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Process Optimization of Poly(ε-caprolactone) Synthesis by Ring Opening Polymerization

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ABSTRACT

The reaction conditions employed for the synthesis of biodegradable polymers via coordinated anionic ring opening polymerization (CAROP) can be very different and may result in differences between the target and actual product molar masses. Influence of three parameters, monomer (ε-caprolactone) concentration, initiator/catalyst molar ratio, monomer/initiator molar ratio, on real polymer molar mass has been studied. Our modelling embodied a mathematical equation through which we calculated the initiator/catalyst (alcohol/stannous 2-ethylhexanoate) ratio for all given monomer concentrations and targeted molar masses of the polymers. We have established that in order to synthesize a polymer of certain molar mass, a lower amount of catalyst would be required when higher monomer concentrations are used. The amount of catalyst required was found to decrease as the target molar mass of the polymer increases. This reduction becomes sharper with increasing monomer concentration. For example, the initiator/catalyst ratios of 33, 24 and 10 are needed to synthesize polycaprolactones with molar masses of 10,000, 20,000 and 50,000 Da accordingly at monomer concentration of 1 mol/L. The initiator/catalyst ratio of 40 is less subjected to the influence of monomer concentration and may be used to calculate the universal amount of catalyst required for the synthesis of polymers with a particular molar mass by ring opening polymerization. The proposed mathematical model was confirmed by syntheses of polymers with different molar masses and initiators.

Key Words:

polyesters;
ring opening polymerization;
computer modelling;
polyester;
matrix-assisted laser desorption/ ionization.

INTRODUCTION

Ring opening polymerization (ROP) is a widely studied polymerization process. Polymers prepared by the ROP process are used for a wide range of applications. In practice it is very important to synthesize polymers with a targeted molar mass. It is well known, that the final molar mass of a polymer prepared using the ROP process is defined by the monomer/initiator molar ratio [1,2]. In addition, other factors have also been reported to influence the ROP polymerization process. These include type of polymerization techniques (melt, bulk or solvent) [3], initiator [4], type and concentration of catalyst [5,6], temperature [7], monomer concentration [8], stirring speed [9]

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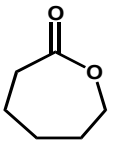
and impurities (water and hydroxyl containing substances) [10]. Transesterification has great influence on polymer molar mass as well [11]. It should also be noted that the conditions for polymerization in a solvent are different from those in melt polymerization reactions, due to the differences in mass transfer. The results of polymerization would finally depend, therefore on the concentration of components in the mixture. However, the mechanistic rational behind the process has not yet been developed. Two types of mechanism have been proposed for the polymerization of cyclic ester monomers, such as ε-caprolactone and 1,5-dioxan-2-one, etc. Kricheldorf et al. have proposed a mechanism where the co-initiating alcohol and monomer are connected to the $Sn(Oct)_2$ complex during propagation [12]. Another mechanism, proposed by Penczek et al., supposes that $Sn(Oct)_2$ complex is converted into a tin alkoxide before ring-opening of the monomer [6,13]. It is probable that various mechanisms take place, depending on the reaction conditions and the initiator (alcohol)/ catalyst ratio used in the reaction. It is very formidable to consider the influence of all the factors mentioned in a synthesis. The synthesized polymer, therefore, deviates from the targeted molar mass as a result of the complexities of the polymerization process.

The purpose of our research was to synthesize a series of polymers, according to experimental design and to develop a mathematical model, which can account for the real molar mass of a synthesized polymer using the main polymerization parameters as the variables. In order to optimize the conditions of synthesis, polycaprolactone (PCL) was used as a model polymer. We do not intend to provide a detailed insight into the ROP mechanism, but rather we describe the trends and behaviour of the ROP process for practical tasks. Application of polycaprolactone increases in many areas and an exact molar mass of the polymer is needed [14]. In this work, based on the experimental design, we provide a mathematical description of polymerization process of PCL in solvent by CAROP. The model can be applied for calculation of the amount of tin octoate needed to obtain exact molar mass of polymer.

EXPERIMENTAL

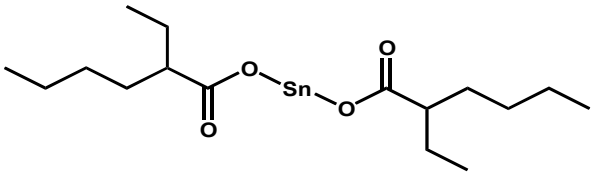
Materials

ε-Caprolactone (99%):

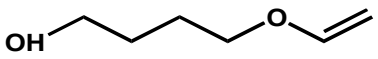


obtained from Fluka, was dried over CaH_2 and distilled under nitrogen at reduced pressure.

Stannous 2-ethylhexanoate (96%), $Sn(Oct)_2$, from Sigma:



hydroxybutyl vinyl ether (HBVE) stabilized by 0.01% of KOH from BASF:



were purified by distillation under reduced nitrogen at reduced pressure. Anhydrous methanol (99.8%) from Aldrich and 1.4-butanediol (99%) from Alfa Aesar were used as received. Anhydrous toluene (99.8%) purchased from Aldrich, was dried over CaH_2 and distilled under nitrogen.

Measurements

Matrix-assisted Laser Desorption/Ionization-Time-of-flight (MALDI-TOF) Mass Spectrometry

Mass spectrometric measurements were performed using a Kratos Axima TOF^2 (Kratos-Shimadzu Biotech, Manchester, UK) time-of-flight instrument, equipped with a pulsed N_2 laser (337 nm, 4 ns pulse width) and time-delayed extraction ion source. An accelerating voltage of 20 kV was used. Mass spectra were recorded in the linear mode. Spectra were acquired by the average of at least 100 laser shots. The matrix, 2,5-dihydroxybenzoic acid (DHB), was dissolved in THF (20 mg/mL). Sodium iodide was dissolved in THF (5 mg/mL) and used as an ionizing agent. The polymer was dissolved in THF (5 mg/mL). Samples were prepared by mixing the matrix solution with the polymer solution and ionizing agent with

their successive fractions of 10:1:1. This mixture (1 μL) was then deposited onto a target sample plate. The average molar mass of polymers was calculated using the standard software programme provided by the instrument manufacturer.

Size Exclusion Chromatography

The molar masses of polymers were determined by size exclusion chromatography (SEC) (Agilent 1100 Series HPLC). Polystyrene standards with a narrow molar mass distribution in the range of 580-400,000 g/mol were used for calibration. Measurements were made at room temperature with linear PL gel 5 μm mixed C columns. Chloroform was used for the solvent with a flow rate of 1 mL/min.

Nuclear Magnetic Resonance Spectrometry (NMR)

^{1}H NMR Spectra were obtained with a Bruker 400 spectrometer. The samples were dissolved in deutero-chloroform in sample tubes of 5 mm in diameter. The solution concentration was 50 mg of polymer in 1 mL of solvent. Degree of polymerization of PCL was calculated as the ratio of integrated signal of two hydrogen atoms of caprolactone -CH_2-O- (δ = 4.049 ppm) and signal of three hydrogen atoms of initiator HBVE -CH=CH_2 (δ = 3.674 and 3.627 ppm).

Synthesis of Polycaprolactone

Syntheses were carried out in a three-necked round bottomed flask (100 mL) equipped with a thermometer, a condenser and magnetic stirrer. The flask was purged with argon, evacuated twice and stored under an inert atmosphere. Argon was blown through the water absorption system with silica gel. A mixture of HBVE and $Sn(Oct)_2$ was added to toluene at 90°C and stirred for 30 min. The quantity of HBVE was taken according to the desired degree of polymerization. We used different initiator/catalyst ratios, ranging from 1 to 50, and different monomer concentrations for optimizing the synthetic procedure. Subsequently, the ε-capolactone monomer was added to the reaction mixture and stirring continued at 110°C for 24 h. The reaction temperature was maintained using a silicone oil bath. The polymer was precipitated by the addition of cold methanol (polymer solution/methanol: 1/10) and dried at 45°C under vacuum for 24 h.

RESULTS AND DISCUSSION

It is clear that many factors affect the molar mass of polymers, produced by the ROP process. These factors include temperature, speed of stirring and concentration of the monomer, the initiator/catalyst ratio and the order by which reactants are added to the reaction vessel. We should take into account that too many factors complicate the mathematical description of the model process and as a result, it is very important to choose the factors, which are most significant in influencing the outcome, when conducting process simulation. However, over-simplification might lead to our mathematical equation becoming inadequate.

Based on published data, using monomer concentration, monomer/initiator (targeted molar mass) and initiator/catalyst molar ratios as the factors of modelling, we cover the most important parameters governing the synthesis process and show their interconnections [6,15,16]. Other factors which influence polymerization reaction (temperature, mixing rate, etc.) were optimized based on our experience, and we used their values located within the range of their minimum influence. Design of this experiment according to the Galois field was carried out using four levels of variation for each parameter to provide good adequacy [17]. A total 16 syntheses of PCL were carried out. The molar ratios of monomer/initiator were chosen to provide targeted PCL molar masses of 2,000, 10,000, 20,000 and 40,000 Da. The monomer concentrations of 0.1, 0.5, 1 and 2 mol/L and the initiator/catalyst molar ratios of 2, 10, 20 and 50 were chosen. The conditions of the experiments and results are given in Table 1.

Several models obtained by the method of least square [18] based on NMR data: the parabolic, polynomial, main effects and pair multiplication models each show good correlation with the data in Table 1. In particular, the model of pair multiplication which makes good correlation with the real data (R^2 = 0.965) and describes the relationships between factors well is more suited as a model for the ROP (eqn 1).

$$M = 2978.34 + 0.108519 \times M_t + 43.8051 \times R + \\ + 2735.07 \times C - 8.24265 \times 10^{-3} \times M_t \times R + \\ 0.267732 \times M_t \times C - 89.0302 \times R \times C \qquad (1)$$

Table 1. Synthetic parameters and their relevant data.

Number	Targeted $\overline{M}_n$ of PCL (Da)	Molar ratio initiator/catalyst	Monomer concentration (mol/L)	PCL molar mass ($\overline{M}_n$), Da (SEC)	PCL molar mass ($\overline{M}_n$), Da (NMR)
1	2,000	2	0.1	3,778	2,280
2	10,000	2	0.5	12,743	9,700
3	20,000	2	1.0	28,039	18,690
4	40,000	2	2.0	46,223	33,633
5	2,000	10	0.5	3,526	2,472
6	10,000	10	1.0	14,090	7,995
7	20,000	10	2.0	28,763	14,701
8	40,000	10	0.1	10,917	5,745
9	2,000	20	1.0	7732	3,981
10	10,000	20	2.0	21,958	11,400
11	20,000	20	0.1	4,103	2,318
12	40,000	20	0.5	6,180	4,002
13	2,000	50	2.0	3,900	2,242
14	10,000	50	0.1	1,902	1,482
15	20,000	50	0.5	6,841	4,111
16	40,000	50	1.0	11,284	2,355

where M and M_t are the molar mass and targeted molar mass of the polymer, respectively in Da; R is the initiator/catalyst molar ratio and C is the monomer concentration (mol/L).

Analyzing the data of Table 1, it is seen that the variation in monomer concentration gives the greatest change in polymer molar mass. If we compare the contribution made by each item of eqn (1) into the result, we can estimate that the factor which exerts the greatest influence on polymer molar mass is monomer concentration, while interesting and important relationships may exist between the following factors: targeted molar mass and monomer concentration and initiator/catalyst molar ratio and monomer concentration. The combinations of the above pairs, one positive and one negative, make the largest contribution in the final molar mass of polymer and the coefficient being the greatest importance

To show all optimal values of initiator/catalyst ratio for each monomer concentration is difficult because there are three variables in eqn (1). For visualization purposes, the relationships between monomer concentration and ratio initiator/catalyst for different fixed PCL targeted molar masses are shown. The curves in Figure 1 reflect the combination of monomer concentration and ratio initiator/catalyst which should, according to the model, give a synthesized polymer without any deviation from the targeted value, for polymers with targeted molar masses (M_t) of 3,000, 5,000, 10,000, 25,000 and 50,000 Da.

An interesting fact is observed in Figure 1. Combination of monomer concentration of around 5 mol/L and initiator/catalyst molar ratio of 40 are suitable for all studied molar masses of PCL because all the curves cross this narrow area in Figure 1. We can see as well, that model displays a deviation in the area of small molar masses of polymer. It may be connected with the influence of time, which was not considered as a factor in the model, but its effect on polymerization is extremely strong in the synthesis of polymer with small molar masses.

Influence of Monomer Concentration on PCL Molar Mass

According to the model and from the data in Figure 1, we can see that it is impossible to achieve a targeted molar mass for the syntheses of PCL with high molar masses at low monomer concentrations.

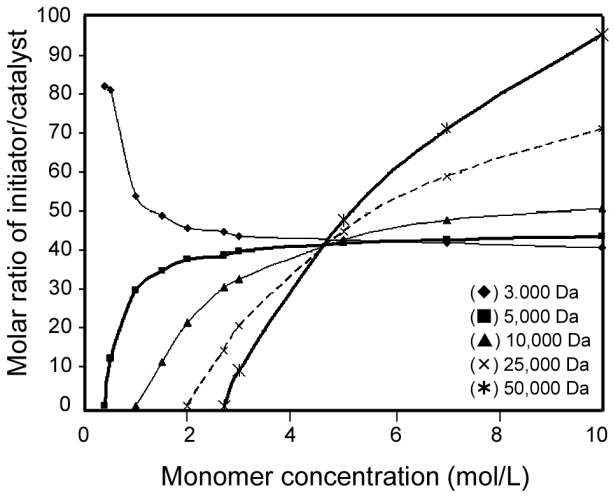


Figure 1. Combination of monomer concentration and initiator/catalyst molar ratio which should result in no deviation of PCL molar mass from the targeted molar mass (M_t).

For example, the results from Table 1 (rows 4, 8, 12 and 16 with targeted molar mass of 40,000 Da) show the influence of monomer concentration. The molar mass of PCL obtained using a monomer concentration of 2 mol/L reached its targeted value, whereas with a PCL synthesized by monomer concentration of 0.1 mol/L was below the M_t value. It is possible, that if the monomer concentration is very low, the transesterification process dominates over the process of macromolecular growth. The same situation is noticed after complete conversion of monomer, when polydispersity index (PDI) starts to increase [19,20]. The results also appear to show an opposite direction to our above findings. The real molar mass of PCL will be higher than targeted at high monomer concentrations (rows 9, 10 and 13 of Table 1). We supposed that the process of chain growth prevails over the macromolecule initiation process, where due to high monomer concentration the obtained polymer molar mass is higher than the targeted one. High monomer concentration provides high rate of polymerization. Catalyst supports the process of macromolecular growth and formation of active species catalyst/initiator. At high monomer concentration and low catalyst quantity (high molar ratio initiator/catalyst), the rate of macromolecular growth is faster than the appearance of active centres of polymerization. The existing of induction time for participation of initiator in polymerization process under certain condition was mentioned by Storey et al. [21].

It is noteworthy that there is a relationship between monomer concentration and catalyst quantity. The best conditions for synthesizing PCL with a molar mass close to the targeted molar mass of 2,000 Da were obtained using a very small amount of catalyst with a high monomer concentration (row 13 of Table 1) or a large amount of catalyst with a low monomer concentration (row 1 of Table 1).

Influence of Catalyst Quantity on PCL Molar Mass

From Figure 1 it is evident that at low monomer concentrations less catalyst was needed for the synthesis of low molar mass. Larger molar mass demanded higher quantity of catalyst. The trend was reversed with a monomer concentration of 5 mol/L. A lower quantity of catalyst was needed for higher molar mass synthesis. This may be connected with the attachment of catalyst to the macromolecules and its participation in monomer insertion and growth of macromolecules that is referred by several authors [21-23]. This possibly depends on transesterification reaction in which the catalyst participates as well.

Practical Calculation of Catalyst Concentration

It is necessary to consider that the initiator/catalyst ratio is a relative factor that depends on the quantity of initiator, which in turn depends on monomer quantity and the targeted molar mass. It would be also useful to see the actual amount of catalyst required to be added into the flask for synthesis. Any trends which may exist as a result of varying the catalyst quantity [$Sn(Oct)_2$] at different monomer concentrations and initiator quantities can be more easily identified if we operate with real amounts rather than with ratios.

We used the fixed target molar masses of 3,000, 5,000, 10,000, 20,000 and 50,000 Da for our polymers. The monomer (ε-caprolactone, M_m = 114 g/mol) concentrations used were varied at three levels; 1.0, 3.0 and 5.0 mol/L and the amount of monomer was kept constant at 5 g. An example of a calculation was made for the targeted polymer of M_t = 5,000 Da.

The degree of polymerization (DP) for PCL M_t = 5,000 Da was calculated from the ratio of targeted polymer molar mass (M_t, g/mol) and molar mass of

monomer (M_m, g/mol):

$$DP = M_t / M_m = 5{,}000/114 = 43.859$$

The quantity of ε-caprolactone (N_m, mol) was calculated from the ratio of the amount of monomer (W_m, g) and molar mass of monomer (M_m, g/mol):

$$N_m = W_m / M_m = 5/114 = 43.85\times10^{-3}\,mol$$

The quantity of initiator (N_{HBVE}, mol) was calculated from the molar ratio between the monomer and initiator at the targeted degree of polymerization:

$$N_{HBVE} = N_m / DP = 43.85\times10^{-3} / 43.859 = 9.997\times10^{-4}\,mol$$

The quantity of initiator (molar mass of HBVE equals 116 g/mol) used was as follows: $m_{HBVE} = 9.997\times10^{-4}\times116 = 0.116$ g

The ratio of initiator/catalyst provided an exact targeted molar mass and was calculated using eqn (1). For a targeted PCL M_t = 5,000 Da and monomer concentration C = 1 mol/L, the molar ratio of initiator/catalyst ($R = N_{ini}/N_{cat}$) was calculated as 30.

The amount of catalyst in moles was then calculated using the following defined ratio:

$$N_{cat} = 9.997\times10^{-4} / 30 = 3.332\times10^{-5}\,mol$$

The amount of catalyst $Sn(Oct)_2$ with a molar mass of 405.12 g/mol was as follows:

$$m(Sn(Oct)_2) = 3.332\times10^{-5}\times405.12 = 13.49\times10^{-3}\,g = 13.49\ mg$$

The full results for these calculations are presented in Table 2.

From these results, we can observe that the absolute quantity of catalyst decreases with respect to the growth of the target molar mass of polymer. For a low molar mass polymer, the amount of catalyst is much higher than for a high molar mass polymer. The reduction of catalyst amount appears to be connected with a reduction in initiator amount and an increase in targeted molar mass. Second reason for this trend may be due to the catalyst participation in transesterification process and its amount needs to be decreased in the synthesis of PCL with high molar mass. Another trend we can see is that the amount of catalyst decreases with higher monomer concentrations except of low molar mass area. It should be noticed that a change in the catalyst quantity for 5 mol/L monomer concentration is expressed more sharply in comparison with 3 mol/L of monomer concentration.

Thus, it is possible to make an assumption that there is a strict balance between monomer concentration, monomer/initiator molar ratio (molar mass of polymer) and the amount of catalyst needed for the synthesis of PCL in solvent. All the factors used in our models are closely connected, such as the monomer and initiator, initiator and catalyst, monomer and catalyst. We can see a close connection among

Table 2. The influence of the targeted molar mass of polymer on the quantity of catalyst.

Targeted $\overline{M}_n$ of PCL (Da)	m_{HBVE} (mg)	Monomer concentration = 1.0 mol/L		Monomer concentration = 3.0 mol/L		Monomer concentration = 5.0 mol/L	
		Initiator/Catalyst ratio	Weight of $Sn(Oct)_2$ (mg)	Initiator/Catalyst ratio	Weight of $Sn(Oct)_2$ (mg)	Initiator/Catalyst ratio	Weight of $Sn(Oct)_2$ (mg)
3,000	193	54.9	12.29	44.0	15.33	42.2	15.99
5,000	116	30.0	13.49	40.6	9.97	42.6	9.51
10,000	58	No solution	-	33.7	6.01	43.6	4.64
20,000	29	No solution	-	24.2	4.18	45.2	2.23
50,000	11	No solution	-	10.6	3.81	47.9	0.84

Table 3. Syntheses of PCL with different initiators under optimized conditions, calculated using our model.

N	Targeted $\overline{M}_n$ of PCL (Da)	Initiator	Monomer concentration (mol/L)	Ratio of initiator/catalyst calculated by the model	Received $\overline{M}_n$ (MALDI-TOF) (Da)
1	5,000	CH_3OH	1	30	5,132
2	10,000	CH_3OH	2	22	10,704
3	5,000	1,4-Butanediol	1	30	6,090
4	10,000	1,4-Butanediol	2	22	10,962

reagents at polylactide polymerization using the system $InCl_3$/BnOH/NEt_3 [24].

The Verification of the Designed Model under Different Conditions

We were interested to see the applicability of our model using different initiators. A model was built based on the results from PCL syntheses carried out using HBVE as the initiator. Additional syntheses were then made using different initiators for the verification of our obtained mathematical model (eqn 1). Methanol was chosen as the simplest alcohol and 1,4-butanediol was chosen as a bi-functional initiator. In each case, $Sn(Oct)_2$ was used as the catalyst. The results are presented in Table 3.

One MALDI-TOF-MS spectrum of PCL synthesized using an optimized ratio of initiator/catalyst is presented as an example in Figure 2.

We can see from Table 3 and from Figure 2 a good correlation between the obtained molar mass of polymers synthesized under optimized condition and those of the targeted values. The molar mass of the synthesized polymers becomes more predictable after optimization and we consider that this model provides a satisfactory, reliable and reproducible method for calculating the reaction parameters of

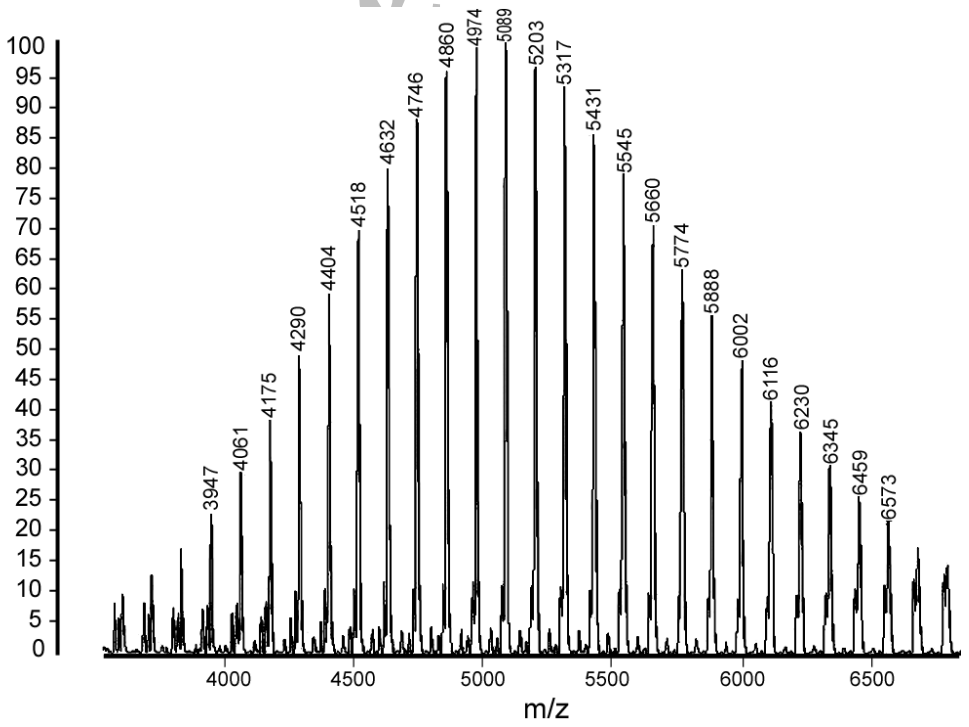


Figure 2. MALDI-TOF-MS of PCL synthesized using methanol as an initiator with a targeted molar mass of 5,000 Da.

PCL syntheses using different initiators.

CONCLUSION

The molar mass of polymer synthesized by ROP is undoubtedly defined by the monomer/initiator molar ratio. Other factors play a role in the polymerization process, and can shift the molar mass during synthesis to higher or lower levels. We have established that by balancing three factors; initiator/catalyst molar ratio, monomer/initiator molar ratio (targeted molar mass of polymer) and monomer concentration we can obtain the targeted molar mass of polymer with good mass accuracy. From the results obtained by simulation we have developed the model describing the ROP polymerization process for PCL in solvent. The model of pair multiplication clearly shows the relationships between the above factors.

The main conclusion we have made is that the quantity of catalyst required to prepare a polymer with a molar mass close to a targeted value depends on monomer concentration and monomer/initiator molar ratio. There is a need to balance not only initiator/catalyst ratio but also monomer concentration and catalyst quantity in order to obtain a polymer with a molar mass close to the targeted value. Higher monomer concentrations demand less catalyst, while lower concentrations are required when a higher amount of catalyst is used. Also, increasing the monomer/initiator molar ratio (targeted molar mass of polymer) requires a reduction in the amount of catalyst used. However, lowering the amount of catalyst at targeted polymer molar mass growth is expressed more sharply at higher monomer concentrations. Reliability of model has been checked by counter synthesis of polymers under calculated conditions. Molecular masses of the received polymers calculated by means of MALDI-TOF analysis coincide with targeted values. The conclusions from our work and the resulting mathematical model are applicable for calculation of catalyst amount needed for PCL synthesis in solvent with an exact molar mass. It may also help to provide a better understanding of the ROP mechanism and to assist future investigative studies.

REFERENCES

1. Stevens MP, *Polymer Chemistry*, 3rd ed, Oxford University, 345-351, 1998.
2. Stridsberg K, Ryner M, Albertsson A-C, Dihydroxy-terminated poly(*L*-lactide) obtained by controlled ring-opening polymerization: investigation of polymerization mechanism, *Macromolecules*, **33**, 2862-2869, 2000.
3. Veld PJA, Velner EM, Witte P, Hamhuis J, Dijkstra P, Feijen J, Melt block copolymerization of ε-caprolactone and *L*-lactide, *J Polym Sci Part A: Polym Chem*, **35**, 219-226, 1997.
4. Pantiru M, Iojoiu C, Hamaide T, Delome F, Influence of the chemical structure of transfer agents in coordinated anionic ring-opening polymerization: application to one-step functional oligomerization of ε-caprolactone, *Polym Int*, **53**, 506-514, 2004.
5. Biela T, Kowalski A, Libiszowski J, Duda A, Penczek S, Progress in polymerization of cyclic esters: mechanism and synthetic applications, *Macromol Symp*, **240**, 47-55, 2006.
6. Kowalski A, Duda A, Penczek S, Kinetics and mechanism of cyclic esters polymerization initiated with tin(II) octoate, *Macromol Rapid Commun*, **19**, 567-572, 1998.
7. Grijpma DW, Pennings AJ, Polymerization temperature effects on the properties of *L*-lactide and ε-caprolactone copolymers, *Polym Bull*, **25**, 335-341, 1991.
8. Liu L-Z, Ma H-J, Zhu X-S, Jin Z-H, Fan Y-J, Analysis of effect factors on the molecular weight of polylactide/nano-silica composites, Gaofenzi Cailiao Kexue Yu Gongcheng, *Polym Mater Sci Eng*, **24**, 63-72, 2008.
9. Ipolitov EG, Artemov AB, Batrakov VV, *Physical Chemistry*, Moscow, Academy, 134-140, 2005.
10. Du YJ, Lemstra PJ, Nijenhuis AJ, Huub van Aert AM, Bastiaansen C, ABA type copolymers of lactide with poly(ethylene glycol). Kinetic, mechanistic, and model studies, *Macromolecules*, **28**, 2124-2132, 1995.
11. Kricheldorf HR, Mang T, Jonto JM, Polylactones. 1. Copolymerization of glycolide and ε-caprolactone, *Macromolecules*, **17**, 2173-2181, 1984.
12. Kricheldorf HR, Kreiser-Saunders I, Boettcher C,

Polylactones 31. Sn(II)octoate-initiated polymerization of *L*-lactide: a mechanistic study, *Polymer*, **36**, 1253-1259, 1995.
13. Stridsberg KM, Ryner M, Albertsson AC, Controlled ring-opening polymerization: polymer with designed macromolecular architecture, *Adv Polym Sci*, **157**, 41-65, 2002.
14. Woodruff MA, Hutmacher DW, The return of a forgotten polymer - polycaprolactone in the 21st century, *Prog Polym Sci*, **35**, 1217-1256, 2010.
15. Duda A, Penczek S, Kowalski A, Libiszowski J, Polymerizations of ε-caprolactone and *L,L*-dilactide initiated with stannous octoate and stannous butoxide, *Macromol Symp*, **153**, 41-53, 2000.
16. Kowalski A, Duda A, Penczek S, Kinetics and mechanism of cyclic ester polymerization initiated with tin(II) octoate. Polymerization of *L,L*-dilactide, *Macromolecules*, **33**, 7359-7370, 2000.
17. Asaturian VI, *Theory of Design of Experiment*, Radio i Sviaz, Moscow, 52-65, 1983.
18. Hamming RW, *Numerical Methods for Scientists and Engineers*, 2nd ed, Dover, New York, 254-261, 1973.
19. Kalmi M, Lahcini M, Castro P, Lehtonen O, Belfkira A, Leskela M, Repo T, Tetrakis Sn(IV) alkoxides as novel initiators for living ring-opening polymerization of lactides, *J Polym Sci Part A: Polym Chem*, **42**, 1901-1911, 2004.
20. Dubois Ph, Barakat I, Jerome R, Tessie Ph, Macromolecular engineering of polylactones and polylactides. 12. Study of the depolymerization reaction of poly(ε-caprolactone) with functional alkoxide end groups, *Macromolecules*, **26**, 4407-4412, 1993.
21. Storey RF, Sherman JW, Kinetics and mechanism of the stannous-catalyzed bulk polymerization of ε-caprolactone, *Macromolecules*, **35**, 1504-1512, 2002.
22. Kricheldorf HR, Kreiser-Saunders I, Stricker A, Polylactones 48. $SnOct_2$-initiated polymerizations of lactide: a mechanistic study, *Macromolecules*, **33**, 702-709, 2000.
23. Stolt M, Sodergard A, Use of monocarboxylic iron derivatives in the ring-opening polymerization of *L*-lactide, *Macromolecules*, **32**, 6412-6417, 1999.
24. Pietrangelo A, Knight SC, Gupta AK, Yao LJ, Hillmyer MA, Tolman WB, Mechanistic study of the stereoselective polymerization of *D,L*-lactide using indium(III) halides, *JACS*, **132**, 11649-11657, 2010.