Mechanistic Study of Boron Trifluoride Catalyzed ε-Caprolactone Polymerization in the Presence of Glycerol

G. Jiang, G. S. Walker, I. A. Jones, C. D. Rudd

School of Mechanical, Materials and Manufacturing Engineering, University of Nottingham, Nottingham NG7 2RD, United Kingdom

Received 18 October 2005; accepted 11 January 2006
DOI 10.1002/app.24159
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Boron trifluoride catalyzed ε-caprolactone polymerization in the presence of glycerol can produce poly(ε-caprolactone) with a high weight-average molecular weight and a broad molecular weight distribution. This article reports an investigation of the polymerization mechanism to determine the formation of these molecular weight features through a study of the polymerization kinetics and the molecular structure with NMR. The polymerization proceeds via an activated monomer mechanism, resulting in polymer molecules with hydroxyl chain ends. The broad molecular weight distribution can be attributed to the etherification reactions between hydroxyl chain ends. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 3900–3906, 2006

Key words: kinetics (polym.); molecular weight distribution/molar mass distribution; polyesters; ring-opening polymerization

INTRODUCTION

Poly(ε-caprolactone) (PCL) has found many applications in the field of medicine[1] and environmentally friendly polymeric materials[2] because of its degradability. In the last decades, most of the preparations have been based on the use of organometallic catalysts, such as those of tin,[3] aluminum,[4] and some rare earth metals,[5] because these produce high-molecular-weight polymers with low polydispersities through the coordination–insertion mechanism. In contrast, strong Lewis acids have been hardly used to produce PCL for such applications as these tend not to produce high-molecular-weight polymers because of the extensive back-biting transesterification caused by the catalysts during polymerization.[1,6]

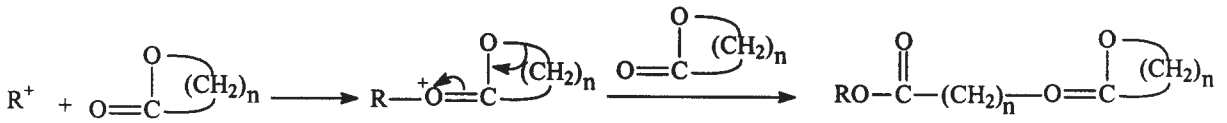
A controlled degradation rate of the polymer is desirable for its utilization in these fields. However, PCL prepared via the organometallic catalyst route has an inherently slow degradation rate, which has to be modified by the copolymerization of ε-caprolactone with other monomers such as L-lactide and glycolide.[7] PCL made with boron trifluoride (BF_3) as the polymerization catalyst, in the presence of glycerol, has a degradation rate comparable to that of copolymers.[8,9] The polymer prepared through this route has shown a high weight-average molecular weight (M_w) and a very broad molecular weight distribution (MWD; a polydispersity index as high as 6.3 can be obtained). In this article, an investigation of the polymerization mechanism that results in the formation of these molecular features for the BF_3-catalyzed polymerization of ε-caprolactone is reported.

MECHANISMS OF ε-CAPROLACTONE CATIONIC POLYMERIZATION

BF_3 is a strong Lewis acid that can initiate the ring-opening polymerization of ε-caprolactone via a cationic mechanism. For the cationic polymerization of ε-caprolactone, there are two suggested polymerization mechanisms: active chain end (ACE) and activated monomer (AM). In the early 1980s, Penczek et al.[10] and Kricheldorf and coworkers[11,12] proposed the ACE mechanism for the cationic ring-opening polymerization of lactones. This was supported by their spectrometric results for the oligomer and the trapped ACE with $(C_6H_5)_3P$. As shown in Scheme 1, the cationic species (R^+) attacks at the exocyclic oxygen atom in the monomer molecule, leading to oxonium cations as active species, which undergo exclusively alkyl–oxygen bond scission. The reason for the attack of exocyclic oxygen is the fact that the exocyclic oxygen is much more nucleophilic than the

Correspondence to: G. S. Walker (gavin.walker@nottingham.ac.uk).

Contract grant sponsor: EPSRC; contract grant number: GR/L38554/01.
Contract grant sponsor: University of Nottingham (through a Ph.D. scholarship to G.J.).



Scheme 1 ACE mechanism: the cationic species (R^+) attacks the exocyclic oxygen of lactones to initiate polymerization.

endocyclic oxygen and the delocalization of the positive charge contributes to the stabilization of the intermediate.

When an alcohol is present in the system, the cationic ring-opening polymerization of lactones may operate according to an alternative mechanism to the ACE one. As early as the 1980s, Belen'kaya et al.[13] noted that the addition of ethylene glycol caused a sharp increase in the polymerization rate when they performed ε-caprolactone polymerization with $(CH_3CH_2)_3O^+SbF_6^-$ as the catalyst. They proposed that the addition of the alcohol converted the process to a mechanism by which chain growth occurred through terminal hydroxyl groups by preliminary transfer of a proton to the monomer. In the 1990s, Okamoto[14] investigated the polymerization of various lactones with $(CH_3CH_2)_3O^+PF_6^-$ as a catalyst in the presence of ethylene glycol. It was determined with NMR that the residue of the alcohol was in the structure of the oligomer and that the chain end of the oligomer was a hydroxyl group and not a CH_3CH_2— group. Moreover, the number-average molecular weight (M_n) of the polymer developed linearly with the monomer conversion during polymerization. It was proposed that the polymerization proceeded via the AM mechanism, as shown in Scheme 2. With the AM mechanism, the cationic catalyst reacts with ethylene glycol first to release a hydrogen ion, which then transfers to the exocyclic oxygen of a monomer molecule; the hydroxyl oxygen of an alcohol molecule then attacks the protonated carbonyl carbon to open the ring. The liberated H^+ can then activate another monomer molecule, which can react with the hydroxyl group at the end of the initiated polymer chain, leading to propagation of the chain. Recently, Endo's group[15–18] investigated ε-caprolactone polymerization with $HCl{\cdot}OEt_2$ and other protonic acids as catalysts in the presence of butanol. Their research suggested that protonic acids could also initiate the cationic ring-opening polymerization of lactones via an AM mechanism under suitable conditions.

Polymers obtained via an AM mechanism have narrow MWDs because of fewer side reactions.[19] A polymer obtained via the ACE mechanism has a broader MWD, but the polydispersity index usually approaches 2 because of intermolecular transesterification side reactions involving ACEs.[19,20]

EXPERIMENTAL

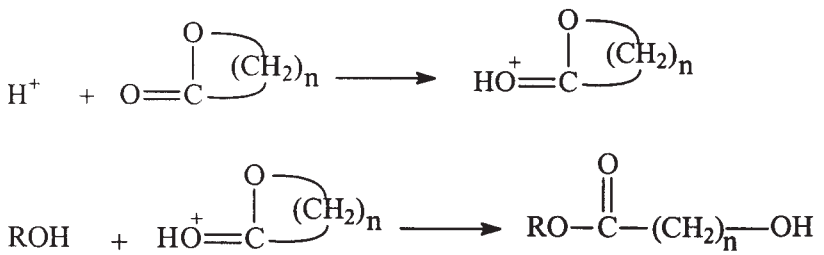
Materials

ε-Caprolactone was acquired from Solvay Interox (United Kingdom) and was distilled *in vacuo* over fresh calcium hydride just before use. The BF_3 used in this work was in the form of boron trifluoride dimethyl ether [$BF_3{\cdot}O(CH_3)_2$]. $BF_3{\cdot}O(CH_3)_2$, glycerol (high-performance-liquid-chromatography-grade), and calcium hydride were obtained from Sigma–Aldrich and used as received.

Polymerization

All glassware was dried *in vacuo* at 140°C overnight. The freshly distilled ε-caprolactone was treated with a predetermined amount of $BF_3{\cdot}O(CH_3)_2$ and glycerol under a blanket of nitrogen. After thorough mixing, the reaction mixture was injected into 2.0-cm^3 reaction vials with a dried syringe. The reaction vials were sealed immediately and then put into an oven that had a predetermined temperature for the polymerization.

For the experiment to determine the relationship between the conversion and polymerization time, the reaction mixture for each formulation was injected into a group of 2.0-cm^3 reaction vials and put into the oven for the reaction. At appropriate time intervals, one glass vial was taken out of the oven, and a sample was



Scheme 2 AM mechanism: the ring-opening polymerization of lactones in the presence of an alcohol.

TABLE I
Variation of the Molecular Weight and Monomer Conversion of PCL with Various BF_3 and Glycerol Concentrations at a Polymerization Temperature of 80°C

Reaction time (h)	BF_3 concentration (mol/dm^3)	Glycerol concentration (mol/dm^3)	M_n (kg/mol)	M_w (kg/mol)	M_w/M_n	Monomer conversion
72	0.0095	0.018	43.0	152.0	3.5	0.87
72	0.0095	0.035	37.5	189.0	5.0	0.91
360	0.0095	0.035	38.8	163.0	4.2	0.99
72	0.0095	0.046	33.6	213.4	6.3	0.96
72	0.0095	0.073	28.5	120.5	4.3	0.99
72	0.026	0.035	35.5	167.7	4.7	0.98

taken from the vial for the analysis of its molecular weight and monomer conversion with gel permeation chromatography (GPC). For the experiment to determine the relationship between the polymer molecular weight and glycerol concentration or BF_3 concentration, a series of reaction mixtures with different concentrations of glycerol or BF_3 were prepared and injected into the reaction vials. After a predetermined polymerization time, the reaction vials were taken out of the oven, and the molecular weights of the polymers were analyzed with GPC.

Characterization

The molecular weight of PCL was measured with a Polymer Labs GPC system with mixed-D columns at 35°C and a refractive-index detector. Chloroform was used as the mobile phase at a flow rate of 1.0 cm^3/min. Calibration was accomplished against narrow polystyrene standards. The monomer conversion was determined with the two peaks in the GPC trace, which were designated as the polymer peak and monomer peak. The peak positions and peak area per unit of weight were calibrated with a monomer and polymer mixture of several predetermined concentrations. The ratio for the peak area per unit of weight of the polymer to the monomer was 1.14.

The molecular structure of the polymer was analyzed with a Bruker 200-MHz ^{1}H-NMR apparatus in a deuterated chloroform solution. The sample used in NMR analysis was purified by double precipitation from a polymer/toluene solution in hexane.

RESULTS AND DISCUSSION

Reaction mechanism

The polymerization was conducted at 80°C to avoid transesterifications so that a high-molecular-weight polymer could be formed.[8] At this temperature, polymers with very high M_w values and very broad MWDs were obtained, as shown in Table I. The polydispersity index reached 6.3 when the glycerol concentration was 0.046 mol/dm^3. The MWD index was much higher than that of PCL obtained with other catalyst systems, which is usually less than 2.[4,12,21,22]

Typical GPC traces tracking the development of the molecular weight during a polymerization are shown in Figure 1. At 1 h, the GPC trace had two shoulders at eluent times of 14.6 and 12.8 min, respectively. At 5 h, the shoulder at 14.6 min shifted to the left and formed a peak at an eluent time of 13.8 min, the shoulder at 12.9 min shifted to 11.6 min, and a new shoulder formed at an eluent time of 9.6 min, corresponding to a molecular weight of over 377 kg/mol. At 48 h, the peak at 13.8 min shifted to 13.1 min, the shoulder at 12.9 min shifted to 10.8 min, and the shoulder at 9.7 min formed a peak. The low-molecular-weight tail did not move toward higher molecular weights during the polymerization. The MWD thus became broader and broader with the polymerization time.

To understand the mechanism for the high M_w and broad MWD values, the effects of both glycerol and BF_3 on the polymerization were investigated. In Figure 2, M_n of the polymer is plotted against the monomer conversion at various glycerol concentrations with a BF_3 concentration of 0.0095 mol/dm^3. M_n of the polymer has a linear relationship with the

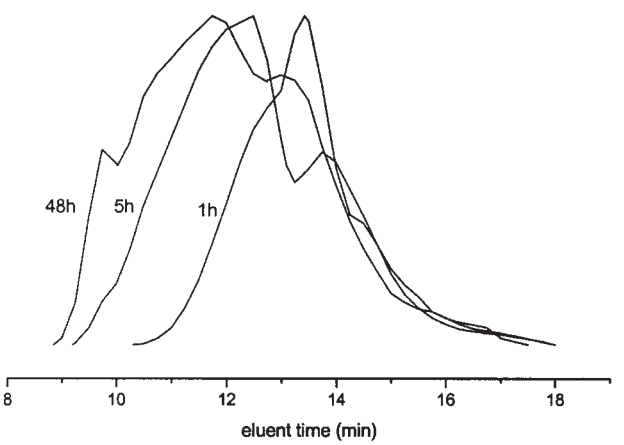


Figure 1 GPC trace development during polymerization at a BF_3 concentration of 0.0095 mol/dm^3 and a glycerol concentration of 0.035 mol/dm^3. The polymerization was conducted at 80°C.

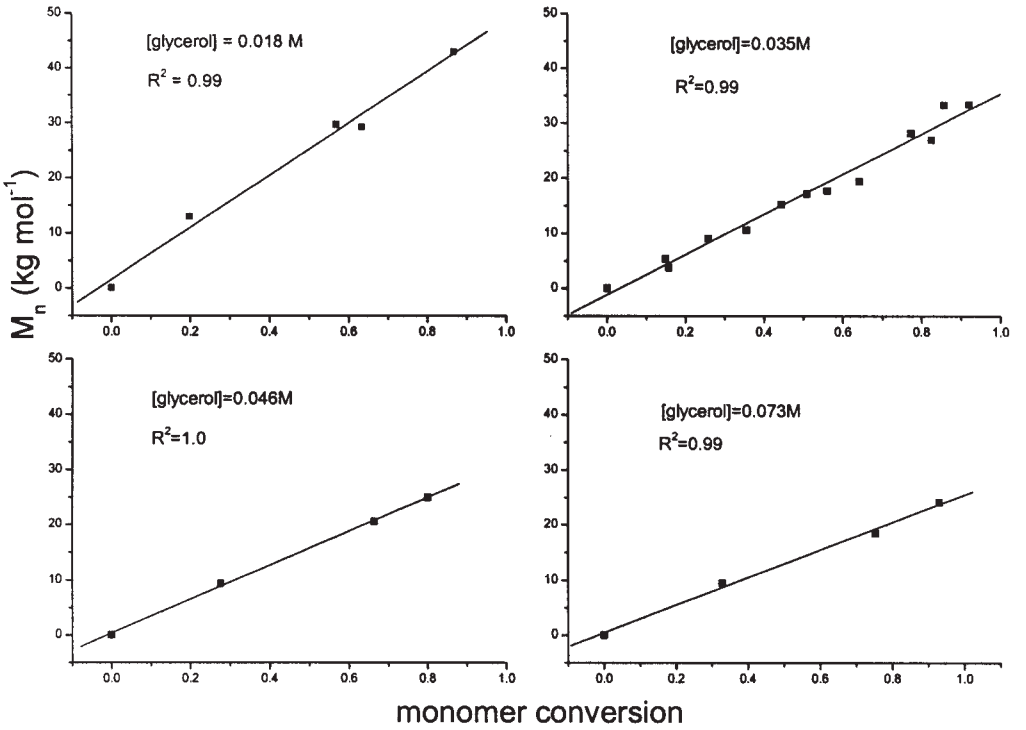


Figure 2 Change in M_n with the monomer conversion at different glycerol concentrations. The BF_3 concentration was 0.0095 mol/dm^3, and the polymerization was conducted at 80°C.

monomer conversion. The linear relationship between M_n and the monomer conversion indicates that the number of polymer molecules did not change during the polymerization.

Figure 3 is the ^{1}H-NMR spectrum of the low-molecular-weight PCL obtained by 2 h of polymerization at 80°C with a BF_3 concentration of 0.0095 mol/dm^3 and a glycerol concentration of 0.035 mol/dm^3. A triplet in the vicinity of $\delta = 3.65$ ppm is due to the $-CH_2OH$ end groups, indicating the presence of hydroxyl group chain ends. The multiplets centered at δ values of 1.40, 1.65, 2.30, and 4.05 ppm correspond to the main-chain protons of PCL. The peak at $\delta = 5.28$ ppm in the spectrum of the polymers is due to the methine proton of a glycerol residue with three ester groups, indicating that a glycerol residue is within the chain of the polymer. The NMR spectrum and the linear relationship between M_n and the monomer conversion suggest that glycerol initiated the polymerization.

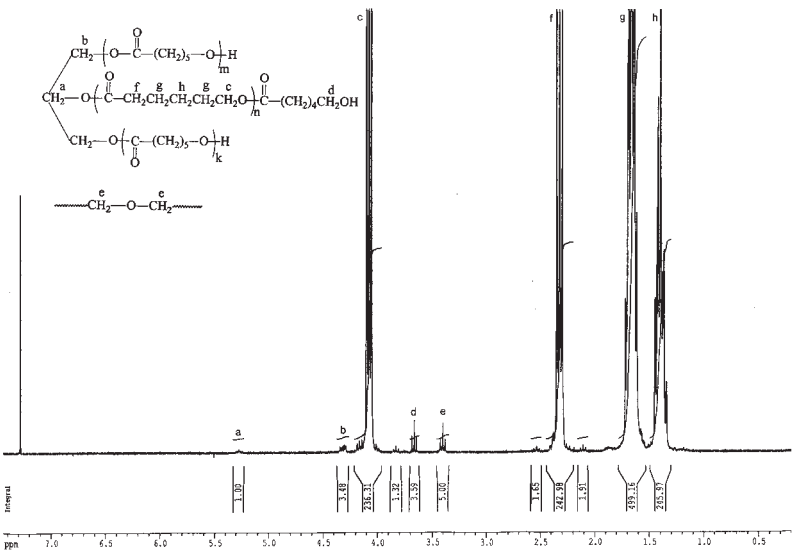


Figure 3 ^{1}H-NMR spectrum of the PCL oligomer prepared with BF_3 in the presence of glycerol.

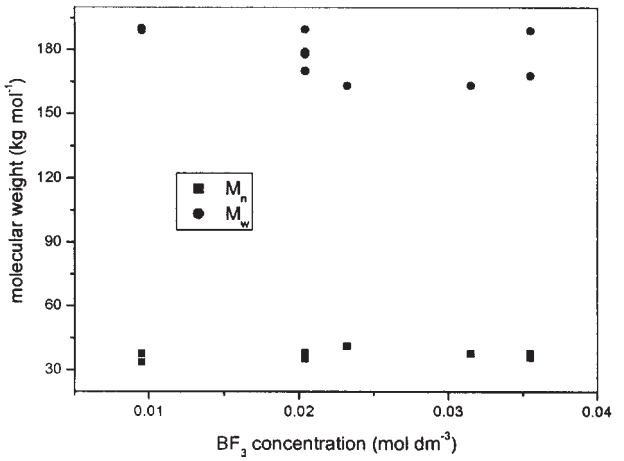


Figure 4 Change in the molecular weight of PCL with the BF_3 concentration. The glycerol concentration was 0.035 mol/dm^3, and the polymerization was conducted at 80°C for 48 h.

Figure 4 shows the variation of the molecular weight of the polymer with the BF_3 concentration. Considering the error of the molecular weight measurement with GPC (3% for M_n and 5% for M_w), we can see that the molecular weight of the polymer did not change significantly with the BF_3 concentration. This indicates that BF_3 did not initiate a polymer chain itself. Otherwise, M_n would have decreased with increasing BF_3 concentration. However, the polymerization rate increased rapidly with an increase in the BF_3 concentration, as shown in Figure 5. For a monomer conversion of 90%, it took 24 h when the BF_3 concentration was 0.026 mol/dm^3, but when the BF_3 concentration was 0.0095 mol/dm^3, the conversion was only 78%.

In a mixture of glycerol and lactone, a cationic species will react with the alcohol first because the hydroxyl group is more basic than the exocyclic oxygen of a lactone molecule.[23] Therefore, the cationic species is converted into a hydrogen ion, which then attacks the exocyclic oxygen of a lactone molecule similarly to the first step of Scheme 1. After this step, there are two possible routes. One is the nucleophilic attack of the hydroxyl group of the alcohol by the carbonyl carbon of the AM (i.e., the AM mechanism). The other is that the exocyclic oxygen from another monomer molecule attacks the α-carbon of the AM molecule, leading to an alkyl–oxygen bond scission reaction, as described in the second step of Scheme 1 (i.e., the ACE mechanism). The two mechanisms are likely to be competing reactions, and the predominant mechanism will depend on the reaction conditions.

If the polymerization had proceeded via the ACE mechanism, that is, the exocyclic oxygen from another monomer molecule had attacked the α-carbon of the AM molecule, one of the polymer chain ends would have been a carboxylic acid group, but no such groups were observed in the NMR spectrum of the oligomer. In addition, BF_3-catalyzed ε-caprolactone polymerization has the following features: the polymer has hydroxyl group chain ends, the backbone of the polymer molecule has glycerol residues, M_n of the polymer has a linear relationship with the monomer conversion, and BF_3 does not initiate a polymer chain itself but can increase the polymerization rate. These characteristics of the polymerization reaction further support the idea that the reaction proceeded by an AM mechanism and are not consistent with an ACE mechanism. From the features of the BF_3-catalyzed ε-caprolactone polymerization at a relatively low temperature (80°C), there is strong evidence that the reaction predominantly proceeded via an AM mechanism.

Etherification between the hydroxyl end groups

The AM mechanism and broad MWD contradict each other. What is the reason for the broad MWD? It can be seen in the NMR spectrum in Figure 3 that there is a triplet around $\delta = 3.4$, which is unique to the BF_3-catalyzed PCL. There was no such peak in the spectra of PCL prepared with organometallic catalysts.[24,25] This peak was assigned to hydrogen atoms associated with an ether bond (—CH_2—O—CH_2—) and was in good agreement with the peak position for other ethers, such as diethyl ether, which has a corresponding peak at $\delta = 3.40$. The ether bond on the polymer chain is most likely due to the etherification reaction between hydroxyl end groups of two polymer chains (as shown Scheme 3) because it is well known that etherification reactions of primary alcohols have an S_N2 mechanism catalyzed by strong acids. BF_3 is a strong Lewis acid and is also recognized as a strong

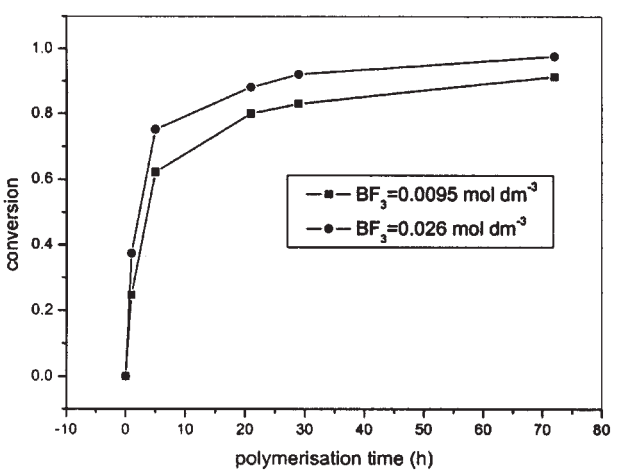
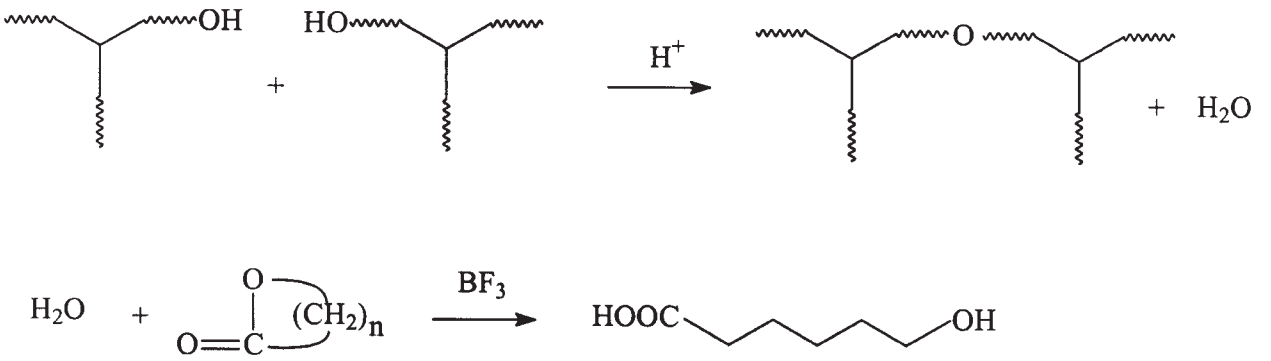


Figure 5 Change in the conversion rate with the BF_3 concentration. The glycerol concentration was 0.035 mol/dm^3, and the polymerization was conducted at 80°C.



Scheme 3 Etherification reaction between two hydroxyl chain ends.

dehydration agent,[26,27] making etherification reactions very likely.

Through the etherification reaction, two or more polymer molecules can be joined together, resulting in a much higher molecular weight. The water produced by etherification can initiate polymerization in the same way as an alcohol, resulting in a lower molecular weight fraction. Very high molecular weight species and very low molecular weight species coexist in the system (Fig. 1), leading to a very broad MWD. Because water produced with etherification can initiate polymerization, the number of propagating chains did not change on account of etherification, and thus M_n and the monomer conversion maintained a linear relationship, as shown in Figure 2.

The etherification can be shown by an analysis of the integral of the NMR peaks. In Figure 3, the relative integrals of hydrogens *a*, *d*, and *e* are 1.00, 3.59, and 5.00 units, respectively. After polymer chains are initiated from the three hydroxyl groups of glycerol, the theoretical value of d/a should initially equal 6. However, every ether link formed will lead to four *d* hydrogens becoming *e* hydrogens. The water formed will initiate another polymer chain, thus creating two more *d* hydrogens. Therefore, the integral representative of the initially formed *d* hydrogens should be

$$e + (d - e/2) = 5 + (3.6 - 2.5) = 6.1$$

This is in very good agreement with the theoretical value of 6.0.

The occurrence of the etherification can also be shown through the analysis of the kinetics of the polymerization. Figure 6 shows the relationship between $\ln([M]_0/[M])$ and the polymerization time (where $[M]_0$ is the initial monomer concentration and [M] is the monomer concentration). The linear relationship between $\ln([M]_0/[M])$ and time in the early stage of the polymerization indicates a pseudoliving character initially for the polymerization. However, the deviation from linearity in the later stages of the polymerization suggests the occurrence of side reactions (i.e., etherification). As shown in Scheme 3, the etherification reaction plus the water initiation of a new polymer chain will reduce the number of hydroxyl end groups by one and also create a carboxyl acid end group. The slowdown of the polymerization rate may be due to the decrease in the number of propagating ends, assuming that the carboxyl groups do not lead to propagation. Because carboxyl groups are able to undergo chain propagation,[28–31] the slowdown of the polymerization rate is due either to a lower rate of propagation for the carboxyl groups or to the fact that the reaction becomes diffusion-limited (if indeed a carboxyl end group has a propagation rate similar to that of a hydroxyl end group.

Through this study, we can see that the kinetics of the BF_3-catalyzed ε-caprolactone polymerization in the presence of glycerol were consistent with an AM mechanism. The broad MWD was due to the etherification reactions between two hydroxyl chain ends.

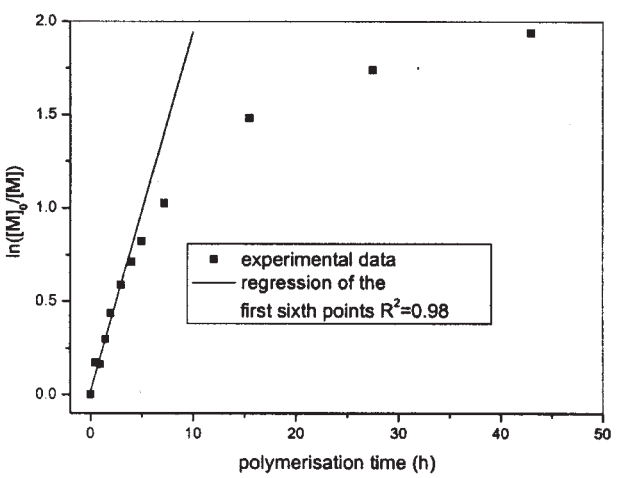


Figure 6 $\ln([M]_0/[M])$ versus the polymerization time. The glycerol concentration was 0.035 mol/dm^3, and the BF_3 concentration was 0.0095 mol/dm^3. The polymerization was conducted at 80°C.

CONCLUSIONS

In the presence of glycerol, BF_3-catalyzed PCL has hydroxyl chain ends and ether bonds in the polymer molecule with glycerol residue within the backbone. During polymerization, M_n has a linear relationship with the monomer conversion. The presence of BF_3 does not affect the molecular weight of the polymer formed but accelerates the polymerization rate. These features are in agreement with an AM mechanism for the cationic polymerization of lactones. Etherification reactions occur during the polymerization, and this is believed to be the reason for the broad MWD obtained.

References

1. Pitt, C. G. Drug Pharm Sci 1990, 45, 71.
2. Hakkarainen, M. Adv Polym Sci 2002, 157, 113.
3. Penczek, S.; Duda, A.; Kowalski, A.; Libiszowski, J.; Majerska, K.; Biela, T. Macromol Symp 2000, 61.
4. Duda, A. Macromolecules 1996, 29, 1399.
5. Agarwal, S.; Mast, C.; Dehnicke, K.; Greiner, A. Macromol Rapid Commun 2000, 21, 195.
6. Lofgren, A.; Albertsson, A. J Macromol Sci Rev Macromol Chem Phys 1995, 35, 379.
7. Duda, A.; Biela, T.; Libiszowski, J.; Penczek, S.; Doubois, P.; Mecerreyes, D.; Jerome, R. Polym Degrad Stab 1998, 59, 215.
8. Christian, P.; Jones, I. A. Polymer 2001, 42, 3989.
9. Jiang, G.; Jones, I. A.; Rudd, C. D.; Walker, G. S. Polymer 2003, 44, 1809.
10. Hofman, A.; Szymanski, R.; Slomkowski, S.; Penczek, S. Makromol Chem 1984, 185, 655.
11. Kricheldorf, H. R.; Sumbel, M. V. Makromol Chem Macromol Symp 1988, 13, 81.
12. Jonte, J. M.; Dunsing, R.; Kricheldorf, H. R. J Macromol Sci Chem 1986, 23, 495.
13. Lyudvig, E. B.; Belen'kaya, B. G.; Barskaya, I. G.; Khomyakov, A. K.; Bogomolova, T. B. Acta Polym 1983, 34, 754.
14. Okamoto, Y. Makromol Chem Macromol Symp 1991, 42, 117.
15. Sanda, F.; Sanda, H.; Shibasaki, Y.; Endo, T. Macromolecules 2002, 35, 680.
16. Endo, T.; Shibasaki, Y.; Sanda, F. J Polym Sci Part A: Polym Chem 2002, 40, 2190.
17. Shibasaki, Y.; Sanda, H.; Yokoi, M.; Sanda, F.; Endo, T. Macromolecules 2000, 33, 4316.
18. Shibasaki, Y.; Sanda, F.; Endo, T. Macromolecules 2000, 33, 3590.
19. Kubisa, P.; Bednarek, M.; Biedron, T.; Biela, T.; Penczek, S. Macromol Symp 2000, 153, 217.
20. Flory, P. J. Principles of Polymer Chemistry; Cornell University Press: Ithaca, NY, 1953.
21. Kowalski, A.; Duda, A.; Penczek, S. Macromol Rapid Commun 1998, 19, 567.
22. Kricheldorf, H. R.; Berl, M.; Scharnagl, N. Macromolecules 1988, 21, 286.
23. Loudon, G. M. Organic Chemistry, 3rd ed.; Benjamin/Cummings: Redwood City, CA, 1995.
24. Dong, C. M.; Qiu, K. Y.; Gu, Z. W.; Feng, X. D. Macromolecules 2001, 34, 4691.
25. Int Veld, P. J. A.; Velner, E. M.; Witte, P. V. D.; Hamhuis, J.; Dijkstra, P. J.; Feiji, J. J Polym Sci Part A: Polym Chem 1997, 35, 219.
26. Mooney, E. F.; Qaseem, M. A. Chem Commun (London) 1967, 5, 230.
27. Nagai, K. B. Chem Soc Jpn 1975, 48, 2317.
28. Bixler, K. J.; Galhoun, G. C.; Scholsky, K. M.; Stackman, R. W. Polym Prepr 1990, 31, 494.
29. Yu, Z. J.; Liu, Z. J.; Zhao, R. X. J Polym Sci Part A: Polym Chem 2003, 41, 3.
30. Korhonen, H.; Seppala, J. V. J Appl Polym Sci 2001, 81, 176.
31. Storey, R. F.; Sherman, J. W. Polym Prepr 1996, 37, 624.