Homopolymerization and Copolymerization Kinetics of Trimethylene Carbonate Bearing a Methoxyethoxy Side Group

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published online 00 Month 2015
DOI: 10.1002/pola.27805

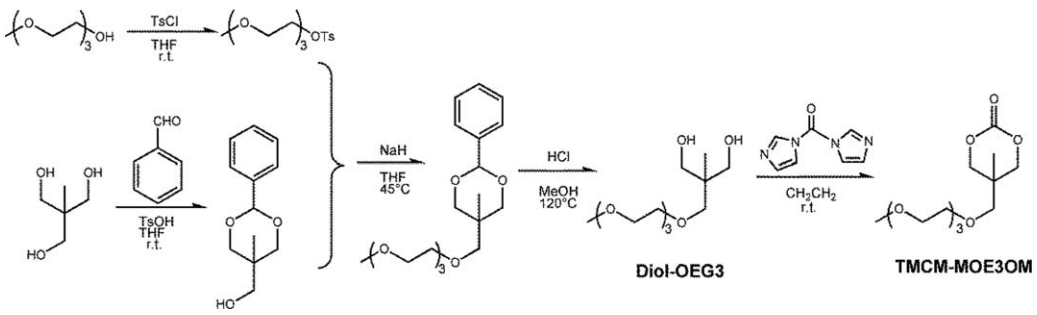
ABSTRACT: The polymerization kinetics of 5-[2-{2-(2-methoxyethoxy)ethyoxy}-ethoxymethyl]-5-methyl-trimethylene carbonate (TMCM-MOE3OM) synthesized using the organocatalyst 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were studied and compared to those with the commonly used catalyst/initiator for ring-opening polymerization of cyclic carbonates and esters, stannous 2-ethylhexanoate. Further, the utility of each of these catalysts in the copolymerization of TMCM-MOE3OM with trimethylene carbonate (TMC) and L-lactide (LLA) was examined. Regardless of conditions with either catalyst, homopolymerization of TMCM-MOE3OM yielded oligomers, having number average molecular weight less than 4000 Da. The resultant molecular weight was limited by ring-chain equilibrium as well as through monomer autopolymerization. Interestingly, autopolymerization of TMC was also achieved with DBU as the catalyst. Copolymerization with TMC using stannous 2-ethylhexanoate as the catalyst yielded random copolymers, while diblock copolymers were formed by copolymerization with LLA. With DBU as the catalyst, copolymers with LLA could not be formed, while blocky copolymers were formed with TMC. These findings should be useful in the incorporation of this monomer in the design of polymer biomaterials. © 2015 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2015**, *00*, 000–000

KEYWORDS: biomaterials; degree of polymerization; kinetics (polym.); polycarbonates; ring-opening polymerization

INTRODUCTION Hydrogels have been extensively investigated as both drug and cell delivery vehicles for biomedical applications. This interest stems from their high water content, which provides for control over the diffusion of drugs for controlled release situations, and nutrients and/or immunomodulating proteins for cell delivery purposes,[1,2] as well as endowing them with mechanical properties that are similar to soft tissues, thereby minimizing inflammation due to mechanical irritation.[3] Hydrogels that can be formed *in situ* following minimally invasive injection are especially advantageous as this implantation strategy reduces healing time and scarring while reducing the risk of infection,[4,5] and the hydrogel formed can conformally fill the implantation site.[6–8]

Polymer-in-water solutions that undergo a phase transition when warmed from room temperature to body temperature are of particular interest as *in situ* gelling systems because the mild nature of the gelation process ensures cell survival and maintenance of biotherapeutic activity.[9,10] These polymers are soluble in water at a given concentration and ambient temperature, and, upon warming to above a threshold temperature referred to as the lower critical solution temperature (LCST), their solubility decreases, and they form physical gels. Recently, Ajiro et al. have reported the preparation of a 5,5-dimethyl-trimethylene carbonate monomer with pendant methyoxyethoxy (MOE) groups.[11] Homopolymers of this monomer exhibited an LCST in water, which was adjustable by modifying the length of the MOE group. In particular, poly(5-[2-{2-(2-methoxyethoxy)ethyoxy}-ethoxymethyl]-5-methyl-1,3-dioxa-2-one), or poly(TMCM-MOE3OM), was soluble in water at 25 °C but exhibited an LCST at 33 and 43 °C for reported molecular weights of 7400 and 960 Da, respectively.[11]

This polymer was synthesized using the organocatalyst 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). DBU as a catalyst has potential advantages for the polymerization of cyclic carbonates such as TMCM-MOE3OM in that polymerization can occur at low temperatures, thereby eliminating side reactions and decarboxylation associated with polymerization at high temperatures, and it is easily removed from the resulting polymer and thus potential toxicity issues are mitigated.[12] For example, using DBU as a catalyst the alcohol-initiated polymerization of trimethylene carbonate (TMC) at 50 °C was complete in 8 h with good control over molecular weight and weight distribution and yielded polymers with high end group fidelity. However, the molecular weights of the poly(TMCM-MOE3OM) obtained by Ajiro et al. using DBU



SCHEME 1 Synthesis pathway for the preparation of TMCM-MOE3OM.

as the catalyst were lower than the theoretical, suggesting poor control over the polymerization with this catalyst.[11] We hypothesized that the reason for the apparent lack of control over poly(TMCM-MOE3OM) molecular weight was due to the formation of a ring-chain equilibrium during polymerization. Ring-chain equilibrium has been reported in the polymerization of other functionalized cyclic carbonates,[13–15] with the equilibrium molecular weight achieved dependent on the degree and type of substitution on the TMC as well as the catalyst/initiator system used. For example, high molecular weight poly(2,2-dimethyl carbonate) can be obtained with stannous 2-ethylhexanoate as the catalyst/initiator,[14] whereas for the same monomer the use of a 2-stanna-1,3-dioxacycloalkane catalyst yielded high monomer conversions but very low molecular weights.[16] Of relevance to this study, the presence of a large (1900 Da) methoxy-poly(ethylene glycol) substituent onto 5-methyl, 5-carboxylate TMC, caused ring-chain equilibrium to dominate such that a high molecular weight polymer could not be formed with DBU as a catalyst.[12] More recently, a DBU and 1-(3,5-bis(trifluoromethyl)phenyl-3-cyclohexyl-2-thiourea (TU) co-catalyst system was reported for the ring-opening polymerization of 1000 Da methoxy-PEG substituted trimethylolpropane carbonate.[17] In this latter paper, the PEG was coupled to the monomer through a carbonate linkage. Although a relatively low molecular weight (10 kDa) polymer was targeted, a molecular weight of only 6.6 kDa was achieved along with a broad dispersity of 2.1.

The utilization of poly(TMCM-MOE3OM) as a biomaterial requires an understanding of the degree to which its degree of homo- and copolymerization can be controlled. One of the objectives of this study was therefore to ascertain whether poly(TMCM-MOE3OM) with controllable molecular weight and high end group fidelity was achievable using either DBU or stannous 2-ethylhexanoate, generally referred to as stannous octoate, as a catalyst. A further objective was to examine the utility of each of these catalysts in the copolymerization of TMCM-MOE3OM with TMC and L-lactide (LLA) as a means of obtaining copolymers with varying functionalities as polymer biomaterials.

EXPERIMENTAL

Triethylene glycol monomethyl ether, *p*-toluenesulfonyl chloride, benzaldehyde, *p*-toluenesulfonic acid, trimethylolethane, 2-methyoxyethyl *p*-toluenesulfonate, sodium hydride in oil (20%w/w), 1,1′-carbonyldiimidazole (CDI), acetic acid, and anhydrous dimethylformamide (DMF) were purchased from Sigma-Aldrich, Canada, and used as received. Benzyl alcohol and DBU were purchased from Aldrich and dried with 3 Å molecular sieves. Tetrahydrofuran (THF) and dichloromethane (DCM) for monomer synthesis and polymerization were distilled with calcium hydride (CaH_2) before use.

Monomer Synthesis

5-[2-{2-(2-Methoxyethoxy)ethyoxy}-ethoxymethyl]-5-methyl-trimethylene carbonate (TMCM-MOE3OM) was synthesized via a five-step process (Scheme 1) based on the protocol described by Ajiro et al.,[11] with the exception that the final crude mixture was dissolved in DCM and extracted with 1 M HCl and saturated NaCl solution to remove the byproduct imidazole salt without using silica gel chromatography. The organic layer was collected and dried by $MgSO_4$. A final yield of 47% (2.4 g) of TMCM-MOE3OM was obtained after evaporation of the DCM.

Polymerization Conditions

Homo- and copolymerizations of TMCM-MOE3OM were performed using the organocatalyst DBU as well as with stannous 2-ethylhexanoate. A typical polymerization procedure is described here for TMCM-MOE3OM homopolymerization using DBU as the catalyst. 0.206 g of TMCM-MOE3OM (0.7 mmol) was dissolved in 1 mL of anhydrous DCM with CaH_2 particles and left to stir overnight. The CaH_2 was removed using a 0.2-μm nylon filter and the monomer solution was then transferred to a flame-dried glass vial in which the DCM was evaporated under reduced pressure. Then, 0.35-mL anhydrous DCM under argon atmosphere was introduced to re-dissolve the monomer. Into the monomer solution, 0.76 mg of benzyl alcohol (0.007 mmol) as initiator and 1.07 mg of DBU (0.007 mmol) were added to start the polymerization at room temperature for 24–48 h. At specific time points, the reaction was stopped by adding a few drops of acetic acid. The solvent was removed under a flow of argon, then directly analyzed for monomer conversion via ^1H NMR spectroscopy. For purification, the reaction mixture was poured into 20 mL of cold hexane/2-propanol (9/1, v/v). The resultant product was recovered by decantation of the supernatant and dried under vacuum at room temperature.

Homo- and copolymerization of TMCM-MOE3OM with stannous 2-ethylhexanoate ($SnOct_2$) as the catalyst were carried

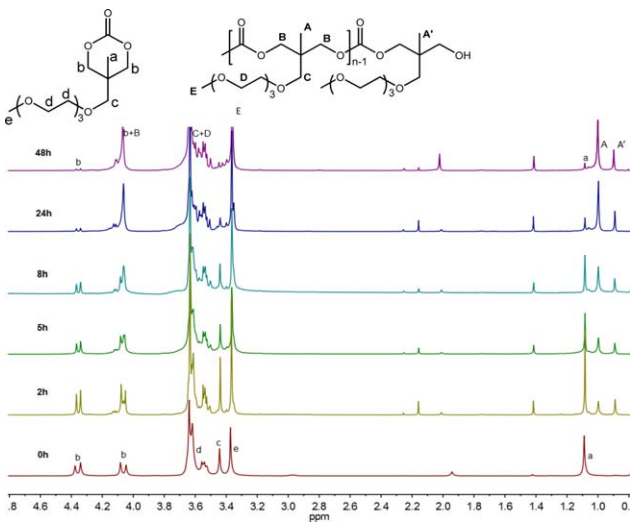


FIGURE 1 Representative ^{1}H NMR spectra of the TMCM-MOE3OM monomer, and its homopolymer, following polymerization for different reaction times using DBU as the catalyst. The reaction conditions were as follows: monomer concentration of 2 M, monomer to initiator ratio of 200:1, monomer to catalyst ratio of 100:1, a temperature of 25 °C, and using benzyl alcohol as the initiator. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

out by bulk melt polymerization at 130 °C. In a typical polymerization, 0.2 g of TMCM-MOE3OM (0.68 mmol), 0.74 mg of benzyl alcohol (0.0068 mmol) and 0.8 mg of $Sn(Oct)_2$ were loaded into a 10-mL glass ampoule. The ampoule was then purged with argon twice, sealed under vacuum, and placed in an oven at 130 °C for 24 h. After cooling, the product was dissolved in DCM and precipitated in an excess of hexane/2-propanol (9/1, v/v). The resultant product was recovered by decantation of the supernatant and dried under vacuum at room temperature.

Characterization

Compositions were determined from ^{1}H NMR spectra obtained from a Bruker Avance 400 MHz spectrometer. The synthesized materials were dissolved in chloroform-d (Fluka, Canada) at 10 mg/mL and their chemical shifts were measured relative to the methyl proton resonance of an internal tetramethylsilane reference. The number average molecular weight (M_n), weight-average molecular weight (M_w), and molar-mass dispersity ($Đ_M$) were measured using size exclusion chromatography (SEC) on a Viscotek GPCmax VE2001 Separation Module equipped with a refractive index (RI) detector. Two porous PAS-106M columns (PolyAnalytik SupeRes Series) were used in series. The calibration curve based on the RI detector was constructed using narrow molecular weight polystyrene standards ranging from 890 to 3.28×10^6 g/mol. THF at 40 °C was used as the mobile phase at a flow rate of 1 mL/min with the polymer sample dissolved in THF at a concentration of 5 mg/mL. The results were analyzed and fitted in Astra v4.90.07 software (Wyatt Technology). The number average molecular weights were also analyzed using a Waters/Micromas MALDI micro MX in linear ion mode using sinnapinic acid as a matrix with capability to detect mass range from 100 Da to at least 200 kDa.

RESULTS AND DISCUSSION

TMCM-MOE3OM Synthesis

The TMCM-MOE3OM synthesis followed the previously reported protocol[11] (Scheme 1) with a single modification. Unlike in the previous protocol, time-consuming column chromatography was avoided, and instead extraction with dilute HCl (1 M) and water was used to remove the unreacted CDI and resultant imidazole salt. The structure and purity of TMCM-MOE3OM was confirmed by ^{1}H NMR (Fig. 1). The extraction proved to be efficient in removing impurities, with the yield reaching 47%, which was higher than the 34% reported previously.[11]

Homopolymerization of TMCM-MOE3OM with DBU

The results of the homopolymerization using the DBU catalyst are summarized in Table 1. The effect of reaction time and monomer to initiator ratio on the monomer conversion and final molecular weight were investigated. Figure 1 shows representative ^{1}H NMR spectra of the TMCM-MOE3OM

TABLE 1 Summary of TMCM-MOE3OM Polymerization Kinetics at 25 °C Using DBU as Catalyst, a Monomer to Catalyst Ratio of 100:1, a Monomer Concentration of 2 M, and Benzyl Alcohol as the Initiator

Run	Reaction Time (h)	M_0/I_0 (mol/mol)	Monomer Conversion (%)	M_n (Da)[a]	$Đ_M$[a]
1	2	200:1	31	1,800	1.40
2	5	200:1	54	2,300	1.45
3	8	200:1	66	2,700	1.47
4	24	200:1	92	3,700	1.58
5	48	200:1	96	3,300	1.71
6	48	100:1	93	3,500	1.67
7	48	25:1	93	2,900	1.64
8	48	No I	94	4,100	1.70

[a] Determined by SEC using THF as mobile phase calibrated with PS standard.

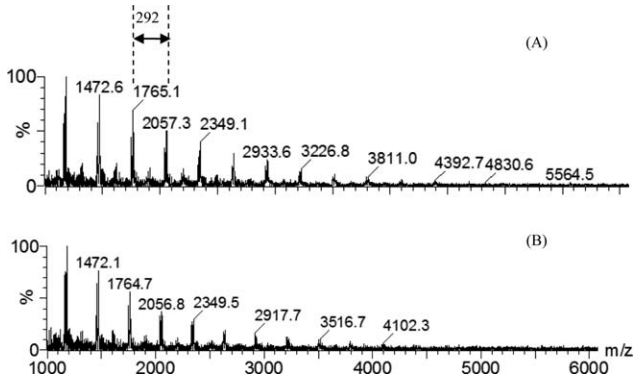


FIGURE 2 Representative MALDI-TOF spectra of poly(TMCM-MOE3OM): (A) $M/I = 100/1$, Run 6 in Table 1, (B) without initiator, Run 8 in Table 1.

monomer and poly(TMCM-MOE3OM) synthesized using the DBU catalyst and benzyl alcohol as initiator, respectively, as a function of time. After polymerization, the peaks at $\delta = 4.37$ ppm (Peak b) and 3.44 ppm (Peak c) corresponding to the methylene protons near the carbonate group and ethylene glycol pendant group in the monomer, respectively, disappeared, while a peak at $\delta = 4.05$–4.1 ppm appeared, corresponding to the methylene protons near the carbonate group in the opened ring of poly(TMCM-MOE3OM). The conversion of the TMCM-MOE3M was calculated using,

$$\text{Monomer conversion} = \frac{(I_{4.07} - I_{4.35})/4}{I_{4.35}/2 + (I_{4.07} - I_{4.35})/4} \times 100\%$$

wherein I represents the integration of the peak corresponding to the subscript ^{1}H NMR ppm.

Under polymerization conditions wherein the monomer to initiator ratio was maintained constant (Runs 1–5), monomer conversion, molar-mass dispersity ($Đ_M$), and number average molecular weight (M_n) increased gradually with

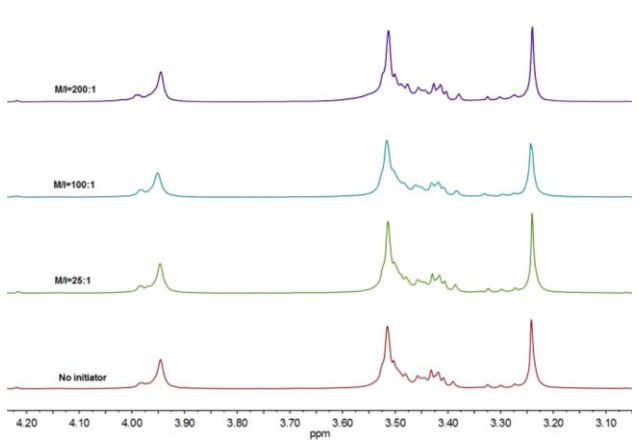


FIGURE 3 ^{1}H NMR spectra of TMCM-MOE3OM polymerization with different monomer to benzyl alcohol ratios (2 M, monomer to catalyst ratio = 100:1, 25 °C. DBU catalyst, reaction time: 48 h). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

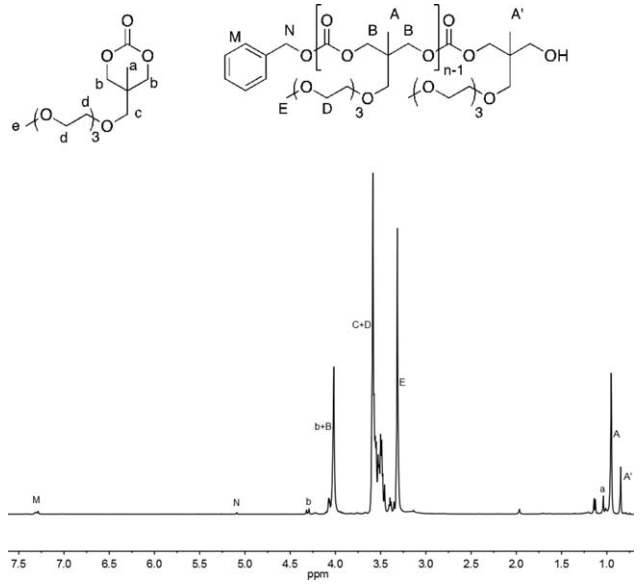


FIGURE 4 ^{1}H NMR spectrum of P(TMCM-MOE3OM) prepared with benzyl alcohol following purification. (Table 1, Run 6).

increasing reaction time, reaching a monomer conversion of 92%, a dispersity of 1.58 and an M_n of 3650 Da by 24 h (Table 1). Increasing the reaction time to 48 h improved monomer conversion to 96%, but M_n decreased slightly to 3300 Da while dispersity increased to 1.71. These molecular weights are far below the theoretical molecular weight, which is approximately 56 kDa, as calculated assuming every initiator molecule initiates a single chain and all chains have the same molecular weight. As these SEC molecular weight results were calculated relative to poly(styrene) standards, they were confirmed by MALDI-TOF measurements. In each case, the SEC measurements and the MALDI-TOF measurements were in good agreement (Fig. 2).

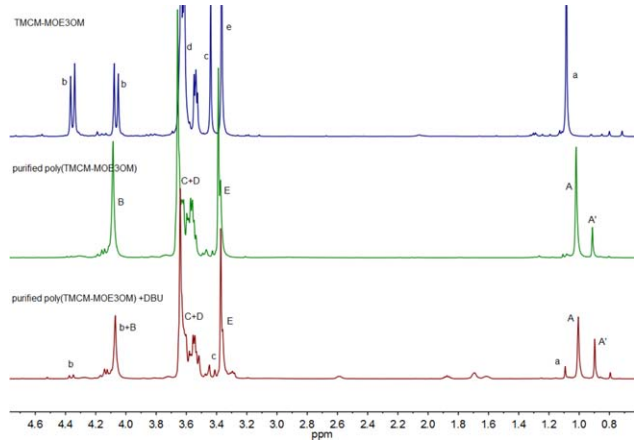
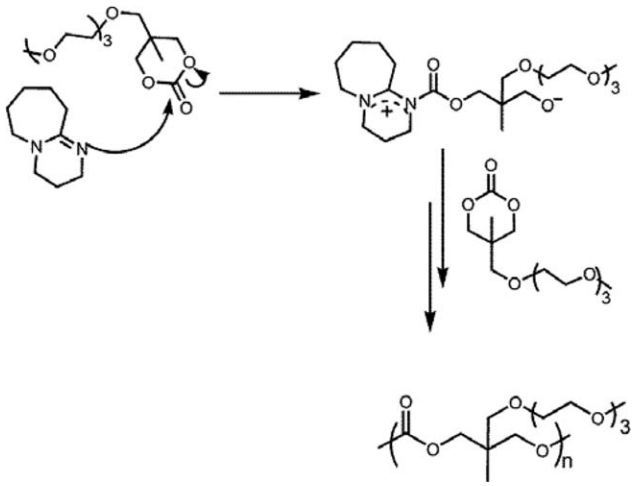


FIGURE 5 ^{1}H NMR spectra of TMCM-MOE3OM monomer (top), purified poly(TMCM-MOE3OM) (middle), and the poly(TMCM-MOE3OM) mixed with DBU for 3 days (bottom). Peak assignments are as shown in Figure 1. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



SCHEME 2 Proposed mechanism for autopolymerization of TMCM-MOE3OM in the presence of DBU.

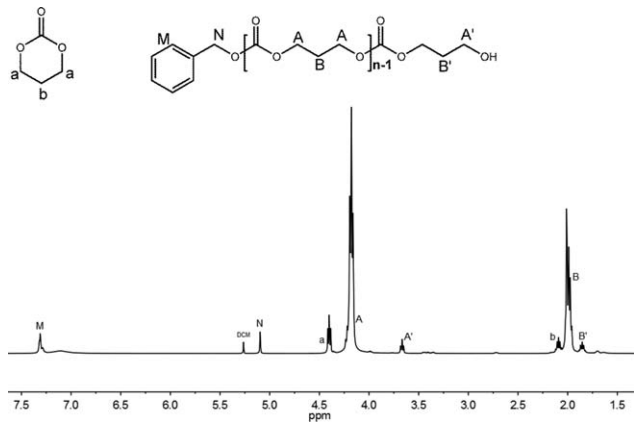


FIGURE 6 ^{1}H NMR spectrum of poly(trimethylene carbonate) prepared using DBU as catalyst and benzyl alcohol as the initiator (Table 2, Run 2, no purification).

Control over molecular weight was then attempted by adjusting the monomer to initiator ratio. However, decreasing the monomer to initiator ratio while maintaining a reaction time of 48 h resulted in no significant change in the obtainable M_n, as measured by SEC before any purification. The M_n remained between roughly 3000–4200 Da (Table 1, Runs 5–7). Further, there were no differences in the ^{1}H NMR spectra of the resultant oligomers (Fig. 3).

Following purification, the calculated M_n from the ^{1}H NMR spectra based on integration of the peaks corresponding to the phenyl group of the initiator (benzyl alcohol), assuming it was present at one terminus of the oligomer chain, yielded much larger values than the theoretical feed ratio. This finding indicated a loss of benzyl alcohol in the purification process. For example, the resulting monomer to initiator ratio for Run 6 was 322:1 (Fig. 4) whereas the starting ratio was 100:1. These results suggested that the degree of polymerization of TMCM-MOE3OM was not controlled by the ratio of monomer to initiator, and that poor end group fidelity was achieved. As noted in the above experimental section, water was absent during the polymerizations, and so initiation by adventitial water did not affect the polymerization. Both findings, therefore, may have resulted from either backbiting during the polymerization leading to ring-chain equilibrium, or from monomer autopolymerization.

The possibility of ring-chain equilibrium was assessed by first purifying the oligo(TMCM-MOE3OM) by precipitation from DCM into hexane/2-propanal (9:1) twice, followed by drying under vacuum, then re-dissolution in anhydrous DCM containing 6.67 mg/L DBU and leaving the polymer in this solution for 72 h at room temperature. After 72 h, the solution was directly analyzed via ^{1}H NMR. The ^{1}H NMR spectra clearly showed the appearance of monomer Peaks (a and c) in the resulting polymer solution (Fig. 5). Moreover, the ratio of the area of the peak corresponding to the pendant methyl group in the repeating unit ($\delta = 1.02$ ppm) to that in the terminal group ($\delta = 0.89$ ppm) clearly decreased, indicative of a decrease in number average molecular weight.

To test whether the TMCM-MOE3OM was capable of autopolymerization, the polymerization reaction was run in the absence of benzyl alcohol. An oligomer with high monomer conversion (94%), but only slightly higher M_n (4100 Da) (Table 1, Run 8) was obtained, demonstrating that TMCM-MOE3OM is capable of autopolymerization in the presence of DBU. A possible mechanism for the autopolymerization, adapted from a mechanism determined for the DBU-catalyzed ring-opening polymerization of 5,5-(bicyclo[2.2.1]hept-2-en-5,5-ylidene)-1,3-dioxan-2-one,[18] is given in Scheme 2. The process is initiated by a reaction between DBU and TMCM-MOE3OM, forming an alkoxide anion. Once the alkoxide anion forms it serves as the initiator that can attack the carbonyl group of remaining

TABLE 2 Summary of TMC Polymerization Kinetics Using DBU as Catalyst and Benzyl Alcohol as the Initiator

Run	Time (h)	M_0:I_0[a] (mol/mol)	Monomer Conversion (%)	M_n (Theor) (Da)	M_n (^{1}H NMR) (Da)
1	24	17:1	94	1,700	1,740
2	24	20:1	91	1,960	2,250
3	24	No I	19	–	1,380
4	72	200:1	80	16,400	16,800

Polymerizations were done at 25 °C, using a monomer to catalyst ratio of 100:1 and a monomer concentration of 2 M.

[a] M_o and I_o are the initial monomer and initiator concentrations, respectively.

TABLE 3 Polymerization of TMCM-MOE3OM in Different Solvents at Room Temperature

Solvent	M_0:I_0 (mol/mol)	Monomer Conversion (%)	M_n[a] (Da)	$Đ_M$[a]
THF	100:1	68	2,100	1.51
DMF	100:1	36	1,650	1.30
DCM	100:1	95	3,040	1.44
DCM	100:0	94	3,450	1.40

In each case, the reaction time was 48 h, the monomer to catalyst ratio was 100:1, and the monomer concentration was 2 M.
[a] Determined by SEC with THF as the mobile phase and calibrated with PS standards.

TMCM-MOE3OM, forming the polymer. Thus, it is likely that both backbiting and monomer autopolymerization of TMCM-MOE3OM limit the maximum molecular weight that can be obtained when using DBU as the catalyst.

As a control, TMC was polymerized using DBU as catalyst and benzyl alcohol as the initiator under the same reaction conditions as TMCM-MOE3OM. The monomer conversion and final M_n of PTMC was monitored by ^{1}H NMR (Fig. 6). Compared to TMCM-MOE3OM, the final molecular weights of PTMC were close to the theoretical values and the molecular weight was controlled to a high degree by changing the monomer to initiator ratio (Table 2). Notably, TMC was also capable of autopolymerization (Table 2, Run 3), but the polymerization proceeded more slowly than in the presence of the benzyl alcohol initiator.

Finally, a series of polymerizations of TMCM-MOE3OM was run with different solvents at the same reaction conditons. With or without benzyl alcohol initiator, high monomer conversions were obtained in DCM (~94%), while low monomer conversion was observed in THF and DMF (Table 3). These results are probably due to hydrogen bonding betweeen DBU and THF or DMF, which inhibited the polymerization.[19] The polymerization behavior in different solvents also implies that through hydrogen bonding DBU was able to activate the monomer and this activation was essential for polymerization.

TABLE 4 Summary of TMCM-MOE3OM Polymerization Kinetics with $Sn(Oct)_2$ as Catalyst, Benzyl Alcohol as Initiator, and Bulk Polymerization at 130 °C

Time (h)	Monomer Conversion (%)	M_n[a] (Da)	$Đ_M$[a]
1	20	1,630	1.14
3	31	2,000	1.24
5	38	2,280	1.26
8	54	2,700	1.36
24	71	3,300	1.51

[a] Determined by SEC using THF as the mobile phase calibrated with PS standard.

Homopolymerization of TMCM-MOE3OM with $Sn(Oct)_2$

Bulk melt polymerizations of TMCM-MOE3OM with $Sn(Oct)_2$ initiated with benzyl alcohol were carried out at 130 °C. A similar trend was observed as for the DBU-catalyzed polymerizations; the M_n first increased with increasing monomer conversion then reached a maximum M_n of about 3300 Da (Table 4). High monomer conversion was obtained, but as polymerization proceeded, a higher dispersity resulted. These results are again attributed to backbiting reactions that would predominate in the later stages of polymerization under high temperature, leading to ring-chain equilibrium.

Thus, it is not possible to obtain a homopolymer of TMCM-MOE3OM with a molecular weight greater than about 4000 Da with a low dispersity using either of these common catalysts. These results are in contrast to those of Ajiro et al., who reported that M_n could be controlled by the monomer

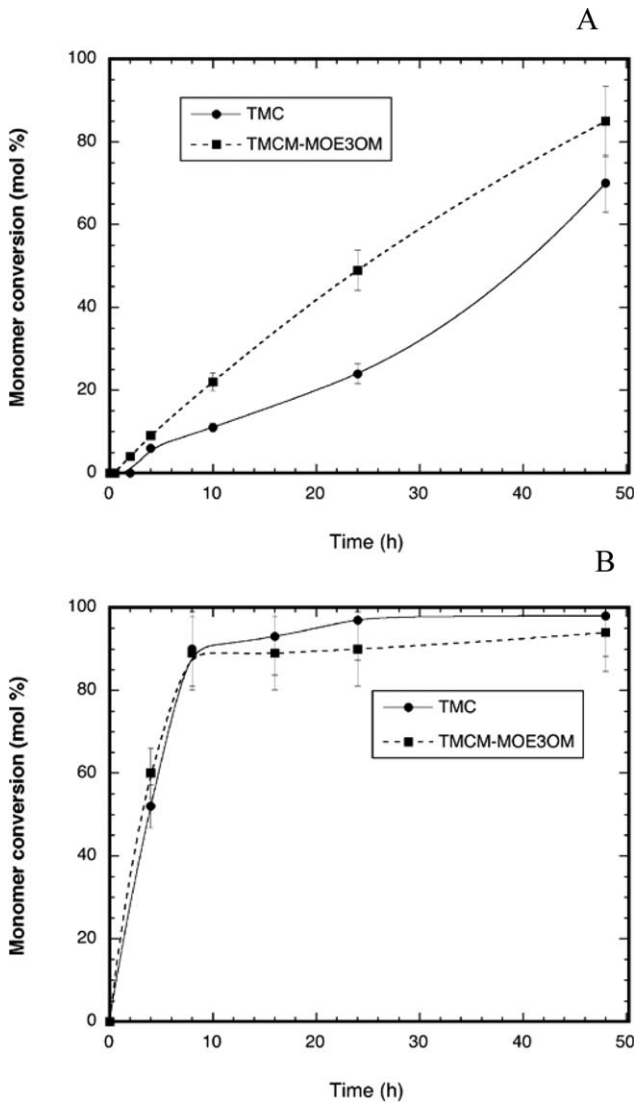


FIGURE 7 Monomer conversion during copolymerization of TMC and TMCM-MOE3OM using (A) DBU and (B) $Sn(Oct)_2$ as catalyst.

TABLE 5 Summary of Copolymerization Results of TMC with TMCM-MOE3OM

Run	TMCM:TMC (mol/mol)	Monomer Concentration (M)	Temperature (°C)	M_0:I_0 (mol/mol)	M_0:C_0[a] (mol/mol)	Copolymer TMCM:TMC	M_n[b] (Da)	$Đ_M$[b]
1	50:50	2	R.T	300:1	300:1	54:46	4,400	2.08
2	33:67	1	R.T	100:1	100:1	29:71	2,200	1.28
3	90:10	2	R.T	100:1	100:1	92:8	3,100	1.34
4	50:50	bulk	130	200:1	300:1	50:50	2,700	1.64

Runs 1–3 were catalyzed with DBU, 4 with $Sn(Oct)_2$. All reactions were for 48 h.
[a] M_o:C_o represents the initial monomer to catalyst molar ratio.
[b] Determined by SEC using THF as the mobile phase calibrated with PS standard.

TABLE 6 Summary of LLA Polymerization Kinetics by DBU

Run	Monomer Concentration (M)	Reaction Time (h)	Monomer Conversion (%)
1	0.7	0.5	78
2	0.7	1	89
3	0.7	2	95
4	0.7	5	97
5	0.7	8	98
6	0.7	24	99
7	0.7	48	99

to initiator ratio, although lower than theoretical molecular weight was obtained, using DBU as the catalyst and benzyl alcohol as the initiator, under the same reaction conditions of solvent and temperature we have used.[11] Ajiro et al. also reported a maximum M_n of 11 kDa in contrast to the approximately 4 kDa obtained in this study, along with a dispersity of 1.4. These differences may be attributable to the fact that Ajiro et al. first purified their homopolymers before measuring the molecular weight. The purification step likely removed the low molecular weight fraction, thus increasing the average molecular weight and reducing the dispersity. Further, Ajiro et al. utilized PMMA as standards in their universal calibration for their SEC measurements, whereas we have used polystyrene standards. Ajiro et al. also have reported different molecular weights for TMC-MOE1OM when measured using SEC with different polymer standards.[20] Our SEC molecular weight results are consistent, however, with those we have obtained from mass spectrometry.

Copolymerization of TMC and LLA with TMCM-MOE3OM Catalyzed by DBU and $Sn(Oct)_2$

TMC and LLA are both widely used monomers for making biodegradable polymers. Copolymerization of TMCM-MOE3OM with these monomers is potentially of interest as doing so might introduce thermoresponsive properties and increase the hydrophilicity of these polymers, and therefore serve as a means of adjusting their degradation via hydrolysis. The copolymerization of TMCM-MOE3OM with each of these monomers was therefore investigated, again using DBU and $Sn(Oct)_2$ as catalysts.

The copolymerization of TMC with TMCM-MOE3OM using $Sn(Oct)_2$ but not DBU yielded random copolymers (Fig. 7). In each case, the final copolymer composition was close to the target feed ratio, but the resultant M_n was still lower than the theoretical value (Table 5). This latter result indicates that ring-chain equilibrium still occurs in the late stage of copolymerization.

The homopolymerization of LLA was first examined as a basis to study the reaction kinetics profile of the copolymerization of TMCM-MOE3OM with LLA. Compared to TMC and TMCM-MOE3OM, LLA polymerized much faster when catalyzed by DBU under the same reaction conditions. At relatively low monomer concentration (0.7 M), the monomer conversion reached to greater than 95% within 2 h (Table 6)

TABLE 7 Summary of Copolymerization of LLA with TMCM-MOE3OM

Run	LLA:TMCM (mol/mol)	Monomer Concentration (M)	Reaction Time (h)	M_0:I_0 (mol/mol)	M_0:C_0 (mol/mol)	Temperature (°C)	TMCM Conversion (%)	LLA Conversion (%)
1	50:50	2	48	200:1	100:1	R.T.	0	95
2	67:33	1	48	100:1	100:1	R.T.	0	91
3	50:50	Bulk	48	200:1	300:1	130	50	97

Runs 1 and 2 were with DBU, 3 was with $Sn(Oct)_2$.

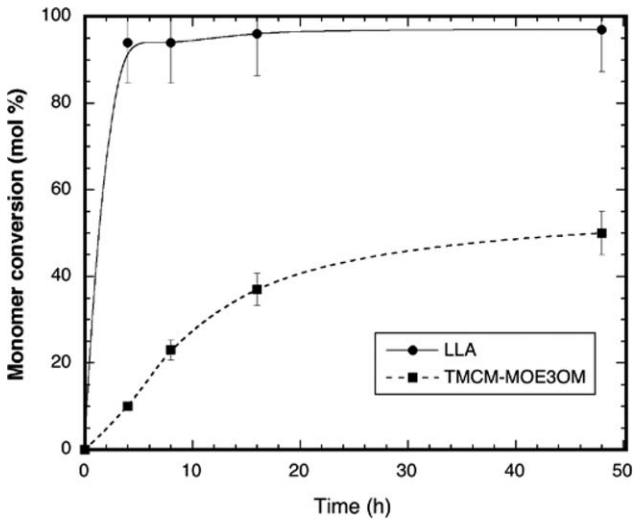


FIGURE 8 Monomer conversion during copolymerization of LLA and TMCM-MOE3OM using $Sn(Oct)_2$ as catalyst.

and a high molecular weight product (29.8 kDa) was obtained. These findings are in agreement with those of others for this polymerization system.[21–23]

As shown in Table 7, LLA did not effectively copolymerize with TMCM-MOE3OM when DBU was used as the catalyst. With targeted 50/50 and 67/33 molar feed ratios (LLA/TMCM-MOE3OM), only LLA was predominantly polymerized into the final polymer, as confirmed by ^{1}H NMR. This finding is in agreement with that of Lohmeijer et al., who found that, with DBU-catalyzed copolymerizations, the faster propagating monomer polymerized first forming a block copolymer with conversion reaching greater than 95%, and thereafter the less reactive monomer was incorporated as a second block, but very slowly.[21] On the other hand, bulk melt polymerization of LLA and TMCM-MOE3OM catalyzed with $Sn(Oct)_2$ did yield a copolymer. However, the resulting copolymer was principally a diblock, as demonstrated by the relative monomer conversions with time, shown in Figure 8. The LLA polymerized rapidly, reaching nearly complete conversion by 4 h, whereas the TMCM-MOE3OM polymerized more slowly, reaching only 50% conversion by 48 h.

CONCLUSIONS

The homo- and copolymerization kinetics of a functional cyclic carbonate monomer bearing a methoxyethoxy pendant group (TMCM-MOE3OM) was investigated using the organocatalyst DBU as well as the commonly used metal catalyst $Sn(Oct)_2$. Compared with nonfunctionalized TMC as well as LLA, ring-chain equilibrium was observed in the polymerization of TMCM-MOE3OM with either catalyst. This equilibrium limited the maximal molecular weight that could be achieved while having no obvious effect on the degree of monomer conversion. The molecular weight was further limited by TMCM-MOE3OM autopolymerization. Interestingly, the maximum molecular weight that was obtained with DBU was independent of the monomer to initiator ratio, which suggests that it can serve as both an initiator and a catalyst. Copolymers could be obtained by copolymerizing TMCM-MOE3OM with TMC with either DBU or $Sn(Oct)_2$ as catalyst, but only with $Sn(Oct)_2$ as the catalyst when TMCM-MOE3OM was copolymerized with LLA, albeit with the formation of a diblock copolymer as the LLA is consumed rapidly while the conversion of TMCM-MOE3OM is far slower. The failure to obtain high molecular weight copolymers of TMCM-MOE3OM and LLA using DBU as the catalyst was due to the large differences in the reactivity of each monomer; with LLA reacting much faster than TMCM-MOE3OM. This study indicates that catalyst selection for the polymerization of substituted TMCs must be carefully investigated to obtain polymers with controlled molecular weights and end group fidelity.

ACKNOWLEDGMENTS

Funding for this project was provided by the Natural Sciences and Engineering Research Council of Canada through a Discovery Grant and the CREATE Biointerfaces Training Program, CREATE Training Program in Bone and Joint Health Technologies.

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