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Hydrogen Bond Donor-Catalyzed Cationic Polymerization of Vinyl Ethers

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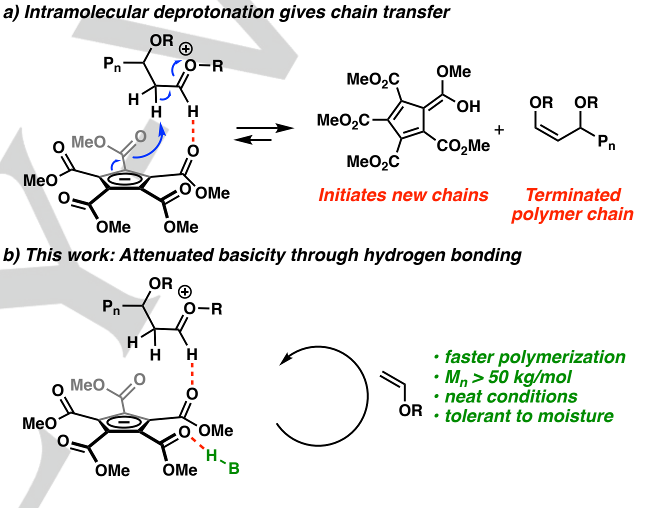
Abstract: The synthesis of high molecular weight poly(vinyl ethers) under mild conditions is a significant challenge since cationic polymerizations are highly sensitivity to chain transfer and termination events. We identified a novel and highly effective hydrogen bond donor (HBD)-organic acid pair that can facilitate controlled cationic polymerization of vinyl ethers under ambient conditions with excellent monomer compatibility. Poly(vinyl ethers) of molar masses exceeding 50 kg/mol can be produced within one hour without elaborate reagent purification. Modification of the HBD structure allowed tuning of the polymerization rate while density functional theory (DFT) calculations helped elucidate crucial intermolecular interactions between the HBD, organic acid, and polymer chain end.

Living polymerizations are a powerful tool that enable syntheses of materials with well-defined structural complexity. [1] However, developing polymerization methods with living characteristics is challenging and often requires specialized reagents and reaction conditions. Specifically, living cationic processes often require rigorously dried solvents, cold temperatures, and additives to avoid deleterious termination and chain transfer events.[2–16] Therefore, designing a robust controlled cationic polymerization under mild conditions that can produce high molecular weight polymers remains a challenge.

In an effort to address these challenges, we recently developed a novel single-component cationic polymerization of vinyl ethers that can be conducted under ambient conditions.[17] This approach employed pentacarbomethoxycyclopentadiene (PCCP-H) as a bench-stable, strong organic acid,[18–20] which rapidly protonated vinyl ethers to initiate cationic polymerization, thereby enabling the synthesis of poly(vinyl ethers) with precise control over the number average molar masses (M_n) and narrow dispersities ($Đ$). We proposed that the polymer chain end exists in equilibrium between a tight ion pair and a covalent adduct rendering the polymerization stable to small amounts of nucleophilic impurities, thus avoiding the need for monomer purification or air free techniques.[17,20,21]

Despite the advantages of this method, targeting polymers with a degree of polymerization (DP) greater than 100 led to materials with lower than expected M_n values and broadened $Đ$s.

We attribute the loss of control to higher amounts of elimination at the chain end and subsequent chain transfer, likely mediated by the PCCP anion (Figure 1a).

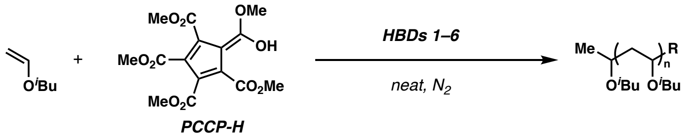

a) Intramolecular deprotonation gives chain transfer

b) This work: Attenuated basicity through hydrogen bonding

Figure 1. a) Proposed mechanism of chain transfer. b) Hydrogen bond donors (HBDs) can attenuate basicity and facilitate higher molecular weight polymers.

We postulated that the proximity of a PCCP-ester to the C–H of the penultimate carbon of the chain end enabled this intramolecular deprotonation. Upon reformation of PCCP-H, a new polymer chain can be initiated through protonation of an additional monomer, resulting in lower than predicted M_n values and broader $Đ$s through this chain transfer process.[22] To address this issue, we proposed that attenuation of the PCCP anion basicity would inhibit deprotonation and allow access to larger molecular weight polymers while maintaining the insensitivity of these polymerizations to moisture and nucleophilic impurities. This goal could be achieved through either modulation of the PCCP structure[23,24] or through additives that interact with the PCCP anion at the chain end. We chose to pursue the second approach because of the modularity of this strategy.

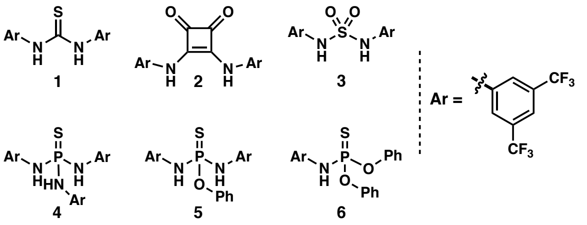
a) Polymerization Results



Entry^a	HBD	M:PCCP-H:HBD	Temp (°C)	Time	$M_{n,exp}$ (kg/mol)	$M_{n,theo}$ (kg/mol)	Đ
1	-	300:1:0	rt	23 h	14.5	24.9	1.38
2^b	**1**	300:1:0.5	rt	23 h	11.5	25.8	1.46
3^b	**2**	300:1:0.5	rt	23 h	13.5	27.9	1.56
4	**3**	300:1:1	rt	1 h	24.5	27.0	1.14
5^b	**4**	300:1:1	rt	1 min	8.8	29.1	2.20
6	**4**	300:1:1	0	1 h	29.8	26.4	1.16
7	**5**	300:1:1	rt	3.5 h	17.3	23.7	1.34
8	**6**	300:1:1	rt	23 h	14.5	27.3	1.39
9	**4**	500:1:1	0	1 h	39.8	38.5	1.18
10	**4**	1000:1:2	0	1 h	65.7	57.0	1.14
11	**4**	100:1:0.2	rt	5 min	10.3	9.9	1.06
12^c	**4**	100:0:1	rt	24 h	n/a	n/a	n/a

^{a}Vinyl ether (100–1000 equiv) was added to PCCP-H (0.007 mmol, 1 equiv) and HBDs 1–6 (0.0014–0.014 mmol, 0.16–0.33 mol%) under inert atmosphere at the indicated temperature. The reaction was quenched with MeOH/NEt$_3$. Unless otherwise noted, M_n and Đ were determined by multi angle light scattering. $^b M_n$ and Đ were determined against polystyrene standards. The MWD of entry 5 was bimodal. ^{c}without PCCP-H.

b) Hydrogen bond donors (HBDs) 1–6



c) Selected GPC traces of poly(IBVE)

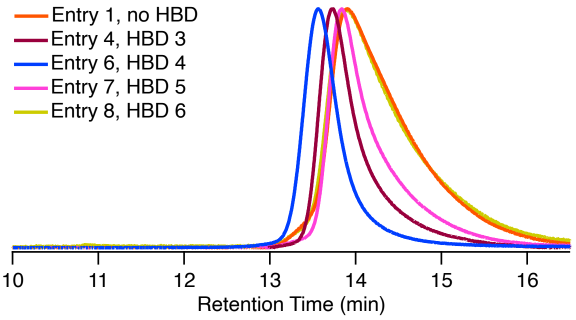


Figure 2. a) Optimization of IBVE polymerization in the presence of HBDs. b) Structures of HBDs. c) Selected GPC traces of catalyzed polymerizations.

Specifically, we hypothesized that hydrogen bond donors (HBDs) could diminish the basicity of the PCCP anion and thereby inhibit chain transfer via interaction with one or more of the PCCP carboxyl groups (Figure 1b). HBDs have found extensive use as catalysts in small molecule synthesis over the last decades due to their structural diversity, high efficiency, and tunability.[25–30] However, utilizing HBDs in the cationic polymerization of vinyl ethers has not yet been explored. In our polymerization, two challenges would have to be addressed: 1) the ideal HBD would bind well to the PCCP anion and moderate its effective basicity, while 2) remaining close to the polymer chain end to prevent termination by nucleophiles. With these features in mind, we investigated the effect of an array of structurally diverse HBDs **1–6** on the cationic polymerization of isobutyl vinyl ether (IBVE) with PCCP-H (Figure 2).

We started our investigation by targeting a DP of 300 in the presence of HBDs **1–6** (0.15-0.33 mol% relative to monomer). The polymerization was terminated at high conversion and analyzed by gel permeation chromatography (GPC). The corresponding uncatalyzed reaction produced a polymer with a Đ of 1.38 and an experimental M_n that was 10 kg/mol lower than the theoretical value (Figure 2a and 2c, entry 1). Upon the addition of Schreiner's thiourea catalyst **1** or squaramide **2**[31,32] no improvement in molecular weight or Đ was observed compared to the reaction without HBD (Figure 2a, entries 2–3). Based on these results, we decided to look into other classes of HBDs, specifically sulfamide **3** and thiophosphoramide **4**. HBD 3 adopts a twisted geometry compared to **1** and **2**, while **4** can donate a third H-bond.[27,33,34] Indeed, upon the addition of **3**, the polymerization reached high conversion within only one hour to yield a polymer with a M_n of 24.5 kg/mol and narrow Đ of 1.14 (entry 4). An even more dramatic rate increase was observed in the presence of **4**, leading to an exothermic and uncontrolled polymerization (entry 5). Upon cooling the reaction to 0 °C, we were able to synthesize poly(IBVE) with a M_n of 29.8 kg/mol and Đ of 1.16. Importantly, the experimental M_n was in excellent agreement with the targeted value suggesting that little to no chain transfer was occurring.

We attribute the success of **4** to its ability to donate three H-bonds, which can bind to multiple methyl esters of the PCCP anion. To probe this hypothesis, HBDs **5** and **6** were synthesized, which can donate two and one hydrogen bonds, respectively (entries 7 and 8).[35] Since aniline was simply replaced by phenol in these structures, these HBDs should closely resemble the geometric and electronic properties of **4**. Employing **5** and **6** under the optimized conditions resulted in little to no polymer. When the polymerization was performed at room temperature, poly(IBVE)s with M_n values of 17.3 and 14.5 kg/mol were obtained, respectively (entries 7 and 8). Interestingly, the GPC traces of the uncatalyzed polymerization and the reaction with **6** are almost identical (Figure 2c), highlighting the need for at least two H-bonds on the thiophosphoramide skeleton to be a competent catalyst. Having established **4** as the optimal catalyst, we decided to target different molar masses. Poly(IBVE) with molar masses up to 66 kg/mol and narrow Đ values were successfully synthesized within one hour (entries 9 and 10).[36] These results highlight the

10.1002/anie.202013419

dramatic improvement to our previous method. Additionally, the polymerization can proceed at room temperature with lower catalyst loading (entry 11). Lastly, no polymer was observed in the absence of PCCP-H when employing **4** as the catalyst (entry 12). The molecular weight is solely controlled by the ratio of PCCP-H to monomer.

With optimal conditions in hand, we decided to explore the robustness and monomer scope of the HBD-catalyzed polymerization. In our previous study, PCCP-mediated polymerizations had been successful under ambient conditions without prior vinyl ether purification. Therefore, we performed the polymerization (DP 300) under ambient atmosphere at 0 °C with monomer that had only been filtered through a plug of basic alumina. After one hour, the polymerization had reached high conversion and the resulting polymer had comparable M_n and $Đ$ as the samples produced under inert and dry conditions (Table 1, entry 1 and Figure 2a, entry 6).[37] Moreover, a variety of vinyl ethers could be polymerized under ambient atmosphere and could achieve higher molecular weights (Table 1, entries 2–3). *n*-Butyl vinyl ether (NBVE), ethyl vinyl ether (EVE), and cyclohexyl vinyl ether (CyVE) were all successfully polymerized with targeted DPs of 300. However, we did observe a slight loss in control for CyVE. Lower polymerization temperatures and the addition of a solvent were required for effective polymerization. Presumably, the increase in steric bulk disrupts the HBD-PCCP complex at the chain end, leading to more chain transfer.

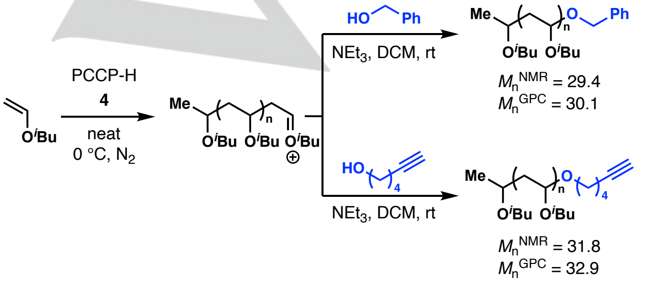
Table 1. Vinyl ether polymerization catalyzed by HBD **4** under ambient atmosphere.

Entry[a]	Monomer	M:PCCP-H:**4**	$M_{n,exp}$ (kg/mol)	$M_{n,theo}$ (kg/mol)	$Đ$
1	IBVE	300:1:1	27.8	26.4	1.16
2	NBVE	300:1:1	22.8	24.5	1.08
3	EVE	300:1:1	13.3	17.9	1.15
4	CyVE	300:1:0.5	31.2	35.2	1.37

[a] Vinyl ether (2.1 mmol, 300 equiv, filtered through a plug of basic alumina) was added to PCCP (0.007 mmol, 1 equiv) and HBD **4** (0.007–0.014 mmol, 0.16–0.33 mol%) under ambient atmosphere at the indicated temperature. The reaction was quenched after 1 h unless otherwise noted with MeOH/NEt_3. [b] 2:1 CyVE:toluene (vol) at –10 °C.

To test the chain end fidelity while achieving higher molecular weights, the polymerizations of IBVE were quenched with excess benzyl alcohol and 5-hexyn-1-ol. Chain-end analysis by ^1H NMR of the purified polymer showed close agreement between the M_n^{NMR} and M_n^{GPC} (Scheme 1 and Figure S20–23), highlighting that good chain-end fidelity is maintained at high conversion and high molar masses.

Scheme 1. HBD-Catalyzed Polymerization Maintains Good Chain-End Fidelity (M_n is reported in kg/mol).



Having demonstrated the effectiveness of **4** on the polymerization of IBVE, the mechanism of action of the HBDs was investigated more closely. We started by monitoring IBVE-polymerization with a target M_n of 10 kg/mol in the presence of 0.1–0.2 mol% of 3–6 (Figure 3). The natural log plot of conversion over time depicts a 50-fold in-crease in polymerization rate when 0.1 mol% of **4** was added to the reaction. Employing HBD 5 (0.2 mol%) afforded a polymerization 10 times faster than the uncatalyzed polymerization, whereas HBD 6 did not lead to an observable change in polymerization rate. Interestingly, the same amount of sulfamide **3** led to 30-fold rate increase, with only two donatable N–H bonds. These findings again suggest that at least two hydrogen bonds are necessary to effectively bind to the PCCP anion. Additionally, the conformation of the HBD, HBD-strength, and presumably additional intermolecular interactions at the chain end all play a crucial role (vide infra). This point is demonstrated by the efficacy of **3** compared to **5**. Of note, all polymerizations maintain excellent control over M_n and $Đ$ of the final polymer (Figure 3, inset and Figures S15–S19).

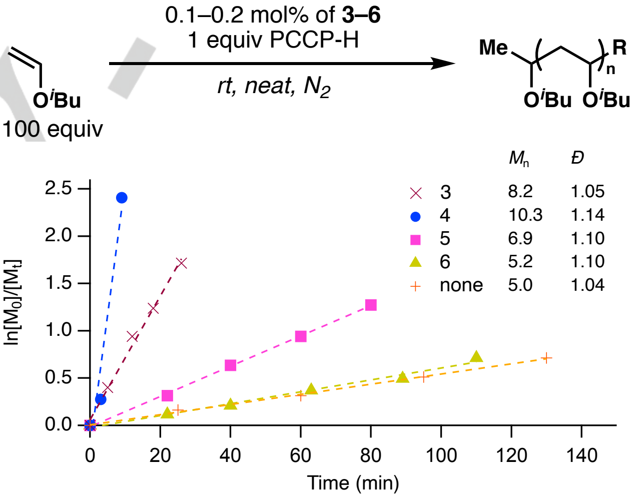


Figure 3. Effect of HBD-catalyzed cationic polymerization of IBVE on polymerization rate.

To further evaluate the role of the HBD in the polymerization, we performed a 1H NMR titration of **4** with $PCCP^{-}/n\text{-}Bu_4N^{+}$ in CD_2Cl_2. Incrementally adding $PCCP^{-}/n\text{-}Bu_4N^{+}$ (guest) to a solution of **4** (host) showed a downfield shift in the N–H resonances of **4**. Fitting the change in chemical shift to a 1:1 host-guest complex binding model revealed essentially quantitative binding of the PCCP anion to 4 (K_{eq} = 3512 M^{-1}).[38] In contrast, a much weaker binding constant was determined for the complexation of PCCP anion with **5** (K_{eq} = 47.3 M^{-1}, see SI for details), corroborating its diminished efficacy as an additive in the polymerization.

Lastly, we utilized DFT-calculations to model the interaction between **4**, PCCP anion and the oxocarbenium ion chain end. Interestingly, the geometry-optimized transition structure revealed several crucial interactions that facilitate the polymerization. As depicted in Figure 4, **4** sits slightly off-center above the PCCP anion and forms two hydrogen bonds with neighboring methyl-ester carbonyls (Figure 4 top, dashed lines).

The third N–H bond coordinates to the π-system of the PCCP anion. The growing polymer chain is located in a pocket between HBD and PCCP anion. The growing polymer chain protrudes from the binding pocket while monomer is shuttled in, forming a key C–H to O interaction between the vinyl α-C–H and an additional PCCP-carbonyl.[16,19] This model also rationalizes the robustness of the polymerization to external nucleophiles in that the cleft formed between the HBD and the PCCP anion could protect the chain end from exogenous nucleophiles while minimizing chain transfer.

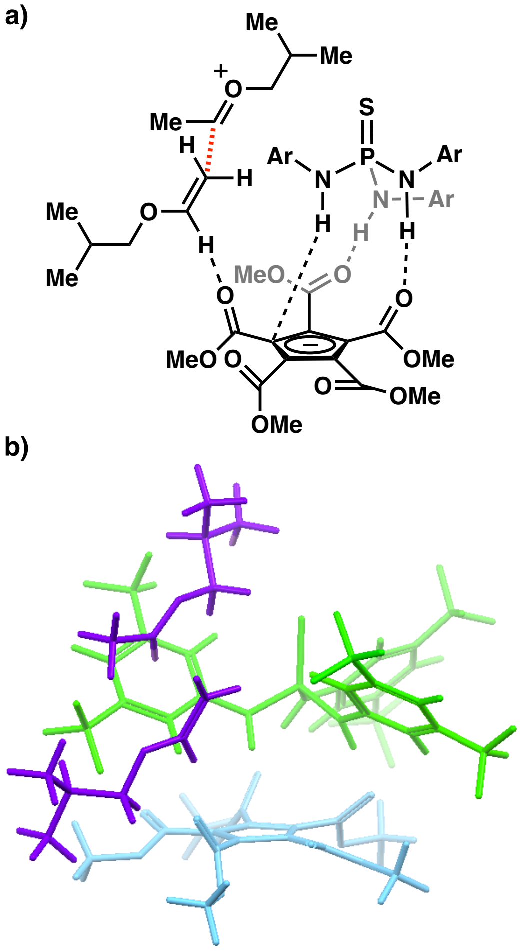


Figure 4. a) Chemical structure and b) Geometry-optimized structure of **4**, growing polymer chain, and PCCP anion.

In conclusion, we have demonstrated the unique ability of thiophosphoramide **4** to catalyze the PCCP-mediated cationic polymerization of vinyl ethers. This system allows for rapid synthesis of poly vinyl ethers with M_n's up to 60 kg/mol. The number of hydrogen bonds plays a crucial role in this mode of catalysis. Importantly, even under ambient atmosphere, excellent control over M_n and $Đ$ are maintained. DFT-calculations suggest the important role of several intermolecular interactions. We deem that every interaction is vital to the level of control exhibited in the polymerization process. This catalytic platform can provide future opportunity to control cationic polymerizations by lever-aging each intermolecular interaction through careful HBD and PCCP design.

Acknowledgements

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Keywords: cationic polymerization • hydrogen bond donor catalysis • ambient conditions

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[36] Under the current conditions, polymers with molecular weights above 66 kg/mol have not been synthesized. The reaction becomes very viscous which causes the stirring and monomer conversion to halt. Current work is investigating the effect of solvents on the polymerization.
[37] The addition of 1 equiv of water leads to slower polymerization, while maintaining good control. Higher amounts of water (10-40) do not prevent polymerization, however, lead to increased chain transfer events (see SI). We hypothesized that water terminates the growing chains and disrupts the hydrogen bond network, causing chain transfer and lower than expected molar masses.
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Entry for the Table of Contents

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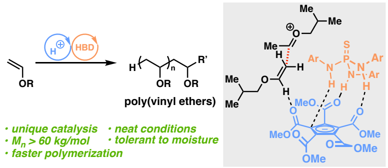

We found that a unique combination of hydrogen bond donor (HBD) and acid catalysis enables rapid vinyl ether polymerization under ambient atmosphere. This controlled polymerization can furnish polymers with molecular weights above 60 kg/mol. Importantly, several key intermolecular interactions between the organic acid and HBD are crucial for successful polymerization.

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