Controlled Lipase-Catalyzed Synthesis of Poly(hexamethylene carbonate)

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Received March 19, 2007; Revised Manuscript Received August 10, 2007

ABSTRACT: High molecular weight (M_w > 25 000) poly(hexamethylene carbonate) (PHC) with polydispersity (M_w/M_n) ≤ 2.2 was successfully synthesized via copolymerization of diethyl carbonate with 1,6-hexanediol catalyzed by immobilized *Candida antarctica* Lipase B (CALB). Because diethyl carbonate is highly volatile, polymerizations were performed by a first stage oligomerization at low vacuum (600 mmHg pressure) followed by a second stage polymerization under high vacuum (1−5 mmHg pressure). Enzymatic polycarbonate synthesis is preferably performed in solution (e.g., in diphenyl ether), although it also proceeds in solventless reactions albeit at reduced rates. Synthesized PHC contains hydroxyl and ethyl carbonate terminal groups. Influence of regulating the ratio of diethyl carbonate to 1,6-hexanediol in the monomer feed on polymer end-group structure was determined. Reaction conditions and monomer feed ratios resulting in PHC with exclusively hydroxyl or ethyl carbonate termini were established. The ability to synthesize PHC products with desired end-group structure is critical to their potential use as macromers in, for example, polyurethane synthesis. Mechanistic features of enzymatic polycarbonate synthesis were elucidated, which explain why high molecular weight PHC can be prepared at high (e.g., 4:1) diethyl carbonate to diol monomer feed ratios whereas conventional chemically catalyzed step-polycondensation reactions of AA−BB type monomers require a 1:1 monomer feed ratio. That is, enzyme-catalyzed polycondensations between dialkyl carbonate and diol proceed via two pathways: (i) reaction between hydroxyl and carbonate end groups with elimination of alcohol and (ii) transesterification between two carbonate end groups with elimination of dialkyl carbonate.

Introduction

Aliphatic polycarbonates are biodegradable materials[1] with potentially important medical applications.[2] They can also be used as thermoplastic additives[3] and as matrix materials in solid electrolytes.[4] High molecular weight aliphatic polycarbonates are suitable for production of extrudates, films, and molded articles.[5] Hydroxyl-terminated aliphatic polycarbonates are particularly useful and have been widely used in industry as building blocks to produce specialty polyurethanes[6] and other polymeric materials.[7] In addition, polymer membranes prepared from polyimides containing aliphatic polycarbonate segments were reported to be effective for selective separation of aromatic/saturated-hydrocarbon mixtures.[8]

Aliphatic polycarbonates are produced chemically through polycondensation of aliphatic diols with dialkyl carbonates, cyclic glycol carbonates, or diphenyl carbonate.[9] Chemical processes require high reaction temperatures (≥200 °C) due to low activity of organometallic catalysts employed. Other chemical methods to synthesize aliphatic polycarbonates include ring-opening polymerization of cyclic aliphatic carbonates catalyzed by organometallic catalysts[10] and copolymerization of epoxides with carbon dioxide.[11]

Enzyme-catalyzed polycarbonate synthesis reactions may proceed with desirable selectivity under mild conditions, avoiding side reactions that plague chemical methods where end-group structural control is desired. Prospective benefits include reduced energy input and reduction of toxic byproducts including residual metals. Routes to high-purity polycarbonate products may be especially beneficial for medical and electronic material applications. Indeed, work has begun to develop routes to polycarbonates via enzyme catalysis. Thus far, two types of enzyme-catalyzed processes, ring-opening and polycondensation polymerizations, have been used for aliphatic polycarbonate synthesis. For example, ring-opening polymerization of trimethylene carbonate catalyzed by various lipases under certain reaction temperatures, particularly Lipase B from *Candida antarctica* (CALB) at 45−70 °C[12a,c] and porcine pancreatic lipase (PPL) at 100−120 °C,[12b] was reported to form poly(trimethylene carbonate) with M_w > 30 000 and M_w/M_n between 2.2 and 4.1. The monomer conversion was 97% in 120 h at 70 °C for CALB and 96% in 24 h at 100 °C for PPL. While a variety of dialkyl carbonate and diol monomers can serve as substrates for the polycondensation reaction, only few cyclic carbonate monomers are readily available for preparing aliphatic polycarbonate via ring-opening polymerization.[12]

Enzyme-catalyzed condensation copolymerization between diphenyl carbonate and diols has been reported.[13] However, this route results in formation of phenol that is a toxic byproduct. Recently, Rodney et al. screened 26 hydrolase enzymes, including various lipases, esterases, acylases, and proteases, for copolymerization of trimethylene divinyl dicarbonate with 1,3-propanediol.[14] Catalyzed by 1 wt % enzyme in bulk at 50 °C for 72 h, the polymerization reactions yielded carbonate oligomers with M_w between 500 and 1300 (M_w/M_n and yields were not reported). The highest molecular weight (M_w = 9000) poly(trimethylene carbonate) was obtained at 40 °C in 72 h using 20 wt % immobilized CALB (Novozym 435 or N435) as catalyst. Polycondensations between trimethylene divinyl dicarbonate with other C_2−C_{12} diols, and between different alkylene divinyl dicarbonates and C_3−C_6 triols, were also discussed. However, vinyl ester or carbonate precursors, such as activated alkylene divinyl dicarbonates, are undesirable

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10.1021/ma070665m CCC: $37.00
Published on Web 10/02/2007

Scheme 1. Two-Stage Process for Copolymerization of Diethyl Carbonate with Aliphatic Diol

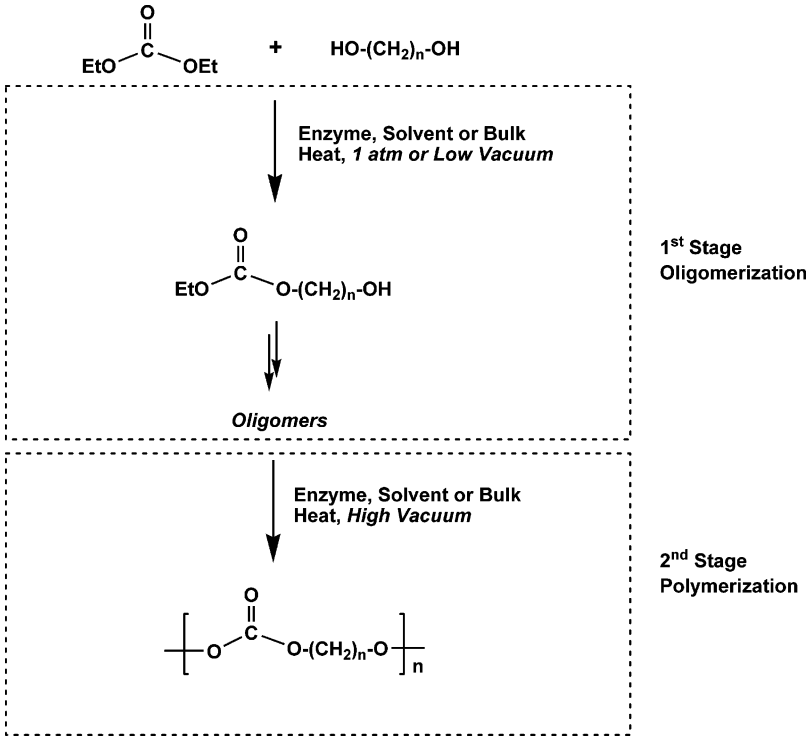
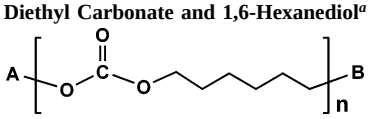


Table 1. Molecular Weight and End-Group Structures of Oligomers Formed during Stage-1 of N435-Catalyzed Polycondensation between Diethyl Carbonate and 1,6-Hexanediol[a]



	end groups		
number of units (*n*)	A: Et; B: OC(O)O−Et	A: Et; B: OH	A: HO−$(CH_2)_6$−; B: OH
1	262 (2.13 min, C_1)[b]		262 (1.97 min, E_1)[b]
2	406 (2.32 min, C_2)[b]	334 (2.11 min, D_2)[b]	406 (2.09 min, E_2)[b]
3	550 (2.48 min, C_3)[b]	478 (2.28 min, D_3)[b]	550 (2.24 min, E_3)[b]
4		622 (2.44 min, D_4)[b]	

[a] Reaction conditions: 80 °C, 600 mmHg, 18 h, in diphenyl ether solution. [b] Retention time and ID of oligomers.

monomers due to their high cost and intrinsic chemical instability.[14]

A desirable, environmentally benign method for preparing aliphatic polycarbonates is via polycondensation routes using dialkyl carbonate and diol as substrates. Matsumura et al.[15] reported polycarbonate synthesis using large quantities of enzyme catalysts (e.g., CALB, 18−31 wt %) from diethyl carbonate and short-chain diol monomers, such as 1,3-propanediol and 1,4-butanediol. The data were reported on reprecipitated polymers, isolated in low yields, representing only high molecular weight fractions of products. Copolymerization reactions were performed at 60−70 °C under 0.5 mmHg pressure for 7 h after initial oligomerization under atmospheric pressure for 24 h. Diethyl carbonate/diol ratios between 1:1 and 4:1 were used during the reactions. The corresponding polymer yields, M_w, and M_w/M_n were 3−43%, 5000−11 000, and 1.2−1.7 for poly(trimethylene carbonate) and 32−60%, 8500−24 000, and 1.5−2.2 for poly(tetramethylene carbonate), respectively.[15] Most recently, CALB-catalyzed synthesis of low molecular weight ($M_n \leq 6000$, M_w/M_n and yields not reported) polycarbonates from dimethyl carbonate and long-chain (C_5−C_8) diols was disclosed in the patent literature.[16] Unfortunately, fractionation by precipitation of products giving low yields that are then used for characterization significantly diminishes the scientific value of corresponding research since valuable information is lost on product molecular weight and molecular weight distribution, critical parameters that determine product quality and subsequent utility. Furthermore, research performed thus far on enzyme-catalyzed polycarbonate synthesis failed to address control of polycarbonate chain-end structure. Indeed, the ability to synthesize products with desired end-group structure is critical to their potential use as macromer building blocks for preparation of higher molecular weight materials through chain extension chemistry (e.g., using diisocyanates).

In this paper, immobilized CALB (N435) catalyzed polycarbonate synthesis was studied. Nonfractionated poly(hexamethylene carbonate), PHC, with $M_w > 25\,000$ was prepared from diethyl carbonate and 1,6-hexanediol. Reactions were performed using a pressure-varied two-stage process to remove the formed ethanol byproduct and avoid premature volatilization of diethyl carbonate. Removal of ethanol drives the equilibrium polycondensation reaction toward polymer formation. Variation of the carbonate/diol feed ratio was studied as a means to regulate chain-end structure. Effective strategies resulted from that enabled the preparation of PHC with predominantly ethyl carbonate or hydroxyl chain terminal units. Structures of PHC and oligomeric intermediates were analyzed by proton and carbon-13 NMR spectroscopy as well as by LC-MS. Mecha-

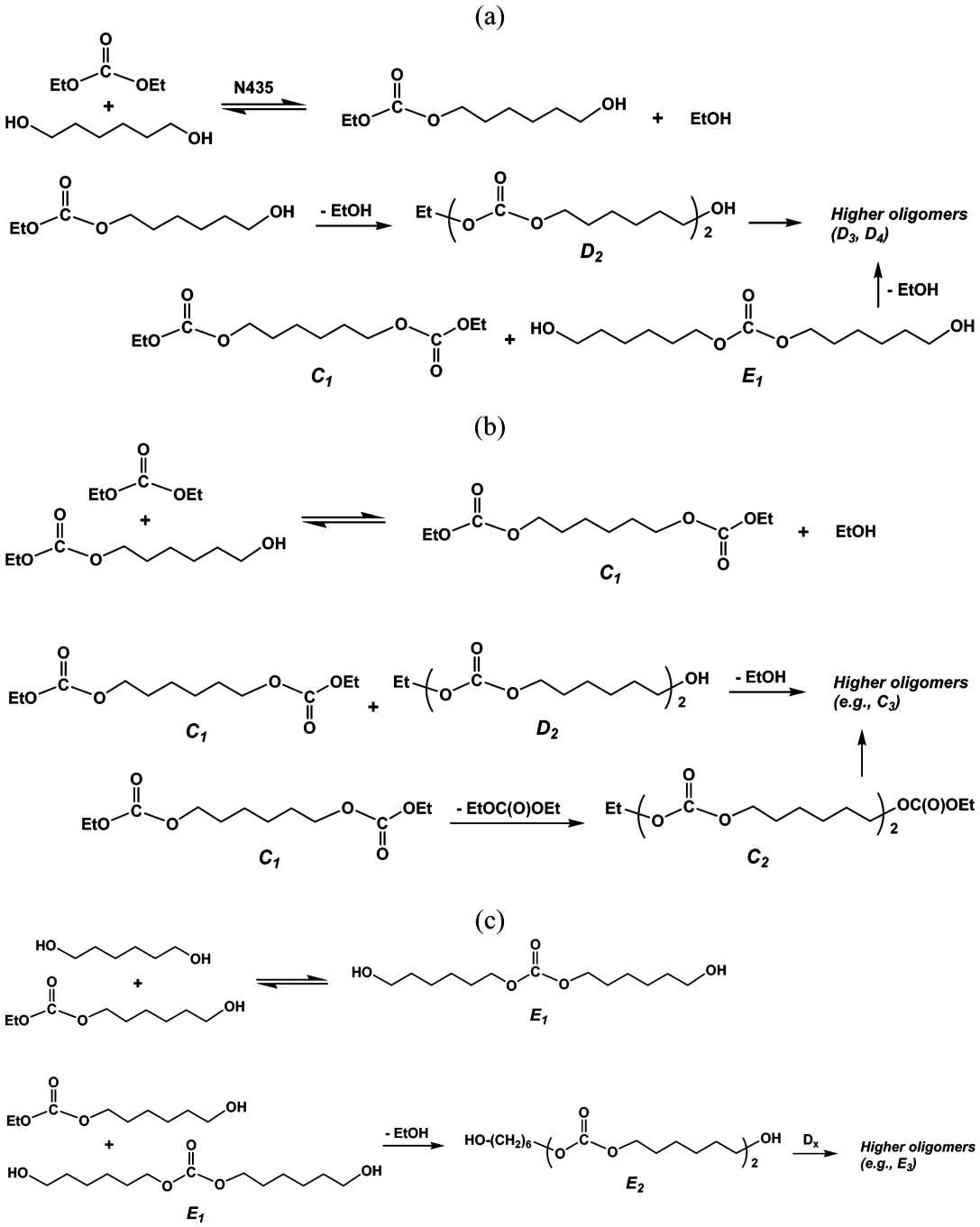


Figure 1. Possible reactions during oligomerization of diethyl carbonate with 1,6-hexanediol.

nistic studies on model compounds gave new insights that explain how high molecular weight PHC is formed by N435 catalysis using diethyl carbonate to diol monomer feeds highly enriched in the former (e.g., 4:1).

Experimental Section

Materials. Diethyl carbonate, dipropyl carbonate, 1,6-hexanediol, and diphenyl ether were purchased from Aldrich Chemical Co. in the highest available purity and were used as received. Novozym 435 (specific activity 10500 PLU/g), abbreviated as N435, was a gift from Novozymes (Bagsvaerd, Denmark) and consists of *Candida antarctica* Lipase B (CALB) physically adsorbed within the macroporous resin Lewatit VPOC 1600 (poly[methyl methacrylate-*co*-butyl methacrylate], supplied by Bayer). Lewatit VPOC 1600 has a surface area of 110−150 m^2/g and an average pore diameter of 100 nm. N435 contains 10 wt % CALB that is located on the outer 100 μm of 600 μm average diameter Lewatit beads.

Instrumental Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE 300 spectrometer or a Bruker AVANCE 600 spectrometer. The chemical shifts reported were referenced to internal tetramethylsilane (0.00 ppm) or to the solvent resonance at the appropriate frequency. Low molecular weight oligomers were analyzed using a LC-MS spectrometer equipped with a Waters 2795 Separations module, containing a Primesep B2 column (dimensions 4.6 × 150 mm, particle size 5 μm, pore size 100 Å), and a Waters Micromass ZQ detector. A mixture of 16:2:1:1 v/v methanol to water, acetonitrile, and 1 wt % aqueous formic acid solution was used as mobile phase that was pumped at a constant flow rate of 1.0 mL/min. The number- and weight-average molecular weights (M_n and M_w, respectively) of polymers were measured on nonfractionated (i.e., without precipitation) products by gel permeation chromatography (GPC) using a Waters HPLC system equipped with a model 510 pump, a Waters model 717 autosampler, and a Wyatt Optilab DSP interferometeric

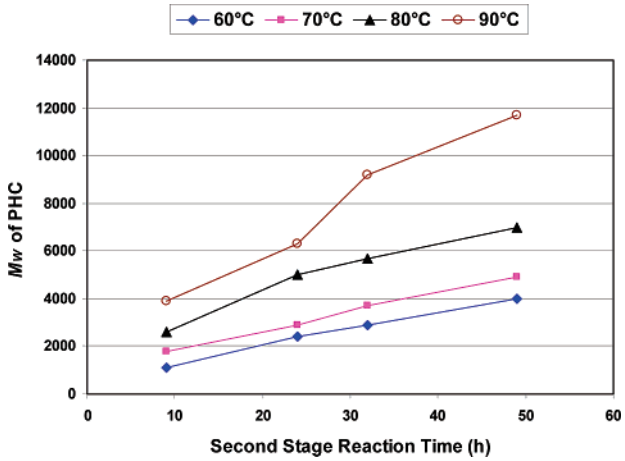


Figure 2. Molecular weight of PHC vs reaction time for copolymerization of diethyl carbonate and 1,6-hexanediol in diphenyl ether (2:1 carbonate/diol ratio; second stage pressure: 3.0 mmHg).

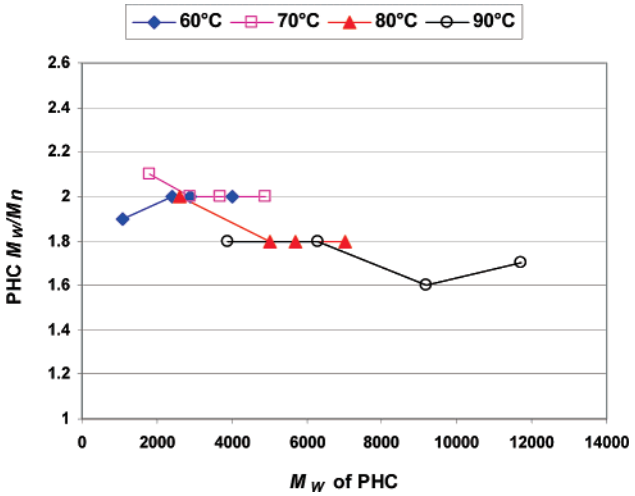


Figure 3. Effects of reaction temperature on PHC polydispersity (M_w/M_n) for copolymerization of diethyl carbonate with 1,6-hexanediol in diphenyl ether (2:1 carbonate/diol ratio; second stage pressure: 3.0 mmHg).

refractometer with 500, 10^3, 10^4, and 10^5 Å Ultrastyragel columns in series. Trisec GPC software version 3 was used for calculations. Chloroform was the eluent at a flow rate of 1.0 mL/min. Sample concentrations of 2 mg/mL, and injection volumes of 100 μL were used. Molecular weights were determined on the basis of a conventional calibration curve generated by narrow polydispersity polystyrene standards from Aldrich Chemical Co.

General Procedure for N435-Catalyzed Copolymerization of Diethyl Carbonate with 1,6-Hexanediol. Copolymerization between diethyl carbonate and 1,6-hexanediol was carried out either in bulk or in diphenyl ether solution on 10−20 g scale using a parallel synthesizer connected to a vacuum line with vacuum (±0.2 mmHg) controlled by a J-KEM vacuum regulator. In a typical experiment, a reaction mixture containing 1:1 to 4:1 (molar ratio) diethyl carbonate and diol, N435 (5−10 wt % based on total weight of monomers, dried at 50 °C under vacuum for 18 h), and optionally diphenyl ether solvent (0.5−2 equiv vs total weight of monomers), was stirred at 50−90 °C under 600 mmHg pressure. After the initial first stage oligomerization for 18−24 h, the reaction pressure was reduced to 1−5 mmHg, and the reaction was allowed to continue for an additional 24−53 h. Aliquots were taken during the first stage oligomerization and second stage polymerization. The low molecular weight oligomers were analyzed by LC-MS spectrometry. Polymer samples were dissolved in chloroform and filtered to remove the enzyme catalyst. Products were not fractionated by precipitation prior to analysis of molecular weight and structure. Polymer molecular weights were analyzed by GPC using polystyrene standards. To determine polymer structures, aliquots were dissolved in chloroform-*d*. The resultant solutions were filtered to remove catalyst particles and then analyzed by ^{1}H and ^{13}C NMR spectroscopy. With respect to determination of yield, under the reaction conditions herein there was no observed loss of 1,6-hexanediol (boiling point = 250 °C) during polycondensation reactions. Furthermore, 1,6-hexanediol was quantitatively converted to PHC. Volatilized diethyl carbonate and ethanol byproduct (but no 1,6-hexanediol) were recovered in a dry ice trap between reactors and the vacuum pump. Thus, yields for copolymerizations of diethyl carbonate with 1,6-hexanediol are quantitative (~100%) with respect to this diol.

Poly(hexamethylene carbonate) (PHC) with variable end-group structure and molecular weight was synthesized by the above general method. The results of ^{1}H and ^{13}C NMR spectral analysis were as follows.

PHC with Both Hydroxyl and Ethyl Carbonate End Groups. ^{1}H NMR ($CDCl_3$) (ppm): 1.41 (4H, m, $-CH_2-$), 1.68 (4H, m, $-CH_2-$), 4.12 (4H, t, $-CH_2-$), weak signals at 1.31 (t), 4.19 (q) attributable to ($CH_3CH_2OC(O)O-$) end groups, weak resonances at 3.64 (t) due to methylene attached to hydroxyl terminal group ($HOCH_2CH_2CH_2CH_2CH_2CH_2O-$).

PHC with 100% Ethyl Carbonate End Groups. ^{13}C NMR ($CDCl_3$) (ppm): 25.4 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 28.5 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 67.8 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 155.3 ($-OC(O)O-$); small signals at 14.3, 63.8, 155.2 attributable to $CH_3CH_2O-C(O)O-$ end groups; resonance at 67.7 attributable to $-OCH_2-$ groups adjacent to terminal ethyl carbonate.

PHC with 100% Hydroxyl End Groups. ^{13}C NMR ($CDCl_3$) (ppm): 25.4 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 28.6 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 67.8 ($-OCH_2CH_2CH_2CH_2CH_2CH_2O-$); 155.3 ($-OC(O)O-$), small signals at 25.5, 28.7, 32.7, 62.8, 67.9, 155.4 attributable to $HOCH_2CH_2CH_2CH_2CH_2CH_2O-C(O)O-$ end groups.

N435-Catalyzed Transesterification of Diethyl Carbonate with Dipropyl Carbonate. A reaction mixture containing diethyl carbonate (4.00 g, 33.9 mmol), dipropyl carbonate (4.95 g, 33.9 mmol), and N435 catalyst (1.00 g) was stirred at 85 °C under atmospheric air pressure in a closed flask equipped with a 5 psig pressure-relief valve for 68 h. Aliquots (~50 mg) were withdrawn at predetermined time intervals. They were dissolved in $CDCl_3$, filtered to remove the catalyst, and then analyzed by NMR spectroscopy. NMR resonances of ethyl propyl carbonate were recorded as follows. ^{1}H NMR ($CDCl_3$) (ppm): 0.97 (3H, t, $CH_3CH_2CH_2O-$), 1.31 (3H, t, CH_3CH_2O-), 1.70 (2H, sextet, $CH_3CH_2CH_2O-$), 4.09 (2H, t, $CH_3CH_2CH_2O-$), 4.19 (2H, q, CH_3CH_2O-). ^{13}C NMR ($CDCl_3$) (ppm): 10.35 ($CH_3CH_2CH_2O-$), 14.44 (CH_3CH_2O-), 22.25 ($CH_3CH_2CH_2O-$), 63.91 (CH_3CH_2O-), 69.55 ($CH_3CH_2CH_2O-$), 155.49 ($-OC(O)O-$).

Results and Discussion

Hydrolysis Reactions during Diethyl Carbonate/1,6-Hexanediol Copolymerizations. Water impurities can cause side reactions such as hydrolysis of diethyl carbonate and cleavage of polycarbonate chains.[15] The result would be chain-end structures that would vary from that predicted by monomer stoichiometry. To minimize hydrolysis reactions, the catalyst (N435), monomers, and solvent (diphenyl ether) were either dried prior to use or purchased in high purity (see Experimental Section). To test whether reaction conditions were suitable to avoid hydrolysis of carbonate monomers, both diethyl carbonate and dipropyl carbonate were each placed in a flask at 85 °C for 2 days under atmospheric air pressure with 10 wt % (relative to carbonate) N435. Proton (^{1}H) and ^{13}C NMR spectra recorded after 2-day incubations of these carbonates with N435 showed no evidence of ethanol or propanol formation. Therefore, the reaction conditions used suppressed hydrolytic reactions of

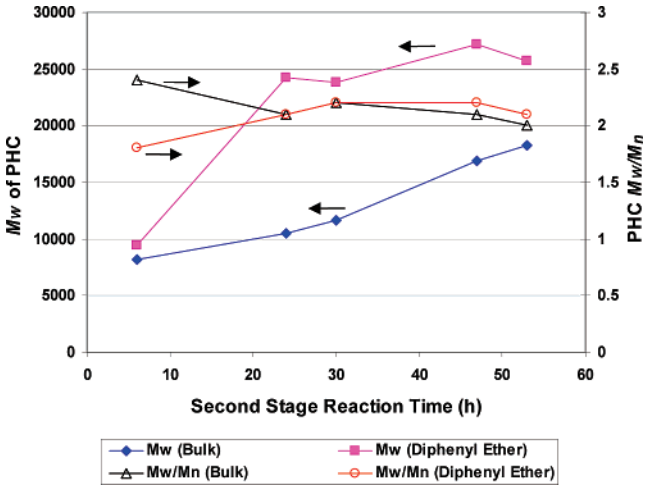


Figure 4. Copolymerization of diethyl carbonate with 1,6-hexanediol at 90 °C in bulk vs in diphenyl ether solution (2:1 carbonate/diol ratio; second stage pressure: 3.0 mmHg).

carbonate monomers and, presumably, of chain end groups containing carbonate linkages. Furthermore, 1,6-hexanediol and diphenyl ether used as received from Aldrich Chemical Co. were sufficiently dry for N435-catalyzed diethyl carbonate/diol copolymerizations. Indeed, comparison of chain growth as a function of time (data not shown) when using dried 1,6-hexanediol (50 °C, 1.0 mmHg, 24 h) and diphenyl ether (4 Å activated molecular sieves, 2 days) gave similar results as when as-received materials were used.

Two-Stage Process for the Copolymerization of Diethyl Carbonate with 1,6-Hexanediol. As illustrated in Scheme 1, polycondensation reactions between diethyl carbonate and 1,6-hexanediol were performed in two stages, where stage 1 and stage 2 were conducted first at low (600 mmHg) and then high (1−5 mmHg) vacuum, respectively. Low vacuum during the first stage allows oligomerization reactions between diethyl carbonate and 1,6-hexanediol to occur without excessive loss of diethyl carbonate that boils at 127 °C. The vacuum pressure was then decreased to 1−5 mmHg during stage 2, enabling conversion of oligomers to polymers. Analysis by NMR of volatile products produced during polymerizations and isolated in a dry ice trap placed between reaction flasks and a vacuum pump showed that it consists of only ethanol and diethyl carbonate.

Product Mixture Formed during First-Stage Oligomerization between Diethyl Carbonate and 1,6-Hexanediol. The oligomerization reaction, with 2:1 (mol/mol) diethyl carbonate/1,6-hexanediol and 7 wt % N435 (vs total monomer), was performed in diphenyl ether (130 wt % vs total monomer) at 80 °C, under 600 mmHg, for 18 h. Analysis of low molecular weight oligomers was performed by LC-MS, and results are summarized in Table 1. Carbonate oligomer pairs C_1−E_1 (262 Da), C_2−E_2 (406 Da), and C_3−E_3 (550 Da) have identical molecular weights but appear at different retention times (see Table 1). Separation of C_1 from E_1, C_2 from E_2, and C_3 from E_3 is due to that C-oligomers have ethyl carbonate−ethyl carbonate end groups whereas E-oligomers have hydroxyl−hydroxyl termini. Since LC separations were performed on a reverse-phase column, E-oligomers, with polar hydroxyl−hydroxyl end groups, have shorter retention times than corresponding C-oligomers with less polar ethyl carbonate−ethyl carbonate termini. The D-oligomers, with molecular weights 334, 478, and 622 Da, have ethyl carbonate−hydroxyl end groups. Thus, LC-MS analyses demonstrate that N435-catalyzed oligomerization during stage 1 gives a mixture of oligomeric products where all three possible end-group structures (ethyl carbonate−hydroxyl, hydroxyl−hydroxyl, and ethyl carbonate−ethyl carbonate) are found. Furthermore, the most abundant chain length in the mixture is trimers. Moreover, no evidence was found for formation of cyclic oligomers, consistent with an earlier report on oligomerization of diethyl carbonate with short-chain (C_3−C_4) diols.[15]

The structures of some intermediates described in Table 1, which were formed during oligomerization reactions and serve as building blocks during stage 2 for polymer synthesis, are shown in Figure 1. In Figure 1a, diethyl carbonate reacts with 1,6-hexanediol forming ω-hydroxylhexyl ethyl carbonate which can then undergo stepwise self-condensation reactions with elimination of ethanol to generate higher oligomers, such as D_2, D_3, and D_4 (see Table 1). D_3 can also be formed via condensation between diethyl hexamethylene dicarbonate (C_1) and di(ω-hydroxylhexyl) carbonate (E_1). Figure 1b shows the reaction between ω-hydroxylhexyl ethyl carbonate with diethyl carbonate to form C_1. Reaction of C_1 with carbonate−hydroxyl terminated oligomers, such as D_2, generates higher oligomers (e.g., C_3, Table 1). Alternatively, C_1 can continue chain growth via self-condensation with elimination of diethyl carbonate to form higher molecular weight oligomers (e.g., C_2, C_3) and polymers. Evidence that this mechanism of chain growth between carbonate terminal units does indeed occur is given later in this paper. Finally, condensation of ω-hydroxylhexyl ethyl carbonate with 1,6-hexanediol occurs to give di(ω-hydroxylhexyl) carbonate (E_1) which can then react with a carbonate-terminated oligomer, such as ω-hydroxylhexyl ethyl carbonate or diethyl carbonate, forming higher oligomers (e.g., E_2, E_3) and polymers (Figure 1c).

Temperature Effects on Polycondensations between Diethyl Carbonate and 1,6-Hexanediol. Reaction temperatures studied include 60, 70, 80, and 90 °C. Copolymerizations were performed using a 2:1 (mol/mol) ratio of diethyl carbonate to 1,6-hexanediol, 6.7 wt % N435 (vs total monomer), in diphenyl ether (130 wt % vs total monomer). During first stage oligomerization reactions, the pressure was maintained at 600 mmHg for 18 h. Thereafter, during the second stage, the pressure was reduced to 3.0 mmHg. Both first- and second-stage reactions were maintained at identical temperatures. Here, as in all studies described in this paper, sample analysis by NMR and GPC was performed on the complete product from reactions. In other words, products obtained were not fractionated by precipitation prior to analysis. Figure 2 illustrates the change in weight-average molecular weight (M_w) of PHC at different reaction temperatures vs reaction time. By performing reactions at higher temperatures, the polymerization rate increased. For example, at 48 h, PHC M_w increased from 4000 to 4900, 7000, and 11 700 by performing reactions at 60, 70, 80, and 90 °C, respectively. In contrast, no polymer (M_n < 400) was formed for reactions of diethyl carbonate with 1,6-hexanediol in diphenyl ether under similar polymerization conditions (90 °C, 600 mmHg for 18 h during first-stage oligomerization and 3.0 mmHg for 48 h during second-stage polymerization) but by replacing N435 with its corresponding macroporous support (Lewatit) without lipase (CALB).

Figure 3 depicts effects of reaction temperature and progress (based on M_w) on PHC polydispersity (M_w/M_n). No apparent effect of temperature on PHC polydispersity was observed. However, polydispersity tends to decrease as reactions progress forming higher molecular weight PHC. This is consistent with step-condensation reactions of low molecular weight constituents

of mixtures occurring more rapidly than the high molecular weight fraction, resulting in a narrowing of the molecular weight distribution with increased reaction time. In other words, longer reaction times permit low molar mass products to diffuse to the catalyst and form products of higher molecular weight. This reduces the low molecular weight fraction, thereby decreasing M_w/M_n. Transesterification reactions may also occur that, if random, can broaden the molecular weight distribution toward values ≥2.0 assuming statistically random, stepwise, polycondensation reactions. Apparently, by 32 h at 90 °C, the addition of low molecular weight oligomers to polymer chains occurs at a greater frequency than random transesterification reactions, allowing the attainment of products with M_w/M_n values down to 1.6 (Figure 3).

Copolymerization of Diethyl Carbonate with 1,6-Hexanediol in Bulk vs in Diphenyl Ether Solution.[17] Polycondensations between diethyl carbonate and 1,6-hexanediol were also studied in bulk. Figure 4 illustrates chain growth for polymerizations performed in bulk vs in diphenyl ether (70 wt % vs total monomer), with 2:1 (mol/mol) diethyl carbonate to 1,6-hexanediol and 7 wt % N435, at 90 °C. In both cases polymerizations were performed at 600 ± 0.2 mmHg for 18 h (stage 1) and then at 3.0 mmHg for 53 h (stage 2). It is noteworthy that solution polymerizations discussed above (see Figures 2 and 3) were performed using 130 wt % diphenyl ether, i.e., almost twice that used here. As shown in Figure 4, PHC chain growth was significantly faster for the solution polymerization. This is largely attributed to the lower viscosity of solution polymerizations, which reduces diffusion constraints between monomers, oligomers, and/or polymer chain reactants. For bulk and solution polymerizations in Figure 4, PHC polydispersity ranged from 2.0 to 2.2 after 24 h. The relatively higher PHC polydispersity (2.1−2.2) observed for the solution polymerization with 70 wt % diphenyl ether relative to 1.6−1.8 with 130 wt % diphenyl ether may be due to a lower tendency for transesterification reactions at lower reactant concentrations. Furthermore, by decreasing the solvent concentration from 130 to 70 wt %, PHC chain growth occurred more rapidly. For example, at 24 h, PHC M_w values were 6300 and 24 200.

Role of Carbonate−Carbonate Transesterification in Promoting Chain Growth during Polycarbonate Synthesis. N435-catalyzed transesterification between carbonate functionalities was studied using a small molecule model system. Reactions were performed between 1:1 (mol/mol) diethyl carbonate and dipropyl carbonate, with 11 wt % N435 (vs total substrate) at 85 °C under atmospheric pressure in a closed flask equipped with a 5 psig pressure-relief valve. Reaction progress was monitored by measuring the carbonyl ^{13}C NMR resonance of ethyl propyl carbonate at 155.49 ppm vs the resonance absorptions of diethyl carbonate and dipropyl carbonate at 155.35 and 155.63, respectively. N435 exhibited high activity in catalyzing transesterifications between diethyl carbonate and dipropyl carbonate, and the only new product detected by both proton and carbon-13 NMR spectroscopy was ethyl propyl carbonate (Scheme 2). No byproducts were formed during the reaction. To prove that the reaction is enzyme-catalyzed, a control reaction was performed under identical reaction conditions but by substituting N435 with the lipase-free immobilization support (Lewatit). The control experiment showed no reaction over a 70 h period. To the best of our knowledge, this is the first report demonstrating enzyme-catalyzed transesterification reactions between carbonate moieties.

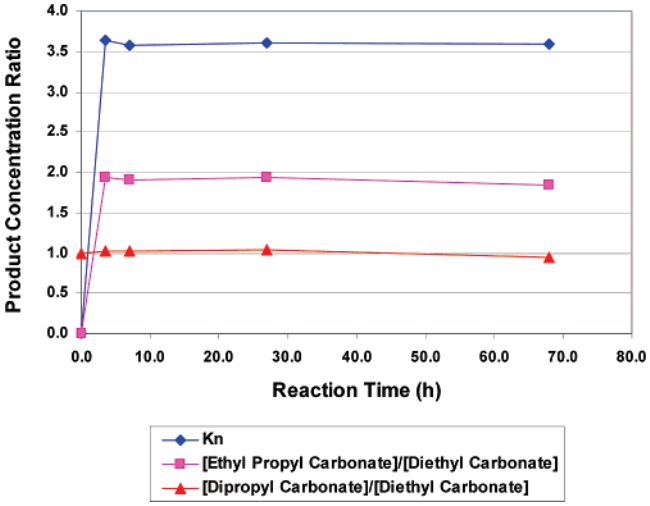


Figure 5. Nominal equilibrium constant (K_n) vs reaction time for N435-catalyzed transesterification between diethyl carbonate with dipropyl carbonate at 85 °C under atmospheric pressure.

Table 2. Bulk Copolymerization of Diethyl Carbonate with 1,6-Hexanediol:[a] Effects of Feed Ratio on PHC Molecular Weight and End-Group Structures

			end group in (mol %)[b]	
carbonate/diol (mol/mol)	M_n	M_w/M_n	−OH	−OC(O)OEt
1:1	1400	1.9	100	0
1.2:1	2900	1.6	94	6
2:1	6600	1.5	22	78
4:1	5400	1.6	0	100

[a] Second stage reaction conditions: 70 °C, 4.0 mmHg, 40 h. [b] Measured on the basis of ^1H NMR absorptions of ethyl carbonate (−OC(O)O−CH_2CH_3) and hydroxylmethylene terminal moieties.

Consistent with the reaction equation (Scheme 2) and the observed clean carbonate transesterification catalyzed by N435, the molar ratio of dipropyl carbonate vs diethyl carbonate in the product mixture remained near 1:1 during the whole 68 h reaction period (Figure 5). The concentration of ethyl propyl carbonate relative to diethyl carbonate quickly (in 3.5 h) reached its maximum value of 1.9 and remained nearly constant thereafter. On the basis of the concentration ratios ([ethyl propyl carbonate]/[diethyl carbonate] and [dipropyl carbonate]/[diethyl carbonate]) measured, the nominal equilibrium constant K_n was calculated using the following formula:

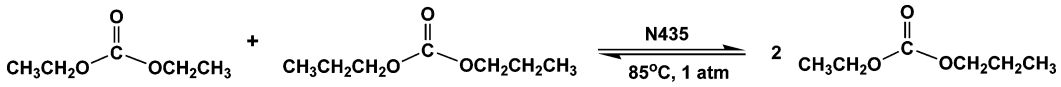
$$K_n = [\text{ethyl propyl carbonate}]^2/([\text{diethyl carbonate}] \times [\text{dipropyl carbonate}])$$

Figure 5 also shows K_n vs reaction time for the transesterification of diethyl carbonate with dipropyl carbonate to form ethyl propyl carbonate. After 3.5 h, K_n increases to and remains at about 3.6, indicating that the reaction reached equilibrium. Thus, K_n becomes the equilibrium constant, K_{eq}, whose value at ≥3.5 h at 85 °C is 3.6.

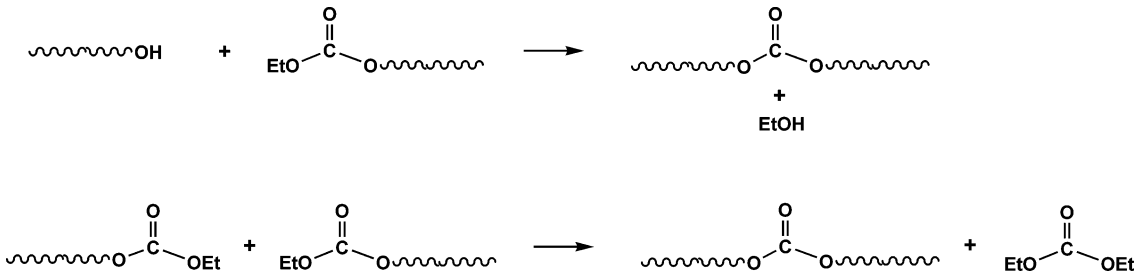
On the basis of the above observations, two types of condensation reactions are proposed as being responsible for chain growth during the copolymerization of diethyl carbonate with diol: (1) reaction between hydroxyl and carbonate end groups and (2) transesterification between two carbonate end groups (Scheme 3).

According to the proposed mechanism, polymers with carbonate−carbonate end groups would continue to participate in chain growth reactions. Hence, use of excess diethyl carbonate relative to diol in the monomer feed should not prohibit the

Scheme 2. Transesterification of Diethyl Carbonate with Dipropyl Carbonate To Form Ethyl Propyl Carbonate



Scheme 3. Proposed Chain Growth Mechanism for Diethyl Carbonate/Diol Copolymerizations



formation of high molecular weight polycarbonates. Indeed, this is consistent with experimental results obtained herein that polycondensation reactions proceed to give high molecular weight PHC by using monomer feed molar ratios of diethyl carbonate to 1,6-hexanediol of both 2:1 and 4:1. The latter case will be discussed in more detail in the following section. The above mechanism is consistent with observations by Matsumura et al.[15] that, in the presence of N435, low molecular weight oligo(trimethylene carbonate) chains with exclusively ethyl carbonate end groups react with each other to form higher molecular weight polymers. However, the authors attributed chain growth of these oligomers to hydrolysis of ethyl carbonate termini. Resulting hydroxyl termini were then believed to react via condensation with ethyl carbonate termini to form chains of higher molecular weight. For such a mechanism to occur, sufficient water in the system would need to be available. Furthermore, hydrolysis reactions would need to occur selectively at chain ends and not randomly along chains. On the basis of the work presented herein, we believe that chain growth observed by Matsumura et al.[15] for ethyl carbonate-terminated oligo(trimethylene carbonate) is due to condensation reactions between ethyl carbonate end groups liberating diethyl carbonate.

Control of PHC Terminal Groups. Hydroxyl-terminated PHC macromers with M_n between 500 and 3000 are widely used in industry as intermediates for producing specialty polyurethane products.[6,9a] Incorporation of carbonate segments was found to enhance polyurethane stability toward hydrolysis. PHC, formed via copolymerization of diethyl carbonate with 1,6-hexandiol, may have various fractions of hydroxyl and ethyl carbonate. Effects of selected reaction variables on PHC end-group structure were investigated. No significant effects of reaction pressure and temperature were observed. An efficient method to regulate PHC end-group structure is by varying the monomer feed ratio. Table 2 summarizes results of experiments where the monomer feed ratio of diethyl carbonate to 1,6-hexanediol was varied from 1:1 to 4:1 (mol/mol). Stage 1 oligomerization reactions were performed at 70 °C, under atmospheric pressure, for 24 h. Subsequently, stage 2 polymerizations were run in bulk at 70 °C and 4.0 mmHg pressure, for 40 h, using 20 wt % N435 (vs diol monomer). Resultant PHC products contained only two types of terminal groups: hydroxyl and ethyl carbonate. The contents of hydroxyl and ethyl carbonate end groups in polymer chains were determined from ^{1}H NMR absorptions. This was accomplished by observing the ethyl carbonate ($-$OC(O)O$-$CH_2CH_3) proton resonances at 4.19 (quartet) and 1.31 (triplet) as well as the resonance at 3.64 (triplet) corresponding to terminal hydroxymethylene ($-$OC(O)O$-$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH_2OH) groups. Parts a and b of Figure 6 display ^{1}H NMR spectra of PHC copolymers with high hydroxyl and ethyl carbonate end-group contents, respectively.

As shown in Table 2, at low (1:1$-$1.2:1) molar ratios of diethyl carbonate to 1,6-hexanediol, PHC consisted of predominantly (94$-$100%) hydroxyl end groups. M_n was between 1000 and 3000 which is useful for applications as macromers,[6,7] and the polydispersity remained below 2.0 (1.6$-$1.9). In contrast, at $\geq$2:1 diethyl carbonate/diol ratio, polymer products consisted predominantly ($\geq$78%) of ethyl carbonate terminal groups. In fact, at 4:1 diethyl carbonate to diol, no hydroxyl terminal groups were detectable by ^{1}H NMR spectroscopy. In other words, by using a 4 to 1 stoichiometry of diethyl carbonate to diol monomers, chain terminal groups were entirely ethyl carbonate moieties. Although similar effects of diethyl carbonate/diol feed ratio on polymer end-group structures were noted by Matsumura et al.[15] during enzyme-catalyzed copolymerization of diethyl carbonate with 1,3-propanediol or 1,4-butanediol, poly(trimethylene carbonate) with 95$-$100% hydroxyl end groups and poly(tetramethylene carbonate) with 95% hydroxyl end groups were isolated in only 3$-$4% and 32% yield, respectively. Similarly, the highest ethyl carbonate end group content reported by enzyme-catalyzed methods was 86% and 60% for poly(trimethylene carbonate) and poly(tetramethylene carbonate), respectively, at corresponding 43% and 60% yield.[15]

Table 2 also shows PHC molecular weight was smaller at low diethyl carbonate/diol feed ratios (i.e., 1:1 and 1.2:1 mol/mol) and increased by increasing this ratio to 2:1 and 4:1. Thus, diethyl carbonate was limiting at low feed ratios, resulting in low molecular weight chains with hydroxyl terminal groups. However, with excess diethyl carbonate, chain growth continues forming higher molecular weight chains. This is consistent with the discussion above that chain growth occurs both by reactions between hydroxyl and ethyl carbonate as well as two terminal ethyl carbonate groups. This enables high molecular weight polymer formation with predominantly ethyl carbonate terminal groups.

Increasing the reaction temperature from 70 to 90 °C had minimal effects on polymer molecular weight at low diethyl carbonate to diol ratios (data not shown). Figure 7 displays PHC M_w and M_w/M_n as a function of reaction time using 1:1 and 2:1 (mol/mol) diethyl carbonate/diol. For both reactions, bulk conditions were used during two stage polycondensations. Stage 1 oligomerizations were carried out at 90 °C, for 16 h, under 600 mmHg pressure, using 20 wt % N435 (vs diol monomer). Subsequently, in the same reaction flask, stage 2 polymerizations were performed at 90 °C, 3.1 mmHg, for 53 h. At 1:1 diethyl carbonate to diol, PHC M_w increased slowly during the initial 24 h and, thereafter, showed no substantial change. For example,

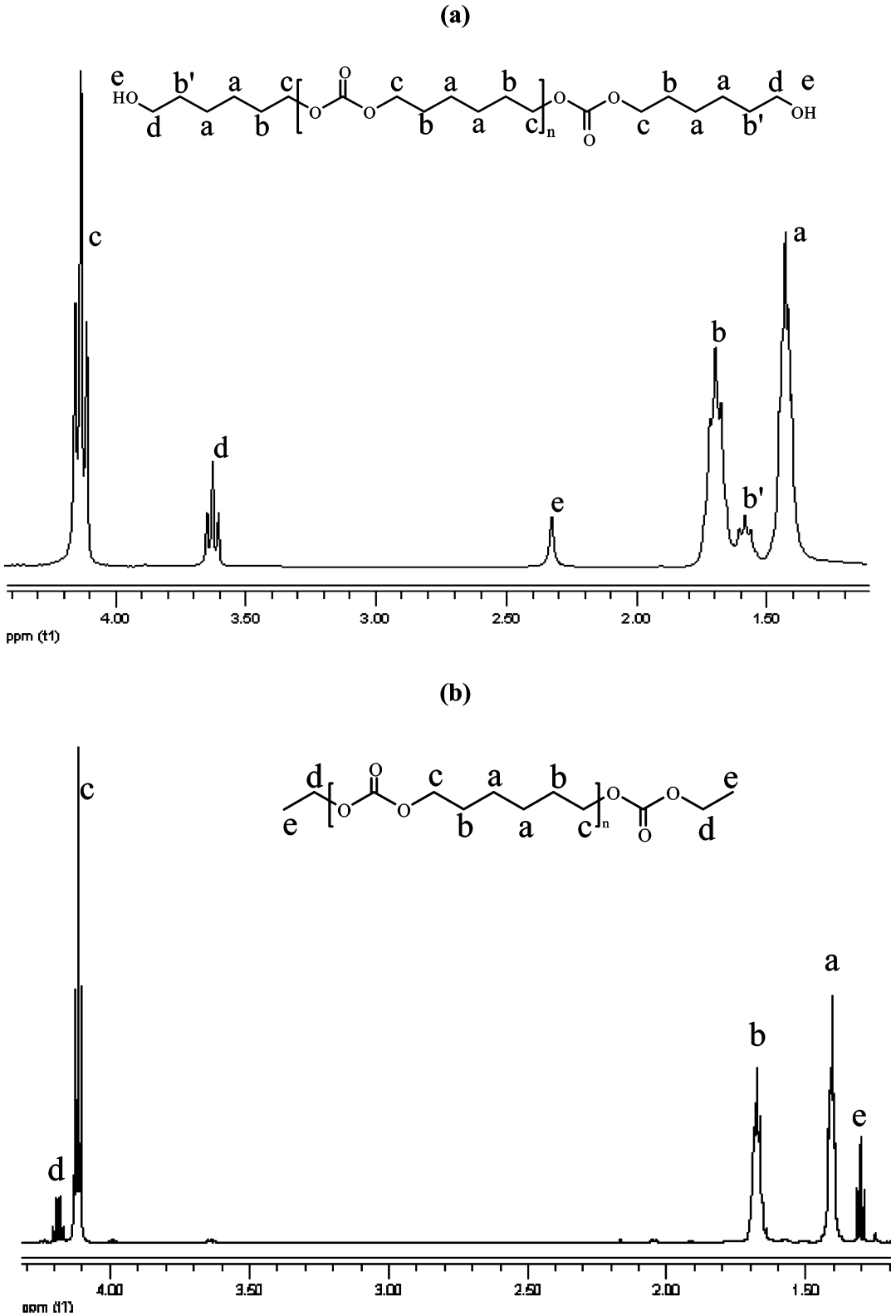


Figure 6. ^{1}H NMR spectra of (a) poly(hexamethylene carbonate) with ~100% hydroxyl end groups and (b) poly(hexamethylene carbonate) with mainly ethyl carbonate termini (solvent: $CDCl_3$).

at 24, 30, and 47 h, the PHC M_w was 2700, 2700, and 3300, respectively. Furthermore, M_w/M_n remained constant at 1.7. Chain end-group structure was also determined by withdrawing aliquots from the reactions at preselected times and recording proton NMR spectra (see Experimental Section). The NMR analysis indicated that, initially (at <24 h), PHC chain ends consisted of both ethyl carbonate and hydroxyl end groups. However, after 24 h, chain end groups were predominantly hydroxyl moieties. Considering the low volatility of 1,6-hexanediol, continuous polycondensation via diol elimination is unlikely under the mild reaction conditions employed herein. Thus, the presence of carbonate end groups is essential for enzymatic polycarbonate synthesis. Hence, once PHC is formed with ~100% hydroxyl end groups, and without addition of an

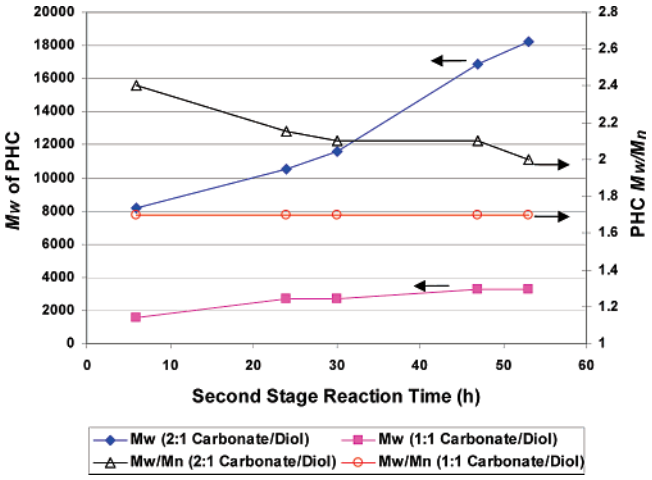


Figure 7. Feed ratio effects on PHC molecular weight (M_w) and polydispersity (M_w/M_n) for copolymerization of diethyl carbonate with 1,6-hexanediol in bulk at 90 °C under 3.1 mmHg pressure.

acyl donor, chain growth will no longer continue. The result is formation of low molecular weight PHC diols using a monomer feed consisting of 1:1 diethyl carbonate to diol.

In contrast, at 2:1 diethyl carbonate to diol, large increases in molecular weight were observed throughout the polymerization. For example, at 24, 30, and 47 h, the polycarbonate M_w was 11 000, 12 000, and 17 000, respectively. As discussed above, for propagation to continue as was observed, a substantial fraction of chain ends must be ethyl carbonate moieties. NMR analysis on the aliquots taken during the course of copolymerization shows that, at 2:1 diethyl carbonate to diol, PHC chains throughout the polymerization had both ethyl carbonate and hydroxyl end groups. Therefore, chains continued to propagate, giving increased molecular weight over prolonged reaction times. Consistent with chain growth is the observation that, by using a 2:1 diethyl carbonate to diol feed, PHC M_w/M_n decreases from 2.4 to 2.0 throughout the course of the second stage polymerization. Similar decrease in M_w/M_n during chain growth was discussed for PHC polymerizations in diphenyl ether at 90 °C (see Figure 3). This trend as above is attributed to that longer reaction times permit low molar mass products to diffuse to catalyst and form products of higher molecular weight, thereby reducing the low molecular weight fraction and decreasing M_w/M_n. At 1:1 diethyl carbonate to diol and at >24 h reaction time, PHC chain ends are exclusively hydroxyl, preventing further events of chain propagation and corresponding decreases in M_w/M_n with prolonged reaction times.

Summary of Results

By using N435 as catalyst, high molecular weight (M_w > 25 000) PHC was successfully synthesized via condensation copolymerization between diethyl carbonate and 1,6-hexanediol in diphenyl ether solution. Enzyme-catalyzed PHC synthesis also took place in bulk reactions but at a reduced polymerization rate. By minimizing water content in the catalyst and reaction mixture, formation of PHC by N435-catalysis occurred with high fidelity of end-group structure, i.e., where end groups consisted of exclusively ethyl carbonate and hydroxyl moieties. Furthermore, by systematic changes in the monomer feed ratio, end-group structure was controlled giving exclusively either ethyl carbonate or hydroxyl terminal groups. PHC is a polymeric material of commercial importance, and hydroxyl-terminated PHC macromers are useful intermediates for the industrial production of hydrolysis-resistant polyurethanes.

Mechanistic studies show that polycondensations between dialkyl carbonates and diols proceed by two pathways: (a) reaction between hydroxyl and carbonate end groups with elimination of alcohol and (b) transesterification between two carbonate end groups with elimination of dialkyl carbonate. The latter is supported by that N435 actively catalyzes transesterification reactions between dialkyl carbonates. The proposed chain growth mechanism also explains why polycarbonates were readily formed under dry conditions when the molar ratio of diethyl carbonate to 1,6-hexanediol is as high as 4:1.

Acknowledgment. The authors thank the National Science Foundation (NSF) and industrial members (BASF, DeGussa, DNA 2.0, Estée Lauder, Genencor, Grace Chem. Co., Grain Processing Corp., and Novozymes) of the NSF-Industry/University Cooperative Research Center (NSF I/UCRC) for Biocatalysis and Bioprocessing of Macromolecules at Polytechnic University for their financial support, intellectual input, and encouragement during the course of this research.

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(17) Note: DSC analysis on the PHC with a M_w of 17 000 and M_n of 11 500 shows that the polymer has a T_m of 57.5 °C and a T_g of 13.5 °C. The bulk copolymerization of diethyl carbonate with 1,6-hexanediol at ≥60 °C proceeded in the molten polymer.

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