Kinetics of Enzymatic Ring-Opening Polymerization of ϵ-Caprolactone in Supercritical Carbon Dioxide

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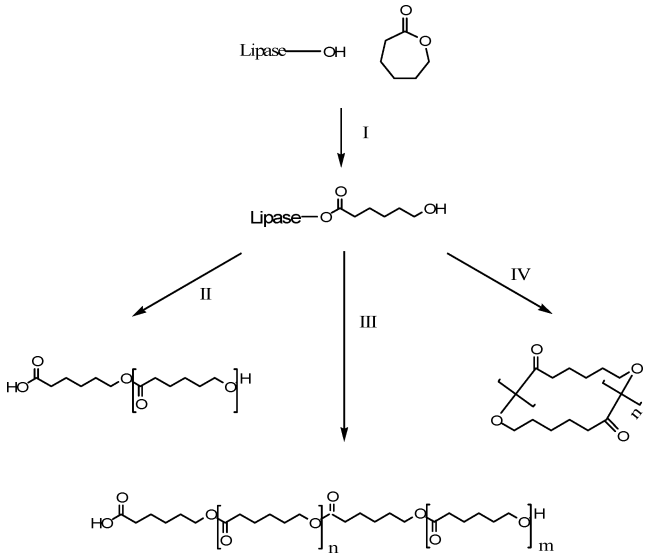
ABSTRACT: The kinetics of enzymatic ring-opening polymerization (eROP) of ϵ-caprolactone in supercritical carbon dioxide ($scCO_2$) was investigated using a new, high-pressure sampling autoclave. The polymerization was performed using *Candida antarctica* lipase B (CALB) as catalyst and was found to be approximately first order with respect to monomer up to 80% conversion. For the first time we have been able to present kinetic results on the eROP of caprolactone in $scCO_2$. These results show that high molecular weight polymer could be obtained (up to 50 kDa) with polydispersities in the range of 2. The relatively poor molecular weight control was attributed to the large degree of enzyme-catalyzed transesterification that forms both cyclic species (intramolecular transesterification) and linear polymer (intermolecular transesterification). This effect has also been observed for eROP of ϵ-caprolactone in conventional solvents. The formation of cyclic oligomers of poly(caprolactone) (PCL) was investigated as a function of conversion, and comparisons were made to similar studies undertaken in conventional solvents.

Introduction

Over the previous decade, enzyme-mediated polymerization has emerged as a new and important method of preparing polymers. While traditional catalysts often contain toxic and environmentally damaging metal species, enzyme catalysis is often seen as an eco-friendly alternative. Indeed, enzymatic catalysts often exhibit considerable benefits over their chemical analogues; enzymes as catalysts for polymerizations show high enantio-[1] and chemoselectivity.[2] Lipases alone have been shown to effectively catalyze ring-opening polymerization of lactones, lactides, and cyclic carbonates to the corresponding polyesters[3,4] and polycarbonates.[5−7] More importantly, these polymerization catalysts can operate under much milder conditions than metal catalysts and are considered biocompatible alternatives.[8,9] In more recent years, researchers have shown that enzymatic ring-opening polymerization (eROP) can be combined with atom-transfer radical polymerization (ATRP)[10,11] or nitroxide-mediated polymerization (NMP)[12] to yield copolymers with well-defined molecular weight and polydispersity.

Supercritical carbon dioxide ($scCO_2$) has received considerable attention and has many advantages over conventional solvents in that it is nontoxic and has low viscosity and there is no detectable chain transfer to solvent. Moreover, the density of the medium can be finely tuned by slight changes in the temperature and pressure of the system.[13] In previous publications we have shown that eROP of ϵ-caprolactone occurs freely in $scCO_2$ to yield polymer with comparable molecular weight and polydispersity to that formed in conventional solvents.[14,15] Recently, we also showed that eROP can occur concurrently with ATRP in $scCO_2$ to form block copolymers of poly(caprolactone) with poly(methyl methacrylate)[16] or poly(fluorooctyl methacrylate).[17] Indeed, good control over the simultaneous eROP and ATRP polymerization has only been shown to occur in $scCO_2$ (and not conventional solvents) and is attributed to the plasticization of the CO_2-insoluble PMMA chain by $scCO_2$ and free ϵ-caprolactone monomer.

Scheme 1. Mechanism Outlining the Enzymatic Ring-Opening Polymerization of ϵ-Caprolactone and Relevant Side Reactions (I, Enzyme-Activated Monomer; II, Polymer Formation; III, Inter-Transesterification; IV, Intra-Transesterification)



One of the most common enzymes for eROP of ϵ-caprolactone is *Candida antarctic* lipase B (CALB). The immobilized form of the enzyme (Novozym-435) has been shown to be extremely effective at catalyzing the ring-opening polymerization. The mechanism of polymerization has been investigated in great detail (Scheme 1).[18,19] Indeed, many reports exist which investigate the effect of various monomers, initiator, and catalyst

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Table 1. Comparison of Kinetic Data Determined for *Candida antarctica* Lipase B Catalyzed Ring-Opening Polymerization of ϵ-Caprolactone with Various Water Concentrations[a]

entry	water added/ μL	water concn[b]/ wt %	monomer:water[c]	theor M_n[d]/kDa	obsd M_n/kDa	rate const $\times 10^4$/min^{-1}
1	0	0.004	990	110	50	8
2	5	0.029	160	18	19	28
3	10	0.054	80	9	11	77
4	20	0.104	40	4.5	6.5	54
5	100	0.504	8	0.9	1.5	28
6	400	2.004	2	0.2	1	17

[a] All experiments were carried out in duplicate showing <5% error—average value shown. [b] Water concentration is based upon total reaction volume as a function of water added. [c] Monomer:water ratios are based on mole concentrations. [d] Theoretical molecular weights are based on water and monomer concentration.

concentration on the molecular weight and polydispersity of the final polymer.[20−22] While the kinetics of eROP of ϵ-caprolactone has been termed "immortal" by some authors[20]—i.e., the polymerization is believed to show living characteristics—such characterization of eROP is inconsistent with the mechanism (Scheme 1) since the polymerization is simply a series of completely random polycondensation reactions which yields polymer with polydispersities typical for polycondensations. The main reason for this lack of control, especially at higher conversion, is undoubtedly due to the high instance of side reactions that are catalyzed by the enzyme. Inter-transesterification (Scheme 1-III) occurs when an ester group within a polymer chain is activated by the enzyme, which then reacts with the hydroxyl moiety of another chain leading to linear polymer with variable molecular weight. On the other hand, intra-transesterification (Scheme 1-IV) leads to cyclic moieties via activation of an in-chain ester group, followed by reaction with the terminal hydroxyl group of the same chain. In addition to transesterification, degradation of the polymer by hydrolysis can be catalyzed by the enzyme if a suitable nucleophile is present (for example, water). All of these side reactions pose important issues for polymer chemists if molecular weight control is desired in the final polymer.

The motivation for this report stems from the lack of mechanistic information available in the literature for enzymatic polymerizations conducted in $scCO_2$. Specific questions that often arise are: Do the excellent mass-transfer properties of the supercritical fluid promote transesterification side reactions during the polymerization (mechanisms III and IV in Scheme 1)? Does the low solubility of water in the $scCO_2$ (0.001 55 wt %[23]) affect the polymerization? While it has been reported that $scCO_2$ can have a favorable influence on enzymatic polymerizations, an in-depth analysis of the mechanism of eROP in the fluid is required to answer these important questions.

In this paper, we address the issue of measuring the kinetics of eROP in $scCO_2$ for the first time. The inherent difficulty associated with mixture sampling in high-pressure polymer synthesis has necessitated the development of a unique high-pressure autoclave. We present the first detailed results outlining the effect of initiator concentration (water content) on the kinetics of eROP of ϵ-caprolactone in $scCO_2$ and discuss the issue of inter- and intramolecular condensation reactions on the characteristics of the polymerization.

Experimental Section

Materials. ϵ-Caprolactone (CL, 99%) was purchased from Aldrich and dried over CaH_2 for 16 h followed by distillation under reduced pressure with three freeze−pump−thaw cycles. The monomer was stored under argon until required. Novozym-435 (10 wt % *Candida antarctic* lipase B immobilized on a cross-linked, macroporous acrylic resin) was purchased from Novozymes. SFC grade carbon dioxide (99.99%) was purchased from BOC gases.

Polymerization in Supercritical CO_2. eROP of CL was undertaken in a high-pressure autoclave. 0.4 g of Novozym-435 was weighed into the autoclave, and the vessel was sealed and evacuated to <10 mTorr at 35 °C for 24 h. 5 mL of CL was then injected into the autoclave under a positive flow of dry CO_2 to prevent the ingress of moisture into the system. Various volumes of distilled water were injected into the vessel as presented in Table 1. The autoclave was then sealed and pressurized to 1100 psi (7.5 MPa), and stirring started. Once the system was thermally equilibrated, the pressure was increased to 1500 psi (10.3 MPa) for the reaction to begin.

High-Pressure Equipment. The high-pressure autoclave for enzymatic polymerizations has been described previously.[14] The autoclave used in this work has been modified to allow sampling through a small reservoir contained at the bottom of the autoclave by way of a needle valve (High Pressure Equipment Co., Erie, PA). Upon each ejection, ~1 mg of polymer/monomer sample was recovered. Five aliquots were taken at each time interval. The first was discarded, and the following four samples were washed into a vial using chloroform. The solvent was evaporated to leave the polymer/monomer mixture for further analysis. In addition to the sampling port, the autoclave was fitted with a magnetically coupled, mechanical stirrer in order to achieve homogeneous mixing of the contents. Our earlier enzyme autoclaves utilized a magnetic stirrer bar which was shown to be sufficient for the polymerization.[14] However, reproducible kinetic results could not be obtained by this method, and the poor stirring of the contents often led to blockage of the sampling port. The addition of a mechanical stirrer greatly improved the reproducibility of results and decreased the incidence of system blockages.

Characterization. Conversion of polymerization reactions were measured using ^{1}H NMR on a Bruker DPX-300 spectrometer operating at 300.14 MHz for protons. The ejected aliquots from the high-pressure vessel were dissolved in $CDCl_3$ and centrifuged to separate the insoluble Novozym-435 residue. The peak due to methylene protons (4.05 ppm triplet due to polymer OCH_2, 4.2 ppm triplet due to monomer OCH_2) was used for calculating the conversion by $OCH_2^{polymer}/(OCH_2^{polymer} + OCH_2^{monomer})$, and the results are presented in Table 1.

Molecular weight analysis was carried out using a PL-GPC 120 system with THF as the eluent at 40 °C. The molecular weight was calibrated using poly(styrene) standards with toluene as the flow rate marker at a flow rate of 1 mL min^{-1}. The instrument was fitted with an RI detector for molecular weight analysis. Molecular weights were mass corrected by the universal calibration constant.

Enzyme water content was measured using a Mettler DL18 Karl Fischer titrator. The water content was measured by stirring a known mass of predried enzyme in dry methanol for 5 min and then titrating it against Karl Fischer reagent (Aqualine Complete 2). Multiple measurements were made on multiple sample sets, and an average "free" water content of 2292 ± 600 ppm was measured. This translates to a contribution of ~2 μL of water per gram of Novozym-435. For a typical experiment, 0.4 g of enzyme was used; hence, an average contribution of ~0.8 μL of water from enzyme is expected.

Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis was carried out on a

Voyager-DE-STR spectrometer using a dithranol matrix with either NaI or LiCl as the salt. Analyses were performed in both reflectron mode (for isotopic analysis) and linear mode.

Liquid chromatography−mass spectrometry (LC-MS) was performed using an Agilent 1100 series HPLC and an Agilent MSD type SL mass spectrometer. The eluent was methanol and water with acetic acid as additive. The LC experiments were performed at 25 °C with a flow rate of 0.25 mL min^{-1}. MS data were collected in positive AP-ESI mode.

Results and Discussion

Effect of Water Concentration on Conversion and Molecular Weight. It has been demonstrated that the stability and activity of immobilized CALB remains high, even under extreme physical conditions. Gross et al.[20] showed that in conventional solvents there was little variation in the reaction kinetics as a function of temperature, although the most favorable temperature was reported as being 60 °C. More recently, our group[14−17] and others[24] have shown that Novozym-435 loses little activity and operates effectively to catalyze ring-opening polymerization in $scCO_2$, despite the high pressures inherently associated with supercritical fluids. Recently, we have shown that optimum conditions for eROP in $scCO_2$ are achieved by finding a balance between the solubilizing power of the solvent and the best temperature for enzyme activity.[14] The highest conversion and yields are achieved at 1500 psi (10.3 MPa) and 35 °C. Hence, all experiments in this report have been conducted under these conditions using water as initiator.

The theoretical and observed molecular weights for various concentrations of water as initiator are presented in Table 1 for reactions that have run to 100% conversion (by NMR). The reaction time to 100% conversion varies from 8 h (for 10 μL added water) up to 50 h (for no added water). The concentration of water was chosen in order to achieve a broad range of molecular weight samples at 100% conversion. The nucleophile content was taken as the volume of water added before pressurization plus the amount of "free" water available in the Novozym-435 beads after drying. The theoretical molecular weight of polymer chains was calculated on the basis of the molar ratio of monomer to water.

Matsumoto and co-workers undertook eROP of two different lactones (15-pentadecanolide and 11-undecanolide) using *Pseudomonas fluorescense* lipase and showed that in both cases the maximum molecular weight corresponded to the initiator concentration in the medium.[25] Similarly, we show that the theoretical and experimental molecular weights for CALB catalyzed eROP of CL in $scCO_2$ show good agreement for all experiments in Table 1, except for entry 1. The experimental molecular weight measured for entry 1 is less than half the predicted value, suggesting that under these conditions the reaction did not go to 100% conversion, more water was present in the system than expected, or deleterious side reactions were occurring that resulted in molecular weight reduction. Transesterification and hydrolysis side reactions catalyzed by CALB have been shown to occur in the eROP of ϵ-caprolactone, especially at high conversion. The consequences of these side reactions are discussed later. However, we believe that the specific effect (entry 1 in Table 1) is related to the much longer reaction time required to achieve 100% monomer conversion and hence the greater amount of time in which polycondensation reactions can occur (compared to the other entries).

The highest molecular weight polymer was recovered when no additional water was added to the system prior to pressurization (entry 1). Hence, eROP was initiated by adventitious water that was present in the system—most probably coming from the Novozym-435 beads. As expected, the lowest molecular weight was observed for the highest concentration of water (entry 6).

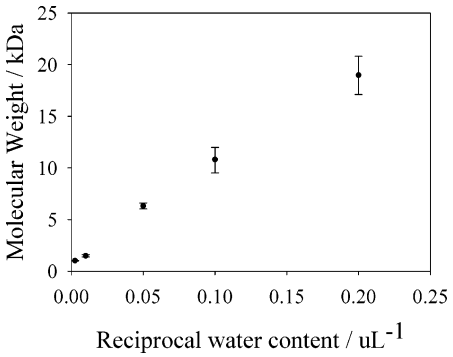

Figure 1. Plot of M_n for final polymer at 100% monomer conversion against the inverse of the amount of water added to the system. The point for zero addition of water is not shown on this plot. Error bars indicate duplicate runs.

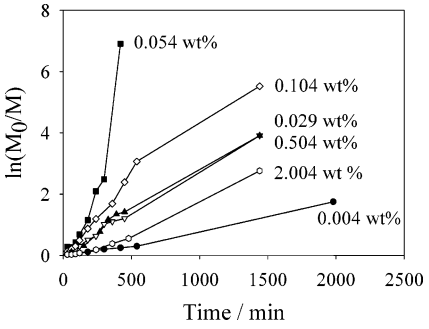

Figure 2. First-order kinetic plots for different water concentrations. Water concentrations are marked on the figure as a weight percent of the total volume. The graph clearly shows nonlinear behavior at longer times (lines are shown to guide the eye).

There is an inverse relationship between molecular weight and the initiator content (Figure 1). Gross et al.[20] showed that for low initiator concentrations the molecular weight of polymer obtained was linearly dependent on the inverse of water concentration (by weight). Our data (Figure 1) also shows linear behavior for all monomer to initiator molar ratios except for very high initiator loadings (2.004 wt %). The off-linear position of the data at this high water loading is likely a result of the high incidence of enzyme-catalyzed transesterification and hydrolysis under these conditions.

The kinetics of polymerization were determined by monitoring the monomer conversion by ^{1}H NMR. The polymerization of ϵ-caprolactone has been shown to be first order in both $scCO_2$ and organic solvents when transition metal catalysts were used to control the polymerization.[26,27]

First-order kinetic plots for eROP of ϵ-caprolactone with varying water concentration in $scCO_2$ (Figure 2) are relatively linear at low conversion for all initiator concentrations. However, deviation from linearity is evident at high conversion, and there exists an optimum water content for conversion rate (0.054 wt %). By assuming first-order kinetics, the rate constant for eROP of ϵ-caprolactone was calculated as a function of water content (Table 1). The results show that the rate constant increases with water content up to 10 μL (0.054 wt %) and then decreases with additional added water. Two contributing factors appear to be present; at lower concentration of water (i.e., $<$0.054 wt % water) the rate of polymerization increases due to the increasing propensity for initiation, while at high water concentrations, monomer activation appears to be affected such that propagation is slowed. This is probably caused by the effect of

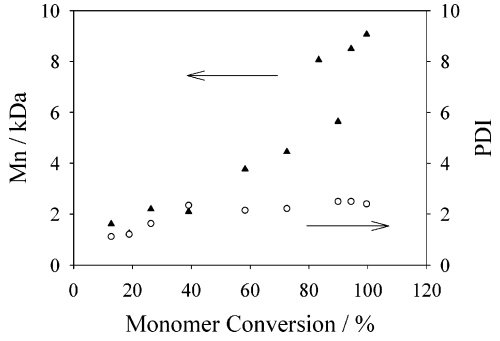

Figure 3. Monomer conversion vs number-average molecular weight (▲) and polydispersity (○) for eROP of ϵ-caprolactone with 0.104 wt % water. The plots show nonlinear molecular weight evolution as a function of conversion and a gradual increase in polydispersity to a final value greater than 2.

high concentrations of water on the hydrophilicity/polarity of the system. It is unclear whether this is simply an "artifact" of undertaking the polymerization in $scCO_2$ or whether it occurs in all solvents; previous reports have not shown such an effect to occur upon increased initiator concentration.[20,28] Indeed, Dong and co-workers demonstrated that increasing the water concentration from 0.1 wt % up to 16 wt % showed an increase in both monomer conversion and rate of conversion for an eROP of ϵ-caprolactone catalyzed by *Pseudomonas sp.* lipase in an organic solvent.[28] The effect of solvent polarity has been investigated by Gross et al.,[29] and it was shown that more polar solvents act to deactivate the enzyme through conformational changes.[28] The effects of increasing polarity/hydrophilicity of the solvent may explain the optimum initiator effect that we observe in our system.

The evolution of molecular weight and polydispersity with time also provides important information on the polymerization kinetics (Figure 3). Gross and co-workers[21] presented data on eROP of ϵ-caprolactone using *Porcine pancreatic* lipase (PPL) with a low initiator concentration. In these experiments Gross reported that the enzyme exhibits good control over the molecular weight and conversion, that there was zero chain termination or chain transfer, and that the enzymatic polymerization shows many features of immortal polymerization.

For controlled, living polymerization (such as that observed for metal-catalyzed ROP of ϵ-caprolactone), a linear relationship between conversion and molecular weight is observed. In addition, controlled reactions typically have polydispersities less than 1.5, and this value remains constant throughout the whole conversion range. Clearly, eROP catalyzed by CALB in $scCO_2$ exhibits quite poor control over the kinetics of polymerization (Figure 3)—this matches that trend shown in conventional solvents. This is not surprising, since the mechanism in Scheme 1 predicts significant side reactions to occur during the polymerization reaction. This is typified by the broad polydispersities and nonlinear molecular weight progression that is evident with increasing conversion. This is accentuated at high conversion when the concentration of monomer in the system is low (Figure 3).[18] Interestingly, Gross et al. compared the number of chains (calculated by NMR) as a function of conversion and showed that the molar concentration of chains increased with water content but remained relatively constant after ~20% conversion.[20] While this suggests immortal-type kinetic behavior, it is important to bear in mind that the calculation of "number of chains" from ^{1}H NMR does not take into consideration formation of cyclics and other transesterification reactions which are known to play an important role in eROP of CL.

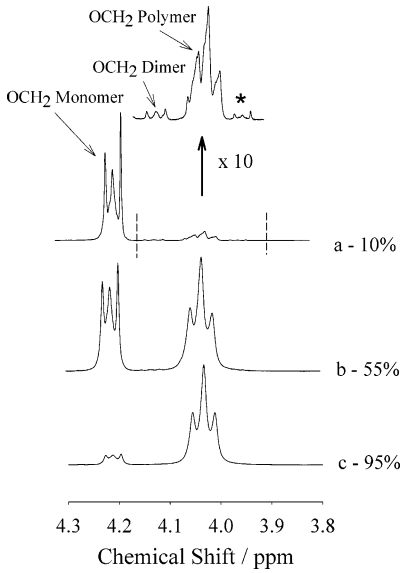

Figure 4. ^{1}H NMR spectrum of polymerization mixture (0.104 wt % water) at various monomer conversions: 10% (a), 55% (b), and 95% (c). An expansion of the spectrum at 10% conversion is shown highlighting the overlap of multiple triplets at 4.05 ppm. Spinning sidebands are marked with an asterisk.

Intra- and Intermolecular Condensation Reactions. While we have shown that eROP of ϵ-caprolactone is probably first order with respect to monomer consumption—at least up to ~70% conversion—intricate control over the kinetics of the system is marred by transesterification side reactions. As shown in the mechanism (Scheme 1), inter-transesterification occurs when a condensation reaction occurs between two separate chains, catalyzed by CALB. The resulting chains have different molecular weight and have the overall effect of decreasing molecular weight control and increasing polydispersity.

Another reaction that can occur is intra-transesterification to form cyclic oligomers of PCL. Iversen and co-workers have investigated the formation of cyclic products during the CALB eROP of ϵ-caprolactone in conventional solvents.[18] They showed that the propensity for cyclic formation is much higher for low monomer concentrations (i.e., at high monomer conversion during a polymerization) because there is a much high propensity for an enzyme-activated chain segment to react with itself (intra-transesterification), rather than free monomer (conventional propagation). Iversen and co-workers fractionated their polymer samples and analyzed the results by MALDI-TOF to determine cyclic molecular weights and dispersities. They showed that in all solvents macrocycles were formed containing up to 23 monomer units. The degree of cyclic formation was dependent largely on the solvent used for the polymerization.

Cyclic products were shown to be evident in all of our samples, regardless of the amount of water present in the system. The presence of cyclic PCL oligomers was inferred by ^{1}H NMR and GPC and quantified by MALDI-TOF MS and LC-MS. In this section, our focus will be on the presence and amount of cyclic species throughout a polymerization reaction.

NMR has proven to be a useful method for determining, in the first instance, the presence of low molecular weight linear or cyclic oligomers in PCL. A section of the ^{1}H NMR spectrum of the reaction product is presented (Figure 4). The triplet at 4.05 ppm (polymer CH_2O) is assigned to methylene protons of the PCL polymer. The triplets at 4.15 ppm (trace amount) and 4.25 ppm are assigned to the corresponding methylene protons in the dimer and monomer, respectively. The NMR spectra at low conversion (10%) show a series of triplets at 4.05 ppm,

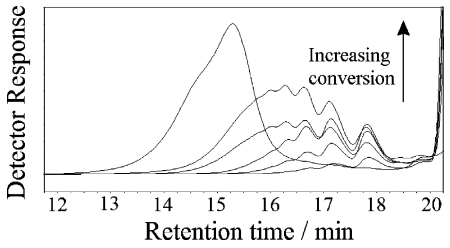

Figure 5. GPC traces of low molecular weight oligomers for increasing monomer conversion for experiment with 0.104 wt % water (entry 4, Table 1). The monomer conversions shown in the figure are 3, 8, 17, 32, 68, and 93% showing the evolution of molecular weight with conversion.

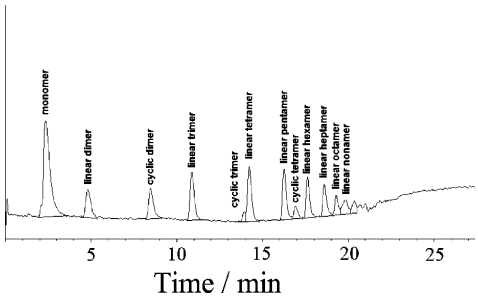

Figure 6. Chromatogram of low molecular weight linear and cyclic oligomeric products resulting from eROP of ϵ-caprolactone with 0.104 wt % water (entry 4, Table 1) taken at 10% monomer conversion. Peaks are identified by the masses detected by mass spectrometry.

suggesting the existence of a diverse mixture of linear and cyclic oligomers. The triplet at 4.15 ppm shows the presence of dimer (either cyclic or linear), and the main signal is due to unreacted monomer in the system. ^{1}H NMR spectra at higher conversion (55−95%) show that linear PCL becomes the dominant species, thus masking any oligomeric signal that might be present in the system. Throughout the whole reaction a small amount of dimer is always present. The unfortunate overlap of signals due to poor chemical shift dispersity affects the ability to quantify oligomeric concentrations by ^{1}H NMR.

GPC evidence also suggests the presence of oligomeric PCL (Figure 5). Each peak in the spectrum correlates to a specific oligomer—either cyclic or linear. As conversion increases, the GPC trace shows that high molecular weight (shorter retention time) oligomers are formed and become the predominant species. Again, the presence of oligomeric cyclic PCL is inferred from the GPC data, but quantification is not possible from these traces.

To determine the identity of the oligomeric species, LC-MS was performed on a sample of PCL formed using 20 μL of water at both 10% and 50% conversion. The resulting mass spectrum for 10% conversion is presented (Figure 6) along with assignment of the mass peaks. In addition to a large monomer peak, a high proportion of oligomeric species were present in the polymer mixture. Both cyclic and linear analogues of the oligomers were detected by LC-MS up to the linear decamer at mass 1158 Da. When a sample of 50% conversion was fractionated and analyzed by MS, all of the same peaks were evident. However, the relative proportion of cyclic species compared to linear analogues was greater than at lower conversion. For example, the ratio of linear to cyclic dimer at 10% conversion was approximately 1:1 compared to 1:2 at 50% conversion. This suggests that linear dimer preferentially propagates to form PCL rather than the cyclic species. This might be explained by the fact that a hydroxyl chain end is much more likely to enter the active site of the enzyme than a large, bulky ring structure.

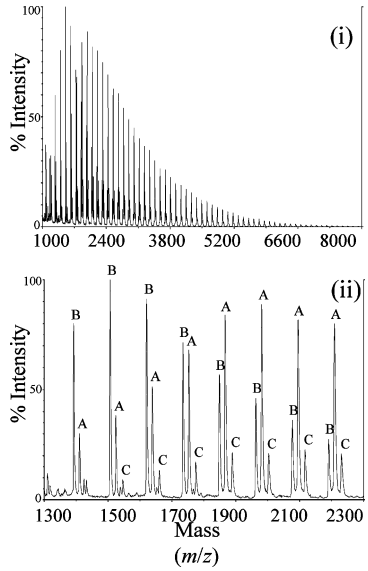

Figure 7. MALDI-TOF MS spectrum of PCL product at 50% conversion for reaction with 0.104 wt % water (entry 4, Table 1). The full spectrum (i) is shown with an expansion (ii) of the region where cyclic peaks (B) are present along with the linear PCL chains (A). The third series (C) is the doubly sodiated species.

To gain a qualitative understanding of the proportions of cyclic to linear species as a function of conversion, MALDI-TOF analysis was performed on the product of eROP of CL at 10, 50, and 100% conversion. The MALDI-TOF mass spectrum of PCL at 50% conversion (entry 4) is presented in Figure 7. Two series are clearly visible in the spectrum. The first ranges from 900 to 12 000 Da (series A) and the second from 900 to 4000 Da (series B). A third series (series C) exists as a shoulder to series A. Series A has been assigned to cyclic PCL (i.e., PCL without end groups). Series B is linear PCL, and series C is a doubly sodiated species and is due to a mass spectroscopy artifact. These three series are present in all MALDI-TOF spectra measured for these samples. To semiquantify the MALDI-TOF data, the area under the cyclic peaks was compared to the area under the peaks assigned to linear PCL. Assuming that linear and cyclic species have the same propensity to fly in each experiment, MALDI data suggest that the ratio of cyclics to linear product increases with conversion up to ~50% conversion. This suggests that a high concentration of cyclic product is formed during the initial stage of the reaction, and this amount then remains fairly constant. In addition, these cyclic oligomers are present right to the completion of the reaction and form a significant part of the final product. This seems to conflict with the expected mechanism which suggests that cyclic product should increase at high conversion because of the much higher likelihood of intramolecular transesterification.[18] This anomaly might be explained by the fact that molecular species with masses below about 900 Da are difficult to measure with MALDI-TOF due to background signal; hence, our calculations are based on those cyclic species with molecular weights greater than 900 Da. The other factor which supports the proposed mechanism of eROP is the increase in molecular weight of cyclic products with conversion. From the MALDI-TOF spectra, the Mp of cyclic PCL increases from 1.3 to 1.6 to 1.8 kDa for 10, 50, and 100% conversion, respectively. This clearly suggests that as conversion increases the incidence of intrachain backbiting to form cyclic products becomes more likely at high conversion and leads to higher molecular weight cyclics.

The mass spectrometry data clearly show the importance of transesterification in side reactions in the kinetics of eROP in $scCO_2$. In addition, the data demonstrate that the classification of this system as immortal or living is not strictly correct, since the polymerization simply involves a series of random polycondensation reactions. Indeed, the ability of CALB to activate any or all carbonyl groups in the system is the main factor for the loss of control in these polymerizations. Such behavior is observed in both $scCO_2$ and conventional solvents[18] though from our data it is unclear whether transesterification is more prevalent in either solvent. Further experiments conducted in the low and very low monomer concentration regime will form the basis of future kinetic work to determine whether backbiting transesterification reactions to form high molecular weight macrocycles will occur more easily in $scCO_2$ because of the influence of the solvent on plasticization and overall chain mobility.

Conclusion

The eROP kinetics of CL in $scCO_2$ have been investigated using a new, high-pressure sampling autoclave. The reaction proceeds via first-order kinetics up to 70% conversion, and the molecular weight of the polymer decreases with increasing water concentration. However, unlike traditional metal catalysts, precise control over the absolute molecular weight and polydispersity cannot be obtained using CALB as catalyst. The transesterification reactions that lead to the broad polydispersity observed in eROP polymerizations of CL were investigated. We showed by numerous techniques that cyclic products were produced during the whole polymerization, and the average molecular weight of the cyclic species increased with conversion. While cyclic products definitely form a significant part of the reaction product, we found no evidence for an increase in concentration of cyclics due to $scCO_2$. Additionally, the low solubility of water in $scCO_2$ did not seem to affect its ability to initiate polymerization. In general, the kinetics of eROP of CL in $scCO_2$ show the same characteristics as the analogous polymerizations in toluene.

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