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A New Polymerization System for Bicyclic Acetals: Toward the Controlled/“Living” Cationic Ring-Opening Polymerization of 6,8-Dioxabicyclo[3.2.1]octane

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ABSTRACT: The bicyclic acetal 6,8-dioxabicyclo[3.2.1]octane, 6,8-DBO, was polymerized in toluene solvent using 1-chloroethyl isobutyl ether as the initiator and zinc iodide as the activator. Initiation of the polymerization proceeded by Lewis acid promoted ionization of 1-chloroethyl isobutyl ether to oxacarbenium ions that subsequently added to 6,8-DBO. The molecular weight control of the polymerization increased with decreasing temperature. For polymerizations conducted at −16 °C the number-averaged molecular weights (M_n) of the polymer as a function of conversion correlated most closely with the expected values ($DP_n = ([6,8\text{-DBO}]_0 - [6,8\text{-DBO}]_t/[1\text{-chloroethyl isobutyl ether}]_0)$), and the molecular weight distributions averaged $M_w/M_n \sim 1.3$. The cationic ring-opening polymerization of 6,8-DBO using 1-chloroethyl isobutyl ether/zinc iodide at −16 °C, therefore, can be considered a controlled polymerization.

Introduction

Living polymerizations are chain growth polymerizations that proceed in the absence of irreversible chain transfer and chain termination.[1−3] Provided that initiation is complete and exchange between species of various reactivities is fast, one can adjust the final average molecular weight of the polymer by varying the initial monomer-to-initiator ratio ($DP_n = \Delta[M]/[I]_0$), while maintaining a narrow molecular weight distribution ($1.0 < M_w/M_n < 1.5$). Also, one has control over the chemistry and structure of the initiator and active end group, so polymers can be end-functionalized and block-copolymerized with other monomers.[4] In practice, it can be difficult to control the chemistry of reactive chain ends to a such an extent that chain transfer and chain termination do not occur. Many times, though, the rates of these side reactions are sufficiently slow that polymerization conditions may be found in which well-defined polymers may be prepared. These types of polymerization methods are termed controlled/“living” polymerizations[5,6] to indicate that while chain transfer or chain termination may occur to some degree, the polymerizations are still as synthetically useful as true living polymerizations.

Polysaccharides display a remarkable range of properties and uses that are a result of the diverse array of structures and conformations these polymers can adopt.[7] Stereoregular linear polysaccharides can be prepared via the cationic ring-opening polymerization (CROP) of anhydrosugars.[8,9] The synthesis of well-defined macromolecules of varying architectures using anhydrosugars would require a controlled/“living” polymerization method with which the structure of the polymer could be controlled precisely. Bicyclic acetals are the structural skeletons of anhydrosugars, and their CROP has been studied to understand the fundamental polymerization chemistry of anhydrosugars.[10] The bicyclic acetal, 6,8-dioxabicyclo[3.2.1]octane (6,8-DBO), possesses the structural skeleton of the widely studied 1,6-anhydrosugars, and because it is readily prepared from acrolein dimer,[11] its polymerization has been investigated by many groups.[12−14] Additionally, the chemical modification of polymers prepared using 6,8-DBO derivatives provides entry into a range of natural and unnatural polysaccharide structures.[10]

Typically, 6,8-DBO has been polymerized using PF_5 in CH_2Cl_2 solvent at −78 °C.[15] At this temperature the resulting polymer contained stereoregular α-1,6-linkages (or trans linkages), but at higher temperatures the polymer contained an increasing amount of β-1,6 linkages (or cis linkages).[14] The yields of polymer were variable, depending upon the conditions used, but at −78 °C the yields ranged from 60% to 90%. The molecular weights usually fell within the range $20\,000 > M_n > 1000$, but higher molecular weight polymer ($M_n \sim 10^5$) was obtained in lower yield using $BF_3{\cdot}Et_2O$ initiator at −78 °C.[13] Molecular weight distributions were reported in one instance that were in the range $1.6 < M_w/M_n < 5.6$.[10] The thermodynamic parameters for the polymerization of 6,8-DBO in CH_2Cl_2 were measured at $\Delta H° = -17.5$ kJ mol^{-1} and $\Delta S° = -59.4$ J mol^{-1} K^{-1},[16] which translates into a ceiling temperature, $T_c = 21$ °C (for $[M]_{eq} = 1$ M). Thus, at higher temperatures these are equilibrium polymerizations, and this fact must be taken into account during kinetic experiments.

The currently accepted initiation mechanism for the polymerization of bicyclic acetals and anhydrosugars using PF_5 is shown in Figure 1.[17,18] A Lewis acid−base complex of monomer and PF_5 undergoes nucleophilic ring-opening by another equivalent of monomer. A second equivalent of PF_5 abstracts a fluoride anion from the initiating end of the polymer chains to form a neutral $-OPF_4$ end group and a PF_6^- counteranion. Fewer chains than expected, on the basis of the initial concentrations of monomer and PF_5, are actually generated using this polymerization method, because PF_5 is such a strong Lewis acid that it can bind tightly and unproductively to other Lewis basic sites or participate

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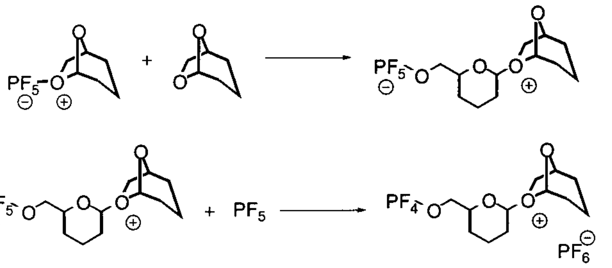


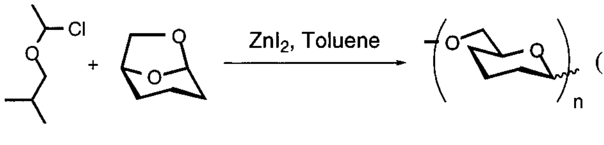
Figure 1. Initiation steps for the polymerization of 6,8-DBO using PF_5.

in side reactions. An additional consequence of the initiation mechanism in Figure 1 is that at most one polymer chain can be formed per 2 equivalents of Lewis acid, eliminating opportunities to prepare end-functionalized and multiarmed macromolecules.

Results and Discussion

We were interested in developing new polymerization systems for bicyclic acetals, such as 6,8-DBO, that yield well-defined polymers and can be used to prepare block, graft, and multiarmed (co)polymers. These methods could then be applied to anhydrosugars in the synthesis of well-defined macromolecules based upon polysaccharides. In selecting a candidate polymerization system, we opted to generate propagating cations from a covalent initiator,[19] instead of activating the monomer as done using the PF_5 initiation system. In such a system, the composition of the initiator could be varied to specify the structure of the initiating end of the polymer chain and to create multifunctional initiators. Additionally, the Lewis acidity of the activator needed to generate propagating cations from the initiator could be varied to control the chemistry of the polymerization. For these polymerizations of 6,8-DBO, the covalent initiator used was 1-chloroethyl isobutyl ether, and the activator used was zinc iodide. The 1-chloroethyl isobutyl ether/zinc iodide polymerization system has been shown to initiate the living cationic polymerization of isobutyl vinyl ether (IBVE).[20] Because the CROP of 6,8-DBO at higher temperatures is thought to proceed via ring-opened oxacarbenium ions[15] and because these intermediates are isoelectronic with the propagating carbocations in IBVE polymerizations, we hypothesized that this system might be adapted for use in controlling the polymerization of 6,8-DBO.

Thus, an anhydrous ether solution of HCl was added to IBVE at 0 °C to prepare 1-chloroethyl isobutyl ether, and this solution was added to a solution of 6,8-DBO in toluene at 20 °C. When a solution of zinc iodide was then added, we observed a decrease in monomer concentration over time, and GPC analysis of aliquots of the polymerization showed an increase in molecular weight (M_n) over time. A polymer was isolated whose ^1H NMR chemical shifts matched those reported for poly(6,8-DBO);[13,14] therefore, the 1-chloroethyl isobutyl ether/zinc iodide system initiated a polymerization of 6,8-DBO (eq 1).



(1)

Table 1. Control Experiments for the Polymerization of 6,8-DBO at 20 °C in Toluene

expt no.	$[IBVE]_0$, mM	$[HCl]_0$, mM	$[ZnI_2]_0$, mM	$[6,8\text{-DBO}]_0$, M	monomer conversion[a]
1		62.0		4.71	none
2	46.8		1.86	3.56	none
3	54.2	54.2		3.76	none
4	54.2	52.8	2.23	3.67	83%

[a] After 1 h.

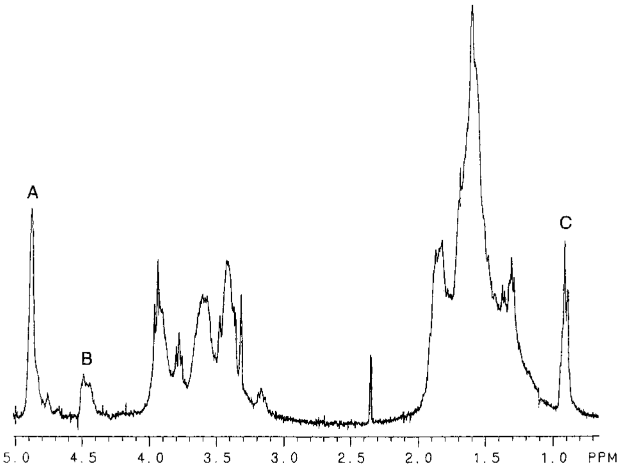


Figure 2. ^1H NMR spectrum of poly(6,8-DBO) from a polymerization in toluene at −16 °C: $[6,8\text{-DBO}]_0 = 2.87$ M; [1-chloroethyl isobutyl ether]$_0 = 0.289$ M; $[ZnI_2]_0 = 1.50$ mM. A and B are equatorial and axial backbone acetal proton signals, respectively, and C is the methyl proton signal for the isobutyl polymer end group.

The first question we sought to answer was whether the polymerization was initiated via the Lewis acid activation of 1-chloroethyl isobutyl ether to oxacarbenium ions or by a Lewis acid monomer activation mechanism similar to that of the PF_5-initiated polymerizations. Four control polymerizations were performed at 20 °C, and Table 1 shows the conditions and results for the four experiments. In the absence of either hydrogen chloride or zinc iodide (experiments 2 and 3), no polymerization occurred. However, when all three components were added to the monomer solution in the appropriate sequence, the polymerization of 6,8-DBO proceeded to high yield (experiment 4). The possibility that residual HCl in solution initiated the polymerization was excluded, because the addition of HCl alone to a solution of 6,8-DBO did not initiate the polymerization (experiment 1). Further evidence for initiation by the activation of 1-chloroethyl isobutyl ether came from ^1H NMR spectra of short chains prepared at −16 °C using this polymerization system (Figure 2). A signal at <1 ppm due to the methyl protons of the isobutyl group was observed in the spectra of isolated, purified polymer samples. Comparison of the integration of this signal with that of the polymer backbone protons yielded a similar number-averaged molecular weight for the polymer as the one determined using GPC. These experimental results support the conclusion that initiation of the polymerization occurred via the Lewis acid activation of 1-chloroethyl isobutyl ether by zinc iodide to form oxacarbenium ions which subsequently added to 6,8-DBO (Figure 3).

After establishing the mechanism of initiation in these polymerizations, we examined the effect of temperature on the polymerization of 6,8-DBO initiated using 1-chloroethyl isobutyl ether and zinc iodide in toluene. When the temperature of the polymerization was varied from 10 to −22 °C, the stereochemistry of

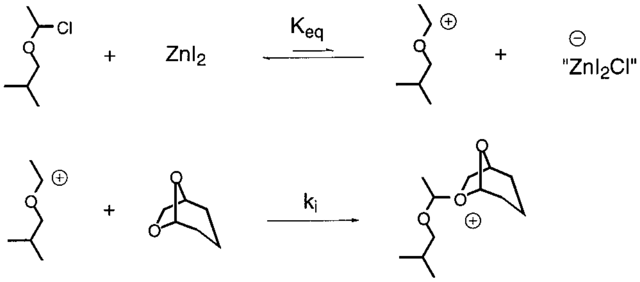


Figure 3. Proposed initiation mechanism for the polymerization of 6,8-DBO using 1-chloroethyl isobutyl ether and ZnI_2.

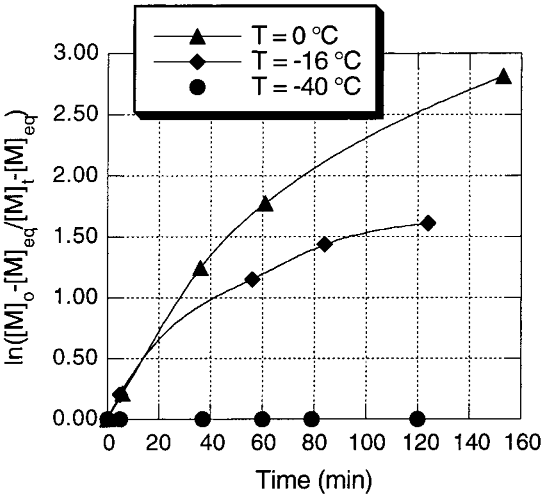


Figure 4. First-order kinetic plots for the polymerization of 6,8-DBO in toluene at 0, −16, and −40 °C: $[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.048$ M; $[ZnI_2]_0 = 2.0$ mM.

the resulting polymer did not vary from an average range of 33−40% β linkages and 60−66% α linkages. This result is consistent with previous observations in which temperatures of −40 °C or below were required to observe stereoregular α-1,6 linkages in the CROP of 6,8-DBO.[10] This temperature dependence of the stereochemistry of polymerization also has been interpreted as evidence for propagation via oxacarbenium ion intermediates at higher temperatures and trialkyloxonium ion intermediates at lower temperatures in the CROP of 6,8-DBO.

Figure 4 shows the kinetic plots for the decrease in monomer concentration versus time for each polymerization at 0, −16, and −40 °C ($[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.048$ M; $[ZnI_2]_0 = 2.0$ mM). In each case the equilibrium monomer concentrations were calculated using the thermodynamic parameters measured for the polymerization of 6,8-DBO in CH_2Cl_2.[16] Two trends were observed. First, the rate of polymerization decreased with each decrease in temperature until, at −40 °C, either no polymerization occurred or the rate of polymerization was very low. Second, the kinetic plots exhibited a deceleration curvature, which indicates either that an irreversible chain termination process occurred or that the equilibrium monomer concentrations calculated using the values measured for CH_2Cl_2 were not an accurate estimate for toluene. The latter explanation became a distinct possibility when we examined the solvent dependence of the rate of polymerization. Shown in Figure 5 are kinetic plots for similar polymerizations of 6,8-DBO in toluene at −16 °C and CH_2Cl_2 at −22 °C ($[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.048$ M; $[ZnI_2]_0 = 2.0$ mM). The rate of polymerization in toluene was smaller than measured for polymerizations in the higher dielectric CH_2Cl_2 (in which $k_{app} = 6.2 \times 10^{-4}$ s^{-1}). Additionally, the kinetic data for the polymerizations conducted in CH_2Cl_2 could be fit to a straight line, whereas the data for toluene solvent could not.

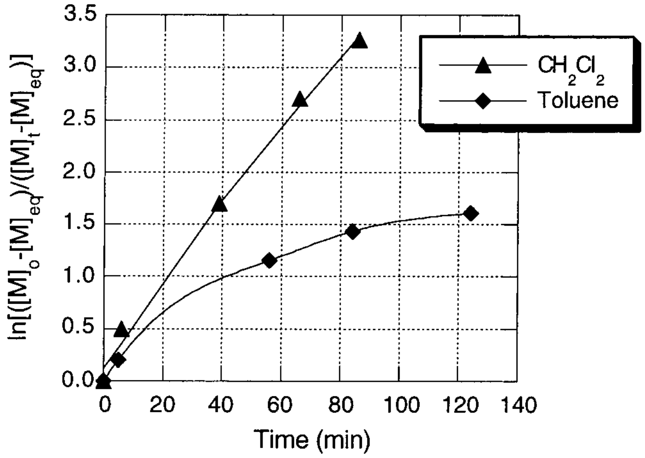


Figure 5. First-order kinetic plots for the polymerization of 6,8-DBO at −16 °C in toluene and −22 °C in CH_2Cl_2. For toluene: $[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.048$ M; $[ZnI_2]_0 = 2.0$ mM. For CH_2Cl_2: $[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.050$ M; $[ZnI_2]_0 = 2.0$ mM.

Figure 6 shows the evolution of molecular weights (M_n) and molecular weight distributions (M_w/M_n) versus conversion for polymerizations at 0 and −16 °C corresponding to Figure 4. The number-averaged molecular weight (M_n) of the polymers obtained from polymerizations performed at 0 °C showed a rapid rise in molecular weight at early conversions, and the corresponding fit to the data showed a pronounced curvature. The molecular weight distributions averaged around 1.5 and were unimodal. If the polymerization at high conversions was not quenched and was allowed to sit for longer periods of time, a decrease in M_n was observed with a corresponding increase in M_w/M_n. Thus, chain transfer to polymer clearly occurs under these conditions. In contrast, at −16 °C the molecular weight of the polymer increased as a linear function of conversion and correlated with values expected on the basis of the initial concentrations of 6,8-DBO and 1-chloroethyl isobutyl ether ($DP_n = ([6,8\text{-DBO}]_0 - [6,8\text{-DBO}]_t/[1\text{-chloroethyl isobutyl ether}]_0)$). The molecular weight distributions were lower than those found for polymerizations at higher temperatures, around 1.3, and unimodal.

The above data prompt the following assessment of the polymerizations. First, because the concentration of the Lewis acid activator was 24−25 times less than the initial concentration of initiator and because the molecular weight of the polymer (M_n) correlated with values expected on the basis of the initial concentrations of 6,8-DBO and 1-chloroethyl isobutyl ether, the intermediate cation concentration must have been generated via the reversible activation of the initiator/dormant polymer chains. Whether the intermediate cations were either oxonium ions or oxacarbenium ions is presently not known and is under investigation, although the stereochemistry of the polymer backbone suggests that oxacarbenium ions were the intermediates. Additional, albeit indirect, evidence for this activation equilibrium comes from the fact that these polymerizations were either very slow or did not proceed at −40 °C. Considering that PF_5-initiated polymerizations of 6,8-DBO occur

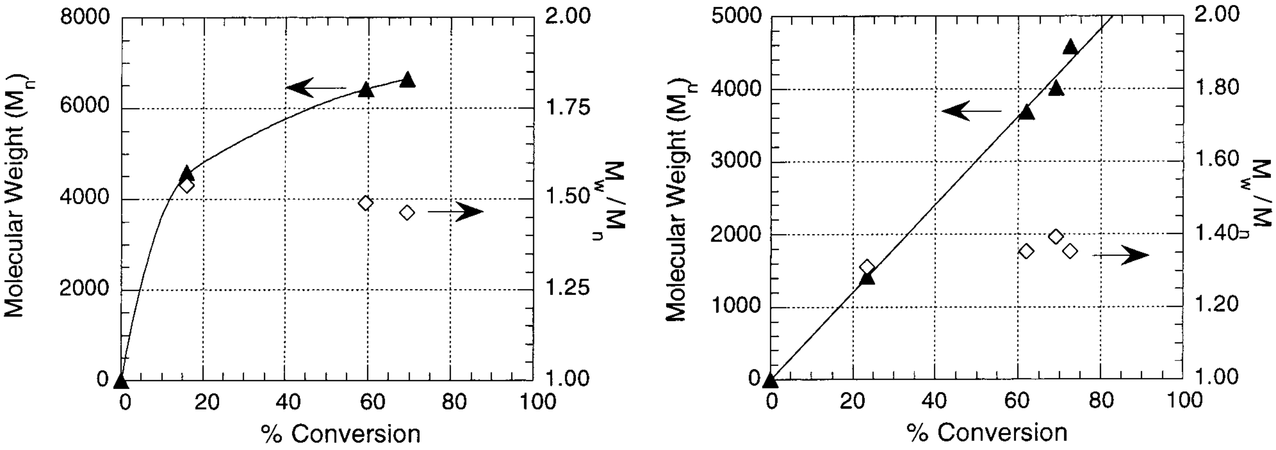


Figure 6. Plots of number-averaged molecular weight (M_n) versus conversion for the polymerization of 6,8-DBO in toluene at 0 °C (left) and −16 °C (right): $[6,8\text{-DBO}]_0 = 3.8$ M; $[1\text{-chloroethyl isobutyl ether}]_0 = 0.048$ M; $[ZnI_2]_0 = 2.0$ mM.

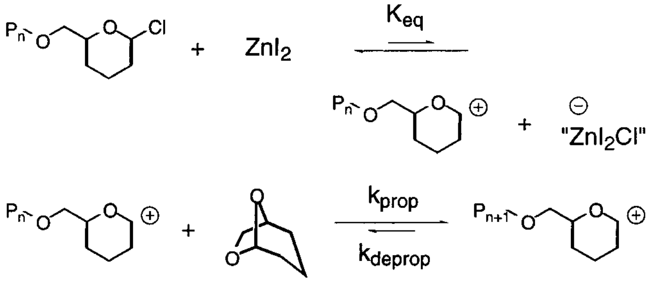


Figure 7. Working propagation mechanism for the polymerization of 6,8-DBO using 1-chloroethyl isobutyl ether and ZnI_2.

at or below even −78 °C, the absence of polymerization at −40 °C must have been a result of the insufficient ionization of the polymer end groups by zinc iodide to produce an observable rate of propagation. Thus, a working propagation mechanism to correspond with the initiation mechanism (Figure 3) is shown in Figure 7, in which only oxacarbenium ion intermediates are shown for simplicity.

This molecular weight behavior indicates that transfer to polymer occurred in these polymerizations at higher temperatures, most likely leading to macrocyclic species (for intramolecular transfer) and broadened molecular weight distributions. The activation energy of chain transfer must have been sufficiently higher than that of propagation such that at −16 °C it became slow and, on the time scale of the polymerization, allowed for more controlled growth of the chains. The molecular weight distributions of the polymers formed at these temperatures were low ($M_w/M_n \sim 1.3$) but were sufficiently high to indicate that either some chain-breaking process still occurred in these polymerizations or that the rate of exchange between dormant and active species was too low. The kinetic data suggest that the former possibility is likely, although the thermodynamics of polymerization need to be measured in toluene to eliminate any curvature in the kinetic plots resulting from errors in estimating the equilibrium monomer concentration. It is clear that the trends in the kinetic and molecular weight data show that lowering the temperature of polymerization toward −40 °C should reduce further the rate of any chain-breaking reaction and increase the overall polymerization control. We are presently investigating the use of stronger Lewis acids to allow these polymerizations to proceed at lower temperatures. Conducting and studying these polymerizations at temperatures approaching −40 °C should also help to separate out the contribution of chain-breaking reactions to the observed molecular weight distributions from any contribution of slow exchange between the dormant and active chain ends.

In summary, 6,8-DBO was polymerized in toluene solvent using 1-chloroethyl isobutyl ether as the initiator and zinc iodide as the activator. Initiation of the polymerization proceeded by Lewis acid promoted ionization of 1-chloroethyl isobutyl ether to oxacarbenium ions that subsequently added to 6,8-DBO. The molecular weight control of the polymerization increased with decreasing temperature. For polymerizations conducted at −16 °C the number-averaged molecular weights (M_n) of the polymer as a function of conversion correlated most closely with the expected values, and the molecular weight distributions averaged $M_w/M_n \sim 1.3$. The cationic ring-opening polymerization of 6,8-DBO using 1-chloroethyl isobutyl ether/zinc iodide at −16 °C or lower temperatures, therefore, can be considered a controlled polymerization. Future work will involve modifying the polymerization conditions to allow these polymerizations to proceed at −40 °C or below, at which temperatures we expect that both chain termination and chain transfer reactions will be slow on the polymerization time scale.

Experimental Section

Materials. IBVE was purified by washing with 10% aqueous NaOH and then deionized water. The IBVE was stirred over CaH_2 overnight and distilled. Dry ZnI_2 (Aldrich) was obtained under a nitrogen atmosphere and transferred into a drybox. 6,8-DBO was prepared according to the procedure of Sweet and Brown,[11] distilled from CaH_2, and stored in a drybox. Toluene and diethyl ether were distilled from Na/benzophenone before use. CH_2Cl_2 was stirred over concentrated H_2SO_4 for 24 h, extracted with 10% $NaHCO_3$ and deionized water, dried over anhydrous $MgSO_4$, and distilled from P_4O_{10} before use. Unless specified otherwise, all other reagents were purchased from commercial sources and used as received. Reagents were handled under nitrogen atmospheres using standard drybox and Schlenk techniques.

Measurements. Number-averaged molecular weights (M_n), weight-averaged molecular weights (M_w), and molecular weight distributions (M_w/M_n) were determined using gel-permeation chromatography in THF at 30 °C. Three Polymer Standards Sevices columns (100 Å, 1000 Å, and linear) were connected in series to a Thermoseparation Products P-1000 isocratic pump, autosampler, column oven, and Knauer refractive index detector. Calibration was performed using polystyrene samples (Polymer Standard Services; $M_p = 400-1\,000\,000$; $M_w/M_n <$

1.10). ^{1}H NMR spectra (300 MHz) and ^{13}C {^{1}H} spectra (75 MHz) were recorded using General Electric QE-300 NMR spectrometers.

Preparation of Initiator, 1-Chloroethyl Isobutyl Ether. To a solution of 1 equiv HCl in anhydrous diethyl ether (Aldrich) at 0 °C was added 1 equiv of IBVE dropwise. The complete conversion of IBVE to 1-chloroethyl isobutyl ether was confirmed using ^{1}H NMR spectroscopy.

Procedure for the Polymerization of 6,8-DBO. Under nitrogen in an oven-dried Schlenk flask, a solution of 6,8-DBO in toluene was prepared using the appropriate quantities of reagents and stirred using a magnetic stirrer. Sequentially, solutions of freshly prepared 1-chloroethyl isobutyl ether in diethyl ether and of zinc iodide in diethyl ether were added using dry syringes. At predetermined intervals, a 1.00 mL aliquot of the polymerization solution was removed using a dry syringe and quenched using triethylamine/CH_3OH (1-to-1 volume ratio) in 5.00 mL of tetrahydrofuran containing a known amount of internal standard (benzophenone). Monomer conversions were determined using standardized GC chromatograms. The remainder of the polymerization was quenched using triethylamine/CH_3OH, and the polymer was isolated by removing volatile materials under vacuum. The polymer was freeze-dried from benzene to leave a colorless powder. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 4.87 and 4.35 (broad singlets, 1H, α and β acetal protons), 3.92−3.40 (broad, 3H), 1.84−1.10 (broad, 6H), 0.89 (broad, end group CH_3). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 97.6−96.9 (broad multiline signal), 70.3−70.1 (broad multiline signal), 68.4−67.9 (broad multiline signal), 31.5 (broad), 30.0 (broad), 28.4−28.0 (broad multiline signal), 22.2 (broad), 18.2 (broad).

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