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Aliphatic Polycarbonates with Controlled Quantities of D-Xylofuranose in the Main Chain

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ABSTRACT: Polycarbonates were synthesized by ring-opening copolymerizations of trimethylene carbonate (TMC) with 1,2-*O*-isopropylidene-D-xylofuranose-3,5-cyclic carbonate (IPXTC). Subsequent deprotection of the ketal protecting groups gave controlled quantities of vicinal diol pendant groups. Studies of TMC/IPXTC copolymerization showed that MAO and $ZnEt_2-0.5H_2O$ were the preferred catalysts. The reactivity ratios measured by the Fineman−Ross method and using $ZnEt_2-0.5H_2O$ as the catalyst were 0.31 and 0.20 for IPXTC and TMC, respectively. Hence, even though IPXTC has bulky substituents, IPXTC was more reactive than TMC early in the copolymerization. Consistent with the above, the average IPXTC chain segment length was longer early in the copolymerization but decreased with increased conversion. ^1H and ^{13}C NMR were used to analyze the repeat unit sequence distribution of copolymers. For copolymers with high IPXTC contents, three types of IPXTC linkages were found: head−head, tail−tail, and head−tail. The protecting ketal groups were removed by CF_3COOH/H_2O to give a novel polycarbonate with hydroxyl pendant groups. Longer deprotection times led to higher extents of deprotection but lower molecular weight. Studies by differential scanning calorimeter (DSC) showed that copolymers having from 8 to 83% IPXTC were all amorphous. In addition, a physical aging transition was apparent. The T_g of the copolymer increased with increasing IPXTC copolymer content. Furthermore, the experimental T_g values were in good agreement with that calculated by the Fox equation. After deprotection, the copolymer T_g decreased, which is consistent with the loss of the bulky ketal side group.

Introduction

Aliphatic polycarbonates prepared by the ring-opening polymerization (ROP) of cyclic carbonate monomers have been of considerable interest as bioresorbable materials for medical applications.[1−7] To meet the wide spectrum of requirements for biomedical materials, it is critical that the properties of these materials may be specifically “tailored”. Important considerations are the material physicomechanical properties, degradation mechanism, and rate as well as thermal processability. The introduction of controlled levels of functional groups along the chains of biocompatible materials is important for a number of reasons. For example, carboxylic acid side chains can be used to regulate the rate at which main chain ester linkages are hydrolyzed.[8−10] The decoration of polymer chains with appropriate structures facilitates the attachment of bioactive molecules. Such work is highly relevant to many tissue engineering applications.[11−15] For example, very small concentrations of active peptides can have dramatic biological effects. A surface density of only 1 fmol/cm^2 of an RGD (arginine−glycine−aspartic acid tripeptide) peptide effectively promotes cell adhesion to an otherwise nonadherent surface.[15] Therefore, a copolymer of poly(lactic acid-*co*-lysine) with RGD attached to the lysine residues at a surface concentration of 310 fmol/cm^2 was expected to greatly promote cell adhesion.[11] In addition, pendant functional groups can be used to facilitate chain cross-linking and formation of comblike grafts for further functionalization as well as for use as interfacial materials.

It is noteworthy that the literature gives examples that describe the use of Zn-, Al-, and Sn-based organometallic catalysts,[16−22] anionic initiators,[23,24] lanthanide catalysts,[25] and enzyme catalysts[26,27] that have proved useful for cyclic carbonate ring-opening polymerizations.

Recently, polycarbonates with functional side chain groups have been synthesized. For example, polycarbonates with vinyl[20,28,29] and hydroxyl[30−32] pendant groups have been described. Studies in the literature on the in vivo and in vitro degradability of polycarbonates have shown that by incorporation of hydroxyl moieties in the side chains it was possible to greatly accelerate chain hydrolytic degradability. For example, poly(ethylene carbonate) was not substantially degraded during an in vitro study in phosphate-buffered saline at pH 7.4. It is noteworthy that the same polymer, when placed in the rat peritoneal cavity, underwent rapid enzyme-catalyzed in vivo biodegradation that was nearly complete within 2−3 weeks.[6] In contrast to poly(ethylene carbonate), poly(hydroxymethylethylene carbonate), which has hydroxyl pendant groups, underwent rapid autodegradation into hydroxymethylethylene carbonate five-membered ring products.[33] Similarly, the in vitro degradation of PTMC in pH 7.4 buffer (30 weeks, 37 °C) resulted in only 9% weight loss and a 7% decrease in molecular weight.[34] In contrast, water-soluble poly(hydroxyalkylene carbonate)s undergo rapid degradation in neutral water. The mechanism of degradation was said to involve intramolecular nucleophilic attack by the pendant hydroxyl groups on the carbonate main chain linkages.[32] Hence, it appears that the introduction of hydroxyl groups into aliphatic polycarbonates is a useful strategy for the regulation of bioerosion rate. Such control is of great importance to the utility of aliphatic polycarbonates in medical and pharmaceutical applications.[32]

In our group, we have initiated a program to synthesize polyesters and polycarbonates of medical importance. To this end, research has been directed at the

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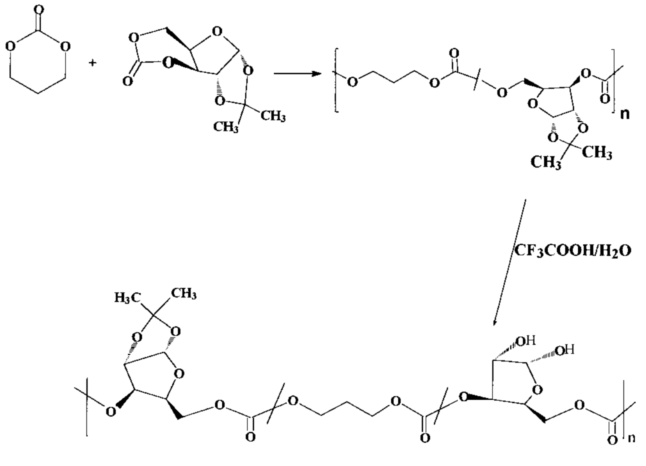
Scheme 1. Preparation of Hydroxyl-Functionalized Polycarbonate by Ring-Opening Copolymerization and Successive Deprotection



decoration of bioresorbable chains with various functional handles. The goal of these activities is to provide a flexible platform for the anchoring of bioactive groups and/or to regulate the bioresorption rate, processibility, and physicomechanical performance. Recently, our work has focused on the preparation and copolymerization of cyclic carbonates bearing different functional groups. For example, high molecular weight polycarbonates bearing vinyl pendant groups were prepared by the polymerization of 4,4-cyclohexene-1,3-trimethylene carbonate.[20] The vinyl pendant groups were partially or completely converted into epoxides by oxidation with chloroperoxybenzoic acid.[20] Random copolymerizations of 2,4,8,10-tetraoxaspiro[5,5]undecane-3-one introduced protected hydroxyl groups to polycarbonates.[21] However, these protecting groups proved to be difficult to remove without substantial chain cleavage.[21] Recently, we found a versatile and easily prepared monomer, isopropylidene-D-xylofuranose-3,5-cyclic carbonate (IPXTC), which is a nontoxic sugar derivative.[35] It was copolymerized with lactide in various molar proportions to give a wide range of hydroxyl-bearing polylactide-based materials.[35] In this paper, we report the synthesis and characterization of hydroxyl-functionalized poly(trimethylene carbonate) by the ring-opening copolymerization of trimethylene carbonate with IPXTC and subsequent deprotection (Scheme 1).

Experimental Section

The catalysts $AlEt_3$, $Al^{i}Bu_3$, $ZnEt_2$, and $Sn(Oct)_2$ were from Aldrich; methylaluminoxane (MAO, 2.03 M in heptane) and isobutylaluminoxane (IBAO, 0.95 M in heptane) solutions were from Akzo Chemical Inc. These catalysts were used as received. Toluene was dried by distillation from melted sodium. All liquid reagents were transferred by syringe under a dry argon or nitrogen atmosphere. 1,2-*O*-Isopropylidene-D-xylofuranose (99%) was purchased from Aldrich and used as received.

Monomer Synthesis. Trimethylene carbonate (TMC) was synthesized by the method reported by Ariga et al. [36] The crude product was washed and recrystallized from dry ether. 1,2-*O*-Isopropylidene-D-xylofuranose-3,5-cyclic carbonate (IPXTC) was prepared by the identical procedure as was described previously for 2,2-[2-heptene-1,5-diyl]trimethylene carbonate (^{c}HTC) synthesis.[20,35]

Preparation of Catalysts. The catalysts AlR_3-H_2O (1:0.5) and $ZnEt_2-H_2O$ (1:0.5) were prepared exactly as was described elsewhere.[20-22,35] Solutions (1 mol/L) of $Sn(Oct)_2$ were prepared in dry toluene.

General Procedure for the Copolymerization. The polymerization ampules (10 mL) were heated at 120 °C, treated with trimethylsilyl chloride, washed with three portions of methanol, dried at 120 °C in an oven, and flame-dried while purging with dried argon. Monomers were transferred into the ampule using a glovebox to maintain an inert nitrogen atmosphere. The ampule was degassed by several vacuum-purge cycles, and then the catalyst solution was introduced by syringe to the ampule. The ampule was sealed under argon and placed in an oil bath for a predetermined reaction time. After the polymerization, chloroform (10 mL) was added to the ampule to dissolve the contents of the ampule and methanol (5 mL) containing 5% (w/w) HCl to dissolve the catalyst residue. And then, all the contents in the ampule were poured into 200 mL of methanol to precipitate the polymer. The precipitate was washed with several portions of methanol, and then the volatiles were removed in a vacuum oven (<3 mmHg, 40 °C, 24 h).

Instrumental Methods. *Fourier Transform Infrared (FTIR) Spectroscopy.* A P-E 1720 FTIR spectrometer was used to obtain the spectra after 16 scans ($2\ cm^{-1}$ resolution) over the range from 4000 to $400\ cm^{-1}$. Samples were analyzed as films cast from chloroform solutions on KBr plates.

Nuclear Magnetic Resonance (NMR) Spectroscopy. Proton (^{1}H) NMR spectra were recorded on a Bruker ARX-250 spectrometer at 250 MHz or a Bruker DRX-500 spectrometer at 500 MHz. ^{1}H NMR chemical shifts in parts per million (ppm) are reported downfield from 0.00 ppm using tetramethylsilane (TMS) as an internal reference. The concentration used was 4% w/v in chloroform-*d*. For the highly deprotected copolymers, deuterated *N*,*N*-dimethylformide was used as solvent. The instrumental parameters were exactly as was described elsewhere.[22] Carbon-13 (^{13}C) spectra were recorded at 62.5 MHz on a Bruker ARX-250 spectrometer in 20% w/v chloroform-*d* solutions. The chemical shifts in ppm were referenced relative to the internal standard $CDCl_3$ at 77.00 ppm. The acquisition parameters used were described in detail elsewhere.[22]

Molecular Weight Measurements. Number- and weight-average molecular weights (M_n and M_w, respectively) were determined by gel permeation chromatography (GPC). The experimental details of the method are published elsewhere.[21,22] Polystyrene standards with a low dispersity (Polysciences) were used to generate a calibration curve. Data were recorded and manipulated using the Windows based Millenium 2.0 software package.

Thermal Analysis. Differential scanning calorimetry (DSC) studies were conducted on a DuPont DSC 912 equipped with a TA 2000 data station. Results of the peak melting temperature (T_m), the physical aging transition temperature (T_p), and the enthalpy of physical aging (ΔH_p) were reported as in first heating of methanol-precipitated sample. The physical aging transition temperature was taken from the temperature at the transition peak. After first heating, the samples were rapidly quenched with liquid nitrogen to −60 °C. Subsequently, they were scanned again at 10 °C/min from room temperature to 200 °C. Data reported for the glass transition temperatures (T_g) were taken in the second heating of these two scans from the midpoint of the transition.

Powder X-ray Analysis. Wide-angle X-ray scattering (WAXS) was performed on a Philips vertical diffractometer with Bragg−Brentano geometry and graphite diffracted beam monochromator at 40 kV/20 mA and Cu Kα radiation (1.5405 Å). A scanning speed of 2°/ min with a sample interval of 0.05° was used.

Ketal Deprotection. Copolymer (1.0 g) was dissolved in 10 mL of CH_2Cl_2. To this solution was added 10 mL of CF_3COOH containing 2 mL of distilled H_2O. After stirring at room temperature for a predetermined time, the resulting solution was poured into 100 mL of methanol. The polymer was separated by filtration, washed, and dried in a vacuum to constant weight.

Results and Discussion

Copolymerization of TMC and IPXTC. It has been demonstrated that Al-based organometallics and $Sn(Oct)_2$

Table 1. Evaluation of Different Catalysts for TMC−IPXTC Copolymerizations[a]

entry	catalyst[b]	yield %[c]	M_n[d] (g/mol)	M_w/M_n[d]	F_{TMC}/F_{IPXTC}[e]	L_{TMC}/L_{IPXTC}[f]
1	$AlEt_3-H_2O$ (1/0.5)	51	11 400	1.5	77/23	
2	$Al^iBu_3-H_2O$ (1/0.5)	52	10 300	1.5	78/22	
3	$ZnEt_2-H_2O$ (1/0.5)	95	14 700	2.3	71/29	2.82/1.11
4	MAO	92	21 700	2.1	71/29	2.28/1.04
5	IBAO	88	18 500	2.1	68/32	2.32/1.06
6	$Sn(Oct)_2$	6	3 530	1.1	n.d.	

[a] 90 °C, (TMC + IPXTC)/cat. = 200 (molar), 22 h, f_{TMC}/f_{IPXTC} = 68/32 (molar). [b] MAO = methylaluminoxane; IBAO = isobutylaluminoxane. [c] Methanol-insoluble copolymer (g)/monomer feed (g) × 100%. [d] Number average molecular weight and molecular weight distribution determined by GPC (see Experimental Section). [e] Copolymer molar composition measured by ^1H NMR. [f] The average IPXTC and TMC repeat unit lengths determined by ^{13}C NMR.

Table 2. Copolymerization of TMC with IPXTC Catalyzed by $ZnEt_2$-H_2O(1/0.5)At Different Feed Ratios[a]

entry	f_{TMC}/f_{IPXTC}[b]	yield (%)[c]	M_n[d] (g/mol)	M_w/M_n[d]	F_{TMC}/F_{IPXTC}[e]
1	0/100	1.4	n.d.	1.5	0/100
2	10/90	45	5 230	1.8	17/83
3	30/70	69	6 470	2.3	38/62
4	50/50	95	15 700	2.2	54/46
5	68/32	95	14 700	2.3	71/29
6	90/10	95	16 500	2.2	92/8
7	100/0	91	16 900	2.5	100/0

[a] $ZnEt_2-H_2O$ (1/0.5), (TMC + IPXTC)/Zn = 200 (molar), 90 °C, 22 h. [b] Monomer feed ratio in mol/mol. [c−e] These footnotes are identical to those described in Table 1.

Table 3. TMC−IPXTC Copolymerization by MAO at Different Monomer Feed Ratio[a]

entry	f_{TMC}/f_{IPXTC}	polym time (h)	yield (%)[c]	M_n (g/mol)[d]	M_w/M_n[d]	F_{TMC}/F_{IPXTC}[e]
1	10/90	22	39	5000	1.5	19/81
2	30/70	22	64	4160	2.8	40/60
3	50/50	22	75	20600	2.7	57/43
4	70/30	2	95	20900	2.5	71/29
5	90/10	2	98	35000	2.1	93/7
6	100/0	2	98	52000	2.2	100/0

[a] 90 °C, (TMC + IPXTC)/Al = 200 (molar). [b] Monomer feed ratio in mol/mol. [c−e] These footnotes are identical to those described in Table 1.

Table 4. TMC−IPXTC Copolymerization Catalyzed by MAO at Different Times

entry	time (h)	TMC[c] % conv	IPXTC[c] % conv	overall[b] % yield	M_n[d] (g/mol)	M_w/M_n[d]	F_{TMC}/F_{IPXTC}[e]
1	0.5	38.7	67.3	53	8 900	1.9	55/45
2	1.0	65.8	82.2	74	15 000	2.3	63/37
3	1.5	88	85.2	86	18 000	2.1	69/31
4	2.0	96	96	96	22 000	2.1	68/32
5	22			92	21 700	2.1	71/29

[a] 90 °C, (TMC + IPXTC)/Al = 200, f_{TMC}/f_{IPXTC} = 68/32 (molar). [b] The overall % yield was determined as follows: insoluble copolymer (g)/monomer feed (g) × 100%. [c] The % conversion of TMC and IPXTC was determined by spectral integration of ^1H NMR recorded on the isolated products. [d,e] These footnotes are identical to those described in Table 1.

are effective catalysts for the ring-opening polymerization of cyclic carbonates and lactides.[20−22] Therefore, alkyl aluminum−water, $ZnEt_2-H_2O$, MAO, and IBAO systems were tested as the catalysts for the ring-opening copolymerization of TMC and IPXTC. The molar feed ratio of TMC to IPXTC, polymerization temperature, and reaction time were fixed at 68/32, 90 °C, and 22 h, respectively. The results listed in Table 1 show that $Sn(Oct)_2$ had poor activity for the copolymerization. The alkyl aluminum−H_2O (1/0.5) systems showed only modest activity. The most promising results were obtained by using the $ZnEt_2-H_2O$, MAO, and IBAO catalysts. For example, with the MAO catalyst, the percent yield was 92 after 22 h and the copolymer M_n was 21 700 g/mol.

Tables 2 and 3 show the results of TMC/IPXTC copolymerizations where the monomer feed was varied, and the catalysts were $ZnEt_2-0.5H_2O$ and MAO, respectively. When the IPXTC content for both of these catalysts was increased from 50 to 70 mol %, the resulting copolymer M_n and/or percent yield values decreased substantially. Inspection of entries 1 of Tables 2 and 3 shows that the homopolymerization of IPXTC under the present reaction conditions was sluggish. A similar detrimental effect of bulky substituents was found for the polymerizations of the cyclic carbonates, 2-methyl-2-phenyltrimethylene carbonate,[37] 2,2-diphenyltrimethylene carbonate,[37] and 5,5-(bicyclo[2,2,1]-hept-2-en-5,5-diylidene)-1,3-dioxan-2-one.[28] These results indicate that the bulky IPXTC substituent makes it difficult to form IPXTC−IPXTC diads along the copolymer chains. However, further study of Tables 2 and 3 shows that there is good agreement between the monomer feed and polymer compositions. These results are consistent with the facile formation of IPXTC−TMC and TMC−IPXTC diads that is further elaborated below. When the polymerization time was reduced to 2 h, high copolymer molecular weights and conversions were achieved for MAO-catalyzed TMC/IPXTC copolymerizations with ≥70 mol % TMC in the monomer feed (Table 3). This result inspired further studies on the influence of reaction time on TMC/IPXTC copolymerizations catalyzed by $ZnEt_2-0.5H_2O$ and MAO.

The effect of reaction time was evaluated by fixing the TMC/IPXTC feed ratio at 68/32, the reaction temperature at 90 °C, and the monomer/catalyst molar ratio at 200. For the MAO-catalyzed polymerizations (Table 4), the M_n and conversion increased regularly with an increase in the reaction time from 0.5 to 2.0 h. A similar study using $ZnEt_2-0.5H_2O$ as the catalyst was also conducted. A large increase in the percent yield and M_n was observed from 0.5 to 1 h (Table 5). Extending the reaction time to 2 h was sufficient to reach a 96% yield. Surprisingly, at early stages of the polymerizations, the content of IPXTC in the product was greater than that in the monomer feed but not larger than 46 mol % of repeat units (see entries 1 of Tables 4 and 5). Extending the polymerization time from 4 to 22 h when using the $ZnEt_2-0.5H_2O$ catalyst resulted in apparent chain cleavage (see entries 4 and 5, Table 5). In contrast, extending the reaction time using the MAO catalyst did not cause any noticeable chain degradation (see entries 4 and 5, Table 4).

Structural Characterization. Figure 1 shows the ^1H and ^{13}C NMR spectra of the copolymer of poly(TMC-*co*-23 mol % IPXTC) that was prepared by using $ZnEt_2-0.5H_2O$ as the catalyst. Assignments of the prominent ^1H and ^{13}C NMR signals in Figure 1 were made based on our previous studies of [L]-LA/IPXTC copolymers,[35] IPXTC homopolymerization,[38] and spectra of TMC homopolymer.[18,34] The ^1H NMR signals of IPXTC repeat units are at 4.35 ppm (H1), 4.50 ppm (H2), 5.11 ppm (H3), 4.63 ppm (H4), 5.96 ppm (H5), and 1.31 and 1.51 ppm (H6,7); the signals corresponding to TMC units are at 4.25 ppm ($OC(O)OCH_2CH_2$, H10) and 2.05 ppm

Table 5. Effect of the Reaction Time on the TMC−IPXTC Copolymerization Using $ZnEt_2$−$0.5H_2O$ Catalyst[a]

entry	time (h)	TMC % conv[c]	IPXTC % conv[c]	overall % yield[b]	M_n[d] (g/mol)	M_w/M_n[d]	F_{TMC}/F_{IPXTC}[e]	L_{TMC}/L_{IPXTC}
1	0.5	28	50	39	10 900	1.8	54/46	1.38/1.44
2	1	76	90	83	17 300	2.0	64/36	2.35/1.35
3	2	96	96	96	18 200	2.0	68/32	2.41/1.17
4	4	98	98	98	19 300	2.0	68/32	2.28/1.04
5	22			95	14 700	2.2	71/29	2.72/1.05

[a] $ZnEt_2$−H_2O (1/0.5), (TMC + IPXTC)/Zn = 200, 90 °C, f_{TMC}/f_{IPXTC} = 68/32 (molar). [b] The overall % yield was determined as follows: insoluble copolymer (g)/monomer feed (g) × 100%. [c] The % conversion of TMC and IPXTC was determined by spectral integration of ^1H NMR recorded on the isolated products. [d−f] These footnotes are identical to those described in Table 1.

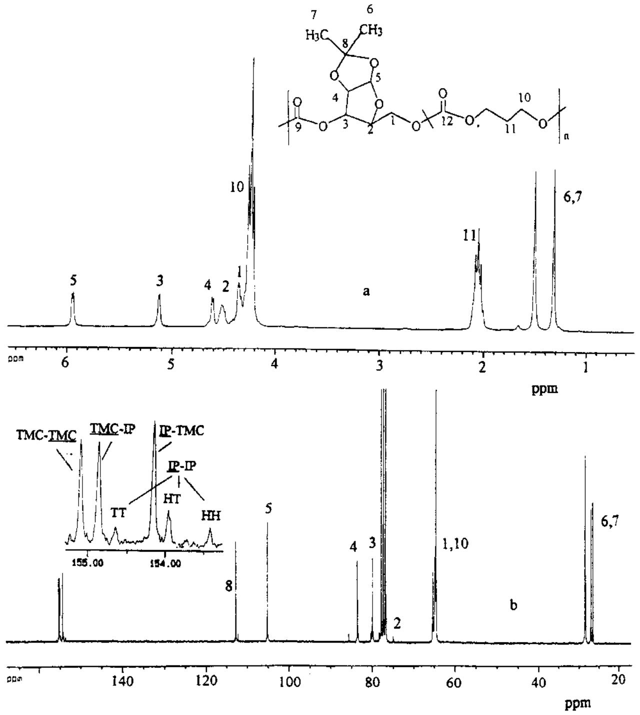
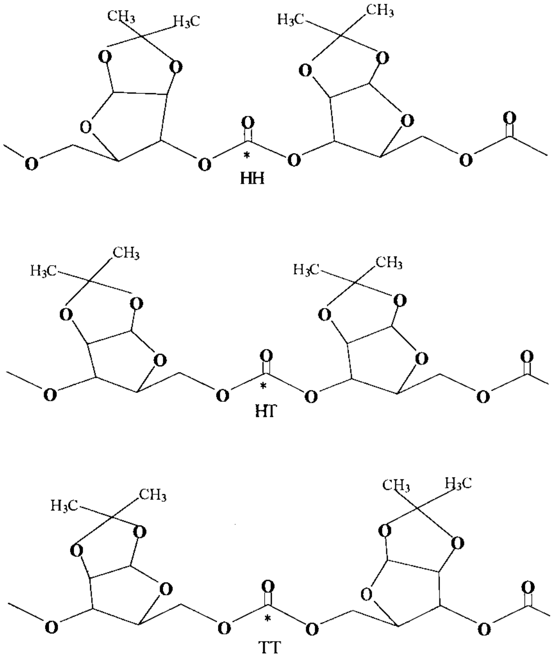


Figure 1. ^1H (a) and ^{13}C NMR (b) spectra of poly(TMC-*co*-23 mol % IPXTC) prepared by $ZnEt_2$−$0.5H_2O$ as catalyst, 90 °C, M/C = 200.

($OC(O)OCH_2CH_2CH_2$, H11). Different chain linkages or directionality effects (see below) may in part explain the complex nature of H1 to H4 signals. In the ^{13}C NMR spectra of the copolymer, signals at 65.05/64.67 ppm (C1), 76.36 ppm (C2, overlapped with the signal of $CDCl_3$), 80.27/80.04 ppm (C3), 83.24/83.13 ppm (C4), 104.97 ppm (C5), 26.85/26.38 ppm (C6,7), and 112.69/112.79 ppm (C8) were due to IPXTC unit carbons. The signals at 28.12/28.22 ppm ($OC(O)OCH_2CH_2CH_2$, C11), and ca. 64.3 ppm (multiplet) ($OC(O)OCH_2CH_2$, C10), which were not resolved from those of IPXTC units, were due to TMC repeat units.

An expansion of the ^{13}C NMR spectrum carbonyl region of poly(TMC-*co*-23 mol % IPXTC) is shown in Figure 1b. The carbonyl carbons of TMC repeat units are at 155.30 and 154.94 ppm. The former occurs at the same chemical shift as the carbonyl signal in the PTMC homopolymer. Hence, the signal at 155.30 was assigned to *C═O of *TMC*−TMC sequences. The other signal at 154.94 ppm was then assigned to TMC units in *TMC*−IPXTC sequences. The upfield signals at 154.62, 153.96, and 153.43 ppm are at the same positions as chemical shifts in the carbonyl region of the IPXTC homopolymer. In addition, the intensity of these signals increased or decreased, corresponding to an increase or decrease in the IPXTC content of the copolymer. Therefore, these three signals were assigned to the *C═O of IPXTC−IPXTC (*IP*−IP) diad sequences that are linked tail−tail (TT), head−tail (HT), and head−head (HH), respectively (see Scheme 2 and Figure 1b).[38] The remaining signal at 154.16 ppm was assigned to the *C═O of IPXTC linked to TMC (*IP*−TMC) units. These assignments were further confirmed by comparison to the shift positions that were calculated with ACD/CNMR software (Version 1.0 for Microsoft Windows, Bruker Inc.).

Scheme 2. The Three Kinds of Linkages of IPXTC−IPXTC Units



The average IPXTC and TMC repeat unit lengths can be calculated by eqs 1 and 2, respectively, where *I* is the peak intensity for the diad given as a subscript. The results of these analyses are given as part of Tables 1 and 5.

$$L_{IPXTC} = [I_{IP-IP}(I_{154.62ppm} + I_{153.96ppm} + I_{153.43ppm}) + I_{IP-TMC}(I_{154.16ppm})]/I_{IP-TMC}(I_{154.16\ ppm}) \quad (1)$$

$$L_{TMC} = [I_{TMC-TMC}(I_{155.30ppm}) + I_{TMC-IP}(I_{154.94ppm})]/I_{TMC-IP}(I_{154.94ppm}) \quad (2)$$

Alternating Character of the Copolymers. To determine the reactivity ratios of LA and IPXTC, the compositions of copolymers were determined as a function of the comonomer feed ratio for polymerizations that did not exceed 10% conversion. The reactivity ratios of TMC and IPXTC determined by the method of Fineman−Ross[39] were 0.20 and 0.31, respectively, when using $ZnEt_2$−$0.5H_2O$ as the catalyst, at 90 °C and M/C = 200. This was very different than the results of

IPXTC/[L]-LA copolymerizations in which a wide range of Al-, Zn-, and Sn-based catalysts had a much lower reactivity for IPXTC than [L]-LA.[35] The unexpectedly high reactivity of IPXTC relative to TMC found herein is peculiar. One explanation is that IPXTC may bind with higher affinity than TMC to the organometallic active site. Studies of ring strain as well as monomer−catalyst binding will hopefully provide greater insight into this subject in future work.

The average IPXTC (L_{IPXTC}) and TMC (L_{TMC}) chain segment lengths were determined by ^{13}C NMR (see above). This work was conducted for copolymers produced by the Al- and Zn-based catalysts (see Tables 1 and 5). In all of theses cases, the monomer feed ratio (TMC:IPXTC) was fixed at 68/32 and the polymerization temperature was 90 °C. Observation of Tables 1 and 5 shows that L_{IPXTC} for the copolymers prepared using MAO, IBAO, and $ZnEt_2-0.5H_2O$ as the catalysts were close in value to 1.0. This is consistent with the discussion above that the kinetics of formation of IPXTC−IPXTC diads is relatively slow. In addition, this agrees with the $r_1 \cdot r_2$ values of reactivity ratios reported above ($r_1 \cdot r_2 = 0$ for an ideal alternating copolymerization). Hence, a propagating chain end containing an IPXTC unit at the terminus will tend to add a TMC repeat unit. Also, the reactivity ratio values using $ZnEt_2-0.5H_2O$ as the catalyst shows that a propagating chain end containing a TMC unit at the terminus will tend to add an IPXTC unit. In other words, this work has led to TMC/IPXTC copolymers that have a tendency toward an alternating copolymer microstructure. If the tendency toward an alternating copolymer is of kinetic origin, it may be that the IPXTC monomer binds with greater affinity than TMC at the active site. However, steric hindrance may make it unfavorable to form homodiads. Similar arguments of binding affinity and steric constraints could also be used to explain an alternating tendency that is of thermodynamic origin. It is noteworthy to mention that prolonged polymerization resulted in a decrease in the average IPXTC segment length. This is likely due to transesterification type reactions.

Preparation of Hydroxyl-Functionalized Polycarbonate by Deprotection. An important objective of this work was to transform the ketal-protected functionalities along the chain to vicinal diol groups (Scheme 1). Preliminary experiments for this purpose showed that CF_3COOH/H_2O in CH_2Cl_2 was the preferred deprotection system. Studies using BCl_3 for deprotection were not successful due to extensive chain scission that occurred concomitantly with ketal hydrolysis. Other investigations using $FeCl_3$ and $PdCl_2$ showed that these catalysts were useful for deprotection but were difficult to remove from the deprotected product.

Figure 2 shows the ^1H NMR spectrum of the copolymer (37 mol % IPXTC) that was deprotected by using CF_3COOH/H_2O in CH_2Cl_2 at room temperature (see Experimental Section). In this case, the extent of deprotection was 47 mol %. In other words, 47% of the IPXTC repeat units were converted to the corresponding vicinal diol. Deprotection results in a new ^1H NMR signal corresponding to H5′ at 5.50 ppm (Figure 2). The relative integration values of the signals at 5.96 and 5.50 ppm were used to determine the mole percent of deprotection.

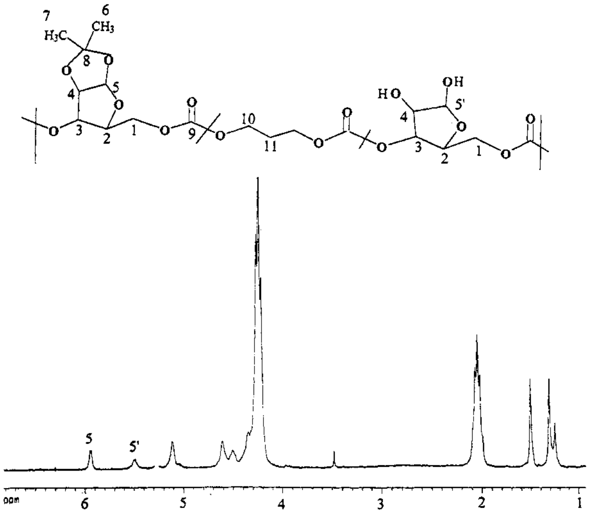


Figure 2. ^1H NMR spectrum of deprotected copolymer (entry 2, Table 5).

The effect of different reaction times using CF_3COOH/H_2O on the extent of copolymer deprotection is shown in Table 6. High extents of deprotection were reached (95%) by extending the reaction to 20 min. The fractional molecular weight change resulting from the time of the deprotection reaction was determined by using values of M_n/M_n^0 where M_n^0 is the molecular weight of the starting copolymer. Values of M_n/M_n^0 for reaction times of 5, 10, and 20 min are 0.96, 0.86, and 0.76, respectively (see Table 6). Therefore, to obtain extents of deprotection less than ~50 mol %, there was little or no apparent chain cleavage. It should be noted that the molecular weights were determined relative to polystyrene so that changes in the hydrodynamic volume were not taken into account. In addition, at present we cannot exclude the possibility that interchain cross-linking reactions occur at a low but substantial frequency. As the extent of deprotection increased, copolymer solubility in chloroform and dichloroethane decreased. For example, poly(TMC-*co*-29% IPXTC) that was 95% deprotected was soluble in *N*,*N*-dimethylformamide but not chloroform. The observed shift in solubility is consistent with changes in the polarity of the deprotected product.

Thermal Properties. Differential scanning calorimetry (DSC) was used to study the thermal properties of TMC−IPXTC copolymers both prior to and after deprotection, and the results are shown in Tables 6 and 7, respectively. The extremes of the T_g range for TMC−IPXTC copolymers are defined by the values of the respective homopolymers. Study of the second heating scans showed that TMC and IPXTC homopolymers have T_g values of −13 °C (literature ref 34, −12 °C) and 128 °C, respectively. Comparison of the experimental and calculated (Fox equation) T_g values showed that they were in excellent agreement over the full range of copolymers studied (Table 7). This is consistent with a copolymer microstructure that tends toward alternating. It is also noteworthy that all of the thermograms for entries 1−7 of Table 7 showed only one T_g.

Inspection of the first heating scan of the IPXTC homopolymer[38] as well as poly(TMC-*co*-IPXTC) with IPXTC contents ≥23% showed prominent endotherm peaks that were not resolved from T_g transitions. Studies described elsewhere[38] have shown that the IPXTC homopolymer is semicrystalline. The WAXS patterns (not shown) on the copolymer samples in Table 7 showed in each case only an amorphous halo (no crystalline reflections). In addition, work by Zhu et al.[34]

Table 6. Deprotection of Poly(TMC-*co*-29% IPXTC)

entry	deprotection[a] time (min)	deprotection[a] degree (%)	M_n[b] (g/mol)	M_n/M_n^0[c]	M_w/M_n[b]	T_p[d] (°C)[a]	ΔH_p[e] (J/g)[b]	T_g[f] (°C)
1	0	0	21 700	1.0	2.1	46	3.5	38
2	5	47.6	20 900	0.96	1.8	41	3.4	34
3	10	85.4	18 600	0.86	1.7	38	3.4	31
4	20	95.2	16 600	0.76	1.6	35	2.4	28

[a] Deprotection conditions: $CH_2Cl_2/CF_3COOH/H_2O$, room temperature, for additional details see the Experimental Section. [b] See footnote *d* of Table 1. [c] The fractional molecular weight change where M_n^0 is the molecular weight of the starting copolymer. [d] Physical aging transition temperature. [e] Enthalpy of the physical aging transition. [f] Glass transition temperature.

Table 7. Thermal Properties of TMC−IPXTC Copolymers[a] That Differ in Composition[a]

entry	F_{TMC}/F_{IPXTC}[b]	T_p (°C)[c]	ΔH_p (J/g)[d]	T_g (°C)$_{calcd}$[f]	T_g (°C)[e]
1	0/100				128
2	17/83	115	6.5	108	109
3	38/62	88	10.0	83	82
4	54/46	62	3.4	60	62
5	71/29	40	6.3	35	37
6	77/23	32	0.9	25	28
7	92/8			1	3
8	100/0				−13

[a] The copolymers were synthesized using $ZnEt_2-H_2O$ (1/0.5), (TMC + IPXTC)/Zn = 200, 90 °C, 22 h. [b] See Table 1, footnote *e*. [c−e] Explanations were given previously in Table 6, footnotes *d*, *e*, and *f*, respectively. [f] Calculated by Fox equation using the compositions determined by ^1H NMR.

showed that high molecular weight PTMC was difficult to crystallize. Interestingly, the average IPXTC segment lengths of poly(TMC-*co*-IPXTC) with 83 and 62 mol % IPXTC were only 4.86 and 2.53, respectively. For copolymers with ≤32 mol % IPXTC units, the average IPXTC segment length is near 1.0 (see above). Hence, it is understandable that the IPXTC components of the copolymers did not crystallize. It was concluded that the endothermic peaks near T_g transitions in the first heating scans correspond to physical aging rather than melting (Table 7). The physical aging transition temperature decreased with decreasing mol % IPXTC in the copolymers (Table 7). The enthalpy of this transition (ΔH_p) varied irregularly from about 6 to 10 J/g for copolymer compositions ranging from 29 to 83 mol % IPXTC. At low IPXTC copolymer content (≤8 mol %, Table 7), the physical aging transition was not observed.

The DSC thermograms of the deprotected copolymers were very similar to those of the corresponding protected copolymers. In the first DSC scans, the deprotected copolymers showed prominent physical aging transitions (see Table 6). It is interesting to consider whether the T_g will increase or decrease with higher extents of IPXTC deprotection. Taking steric bulk as an independent parameter, the removal of the ketal group would cause the T_g to decrease. However, the transition of the ketal to a vicinal diol may introduce effects of hydrogen bonding that might increase the T_g. Observation of Table 6 shows that, by increasing the extent of deprotection from 0 to 95.2% for poly(TMC-*co*-29% IPXTC), the T_g decreased from 38 to 29 °C. Future work will look closely into the nature of hydrogen bonding in deprotected poly(TMC-*co*-IPXTC) copolymers.

Conclusion

Copolymerizations of TMC with IPXTC gave products that tended toward a alternating copolymer microstructure. DSC and WAXS experiments showed that the copolymers of IPXTC with TMC were amorphous and that they undergo physical aging. Comparison of the experimental and calculated (Fox equation) T_g values showed that they were in excellent agreement over the full range of copolymers studied (Table 7). By variation of the copolymer composition from 8 to 83 mol % IPXTC, the T_g was varied from 4 to 109 °C. A high extent of deprotection of the IPXTC ketal groups was reached (95%) using CF_3COOH/H_2O in CH_2Cl_2 at room temperature. To achieve this extent of deprotection, the apparent M_n decreased from 21 700 to 16 600. However, negligible molecular weight loss occurred at 47% deprotection. Deprotection resulted in a decrease in the copolymer T_g. Further extension of this work by exploiting the versatility of the vicinal diol groups is expected to be very important for applications in polymers of biological importance.

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