Poly(hexamethylene terephthalate-*co*-caprolactone) Copolyesters Obtained by Ring-Opening Polymerization

N. González-Vidal, A. Martínez de Ilarduya, V. Herrera, and S. Muñoz-Guerra*

Departament d'Enginyeria Química, Universitat Politècnica de Catalunya, ETSEIB, Diagonal 647, 08028 Barcelona, Spain

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ABSTRACT: A set of aromatic–aliphatic copolyesters were synthesized by ring-opening polymerization of hexamethylene terephthalate (HT) cyclic oligomers and ϵ-caprolactone monomer (CL) at 175 °C using Sb_2O_3 catalyst. A hexamer- and heptamer-enriched cyclic fraction isolated from the product obtained in the cyclo-depolymerization of poly(hexamethylene terephthalate) (PHT) was used. Ring-opening copolymerizations were conducted for HT to CL feed ratios covering the whole range of compositions and for increasing periods of reaction time. The comonomer contents of the resulting copolyesters were similar to those of their respective feeds, and did not vary with reaction time. In contrast, the copolyester microstructure evolved from block to random as the reaction progressed. The thermal properties of the copolyesters was apparently dependent on both composition and microstructure, and therefore changed with reaction time. The hydrolysis of the copolyesters in simulated physiological medium with and without addition of lipase was evaluated. Copolyesters containing more than 10% of CL were readily degraded in the presence of the enzyme. In contrast to PHT and other copolyesters with lower CL contents, the 50/50 copolyester also underwent extensive hydrolysis upon incubation at pH 10.2 and 80 °C.

Introduction

The synthesis of aromatic polyesters by ring-opening polymerization (ROP) of cyclic esters has received considerable attention in the past few years. The advantages of this procedure derive from the low melt viscosity and high reactivity displayed by the cyclic compounds used as feedstock; moreover, there is no generation of byproduct or heat in the polymerization.[1–5] Such characteristics make cyclic esters exceptionally suitable for the preparation of polyester composites via *in situ* polymerization by applying reaction injection molding procedures.[6,7]

The synthesis of cyclic oligomers is currently a very active research area, and various methods are available for their production from the corresponding linear polymers. Carboxylate esters, amides, urethanes, and carbonates are some representative classes of cyclic oligomers synthesized so far by cyclo-depolymerization.[8–12] Particularly interesting are those cyclic oligomers produced from industrial thermoplastic resins, some of which are already commercially available.[13–15]As a consequence, ROP is starting to be considered a serious alternative to the traditional polycondensation method for the preparation of the most extensively used polyesters such as poly(terephthalate)s and poly(isophthalate)s.[16–18] Recently, the method has been successfully extended to the synthesis of copolyesters made up of aromatic and aliphatic units,[19–21] one representative example being the poly(butylene terephthalate-*co*-caprolactone) copolymers prepared from butylene terephthalate cyclic oligomers and ϵ-caprolactone.[22] A valuable up-dated account of the synthesis and polymerization of oligomeric cyclic esters has recently been reported by Brunelle.[23]

In this paper, we describe the synthesis of hexamethylene terephthalate cyclic oligomers $c(\mathrm{HT})_n$ and their use for the preparation of copolyesters—specifically of poly(hexamethylene terephthalate-*co*-caprolactone), abbreviated henceforth as $co\mathrm{PHT}_x\mathrm{CL}_y$—by ROP. A cyclic fraction enriched in hexamer and heptamer, henceforth called $c(\mathrm{HT})_{6-7}$, was used for copolymerization with CL. Poly(hexamethylene terephthalate) (PHT) is a noncommercial polyester of general fundamental and applied interest that has a relatively low T_g (~10 °C), a moderate T_m (~140 °C), and that displays fair mechanical properties. As it is characteristic of aromatic polyesters, PHT exhibits an excellent chemical resistance and is not biodegradable.[24,25] In contrast, poly(ϵ-caprolactone) (PCL) is an aliphatic polyester displaying unsatisfactory thermal and mechanical behavior but a remarkable biodegradability.[26,27] According to basics, copolymers containing HT and CL units are expected to have combining properties that could be adjusted by tuning composition or/and microstructure. In this work, we study in detail the ROP reaction leading to $co\mathrm{PHT}_x\mathrm{CL}_y$, paying special attention to the influence of the reaction time on the molecular size, the composition, the microstructure, and the thermal properties of the resulting copolymers. The study also includes the evaluation of the hydrolytic degradability of these copolyesters compared with that of the parent homopolymers PHT and PCL.

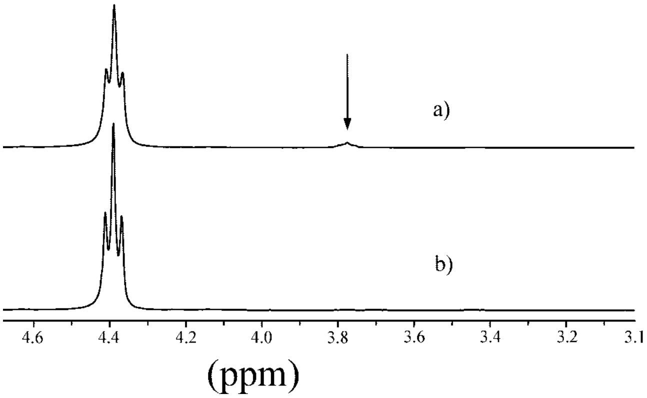

Figure 1. ^{1}H NMR spectra of the product resulting from the thermal cyclo-depolymerization of PHT in solution (top) and the hexamer/heptamer enriched fraction obtained by reprecipitation of the crude product (bottom). The arrow points to the signal assigned to CH_2OH end groups of alicyclic oligomers.

Experimental Section

Dimethyl terephthalate (DMT) (99%), hexanediol (HD) (99%), ϵ-caprolactone (CL) (>99%), dibutyltin oxide (DBTO) (98%),

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* Corresponding author. E-mail: sebastian.munoz@upc.edu.

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Scheme 1. Reactions Involved in the Preparation of *c*(HT)$_n$ Cyclics, PHT Homopolyester, and *co*PHT$_x$CL$_y$ Copolyesters

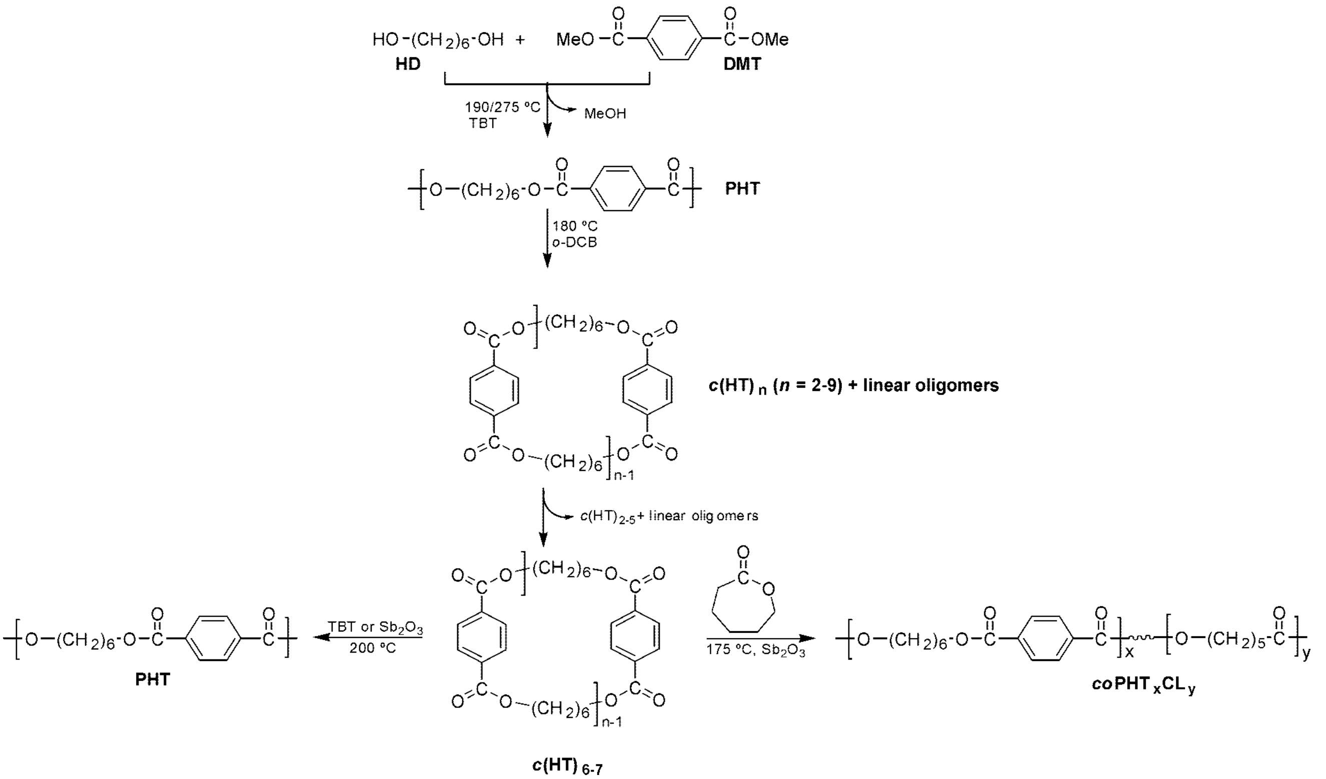

Table 1. Poly(hexamethylene terephthalate): Polymerization Results

Polymerization by Polycondensation

reaction conditions					molecular size					thermal properties				
[DMT]/[HD][a]	TBT[b]	T (°C)[c]	t (min)[d]	yield (%)	[η][e]	M_n[e]	M_n[f]	Mw[f]	PD[f]	T_g (°C)[g]	T_m (°C)[g]	°T_d (°C)[h]	T_d(°C)[h]	RW (%)[h]
1:2.2	0.6	190/275	300/120	84	1.06	47800	31700	63600	2.0	13	139/147	395	417	6

Ring-Opening Polymerization of *c*(HT)$_n$

	reaction conditions				molecular size					thermal properties				
	catalyst[i]	T (°C)[c]	t (min)[d]	yield (%)	[η][e]	M_n[e]	M_n[f]	M_w[f]	PD[f]	T_g (°C)[g]	T_m (°C)[g]	°T_d (°C)[h]	T_d (°C)[h]	RW (%)[h]
PHT1	Sb_2O_3	200	20	92	0.67	18000	20600	44300	2.1	10	134/143	382	411	7
PHT2	TBT	200	30	89	0.65	16900	20500	42600	2.0	9	132/140	384	410	9

[a] Molar ratio or molar concentration. [b] The % mol concentration of catalyst. [c] Reaction temperatures (in polycondensation, for the two reaction steps used). [d] Reaction times (in polycondensation, for the two reaction steps used). [e] Intrinsic viscosity in DCA at 25 °C and number-average molecular weight determined from IV using the Mark−Houwink parameters[40] $a = 0.47$ and $K = 67 \times 10^{-4}$. [f] Molecular weight distribution (number and weight average molecular weight and polydispersity) determined by GPC. [g] Glass transition and melting temperatures observed by DSC. [h] Onset temperature (10% of weight loss), maximum rate decomposition temperature and percentage of residual weight determined by TGA. [i] Catalyst used for ring-opening polymerization at 0.5% mol relative to the monomer content.

lipase enzyme from *Pseudomonas fluorescens* (EC 3.1.1.3, 300U/mg) and 1,2-dichlorobenzene (DCB) (99%) were purchased from Sigma-Aldrich Co. and were used without further purification. Tetrabutyl titanate (TBT) (Merck-Schuchardt) and antimony(III) oxide (97%, Panreac Co) were reagent grade and used as received. The solvents used for purification and characterization, such as chloroform, dichloromethane (DCM), tetrahydrofuran (THF), diethyl ether, dichloroacetic acid (DCA), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), were high-purity grade and used as received.

Measurements. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-300 spectrometer at 25.0 °C operating at 300.1 and 75.5 MHz, respectively. Both polyesters and cyclic compounds were dissolved in deuterated chloroform, and spectra were internally referenced to tetramethylsilane. About 10 and 50 mg of sample in 1 mL of solvent were used for ^1H and ^{13}C, respectively. Sixty-four scans were recorded for ^1H, and between 1000 and 10 000 scans for ^{13}C NMR, with 32 and 64 K data points and relaxation delays of 1 and 2 s, respectively.

Matrix-assisted laser desorption/ionization time-of-flight (MALDI−TOF) mass spectra were recorded in a 4700 Proteomics Analyzer instrument (Applied Biosystems) of the Proteomics Platform of Barcelona Science Park, University of Barcelona. Spectra acquisition was performed in the MS reflector positive-ion mode. About 0.1 mg of sample was dissolved in 50 μL of DCM and 2 μL of this solution were mixed with an equal volume of DCM solution of anthracene (10 mg·mL^{-1}) and the mixture left to evaporate to dryness onto the stainless steel plate of the analyzer. The residue was then covered with 2 μL of a solution of 2,5-dihydroxibenzoic acid in acetonitrile/H_2O (1/1) containing 0.1% TFA and the mixture was left to dry prior to exposition to the laser beam.

High-performance liquid chromatography (HPLC) analysis was performed at 25.0 °C in a Waters apparatus equipped with a UV detector of Applied Biosystems, operating at 254 nm wavelength, and a Scharlau Science column (Si60, 5 μm; 250 × 4.6 mm). Cyclic oligomers (1 mg) were dissolved in chloroform (1 mL) and eluted

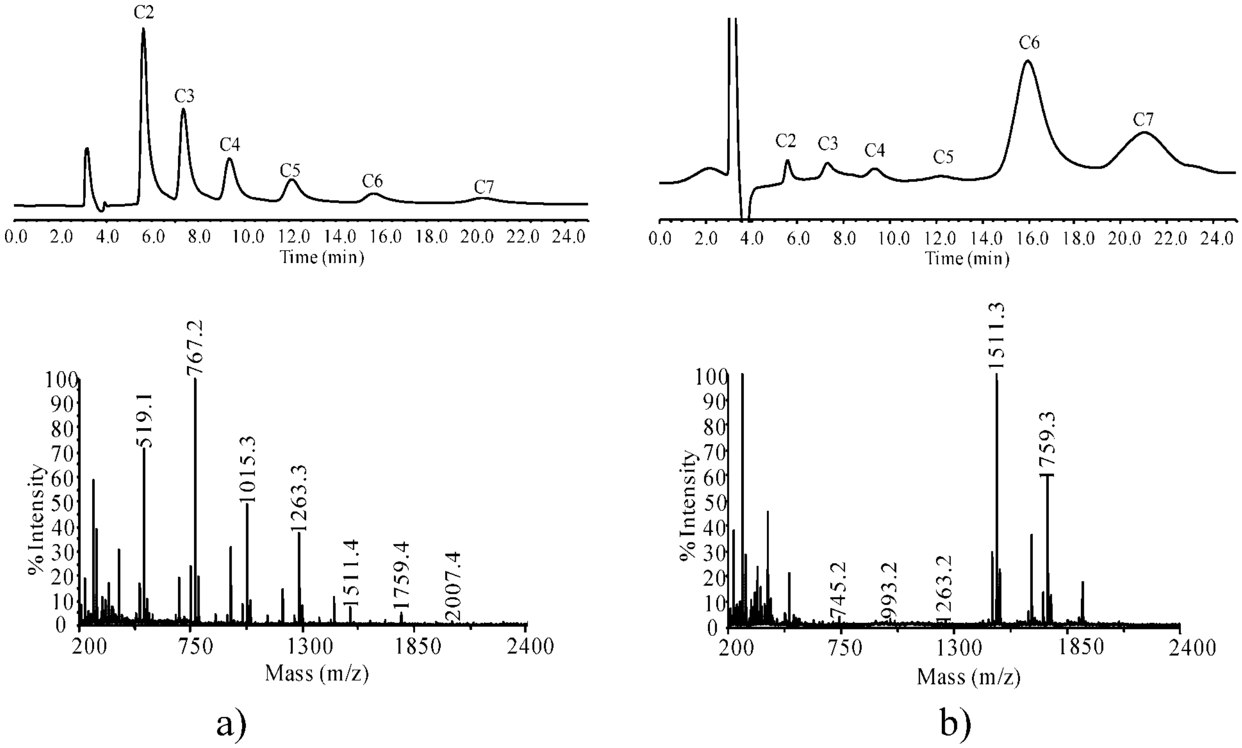

Figure 2. HPLC chromathograms (top) and MALDI−TOF mass spectra (bottom) of cyclic oligomers formed by cyclodepolymerization of PHT in solution. Key: (a) crude fraction; (b) hexamer and heptamer enriched fraction obtained by reprecipitation of the crude product (bottom). (Highest intensity peaks corresponding to either the protonated or Na^+ ionized species for the HPLC separated oligomeric compounds have been labeled; other nonlabeled observed peaks arise from different ionized species coming from cyclic or acyclic compounds).

Table 2. Copolyesters *co*PHT$_x$CL$_y$by Ring-opening Copolymerization of*c*(HT)$_n$and CL

copolyester	t^a (min)	[HT]/[CL]^b	$M_w{}^c$	PD^c	$T_g{}^d$ (°C)	$T_m{}^e$ (°C)	$\Delta H_m{}^e$ (J·g^{-1})	$T_c{}^f$(°C)	$^oT_d{}^g$(°C)	$^mT_d{}^g$(°C)	RW^g(%)
PHT	15	100/0	41200	1.9	10	143	36	109	382	411	7
	120	100/0	50300	2.1	11	143	36	110	385	411	5
*co*PHT$_{90}$CL$_{10}$	15	89.4/10.6	29300	1.8	3	136	34	107	386	412	7
	120	90.6/ 9.4	55200	2.1	4	131	32	93	385	412	6
*co*PHT$_{80}$CL$_{20}$	15	78.8/21.2	25700	1.6	−4	128	29	93	381	412	7
	120	79.8/20.2	48900	2	−16	119	26	76	384	413	6
*co*PHT$_{70}$CL$_{30}$	15	75.3/14.7	30300	1.7	−35	118	25	83	357	414	7
	120	67.3/22.7	50200	2	−16	82	19	30	369	414	8
*co*PHT$_{50}$CL$_{50}$	15	47.4/52.6	38200	1.7	−41	110	18	73	381	413	7
	120	46.3/53.7	53400	2	−32	n.o.	n.o.	n.o.	372	417	6
*co*PHT$_{30}$CL$_{70}$	15	29.4/70.6	24900	1.6	−50	105	11	57	350	350/413	8
	120	28.7/71.3	38200	2	−44	n.o.	n.o.	n.o.	330	350/416	5
*co*PHT$_{10}$CL$_{90}$	15	10.2/89.8	23700	1.4	−56	58	63	31	331	350/415	4
	120	10.2/89.8	40800	1.8	−51	56	54	20	332	350/418	3
PCL	48	0/100	32900	1.7	−60	60	90	30	377	414	3

[a] Reaction times in minutes; in hours for PCL. [b] Composition ratio (mol %/mol %) of HT to CL in the copolymer, determined by ^{1}H NMR. [c] Weight-average molecular weight and polydispersity determined by GPC. [d] Glass transition temperature from melt-quenched samples determined by DSC at 20 °C·min^{-1}. [e] Melting temperature and enthalpy determined by DSC on the second heating at 10 °C·min^{-1}. [f] Crystallization temperature at cooling from the melt at 10 °C·min^{-1}. [g] Onset (10% of weight loss) and maximum rate decomposition temperatures and residual weight determined by TGA under inert atmosphere.

with hexane/1,4-dioxane (70/30 v/v) at a flow rate of 1.0 mL·min^{-1}. Molecular weight analysis was performed by GPC using HFIP containing sodium trifluoroacetate (6.8 g·L^{-1}) in a Waters equipment provided with RI and UV detectors. 100 μL of 0.1% (w/v) sample solution were injected and chromatographed with a flow of 0.5 mL·min^{-1}. HR5E and HR2 Waters linear Styragel columns (7.8 mm × 300 mm, pore size 10^3−10^4 Å) packed with cross-linked polystyrene and protected with a precolumn were used for polymers and cycles analysis, respectively. Molar mass averages and distributions were calculated against PMMA standards. Intrinsic viscosities were measured from polymer solutions in DCA using an Ubbelohde viscometer thermostatted at 25.0 ± 0.1 °C.

The thermal behavior of cyclic compounds and polymers was examined by differential scanning calorimetry (DSC), using a Perkin-Elmer Pyris 1 apparatus. Thermograms were obtained from 4−6 mg samples at heating and cooling rates of 10 °C·min^{-1} under a nitrogen flow of 20 mL·min^{-1}. Indium and zinc were used as standards for temperature and enthalpy calibration. The glass transition temperature (T_g) was taken as the inflection point of the heating DSC traces recorded at 20 °C·min^{-1} from melt-quenched samples and melting temperature (T_m) was taken as the maximum of the endothermic peak appearing on heating traces.

Polymerization and Cyclodepolymerization Reactions. *Synthesis of PHT by Polycondensation.* This polymer was synthesized to be used as source of cyclic oligomers of hexamethylene terephthalate. It was prepared by conventional polycondensation of HD and DMT according to a procedure described in the literature,[28] with minor modifications. HD (65.32 g, 0.453 mol) and DMT (40 g, 0.206 mol) in a feed molar ratio of 2.2:1 were introduced into a three-necked 100 mL round-bottom flask equipped with a mechanical stirrer, a nitrogen inlet, and a vacuum distillation outlet. The temperature was raised to 190 °C and, after complete homogeniza-

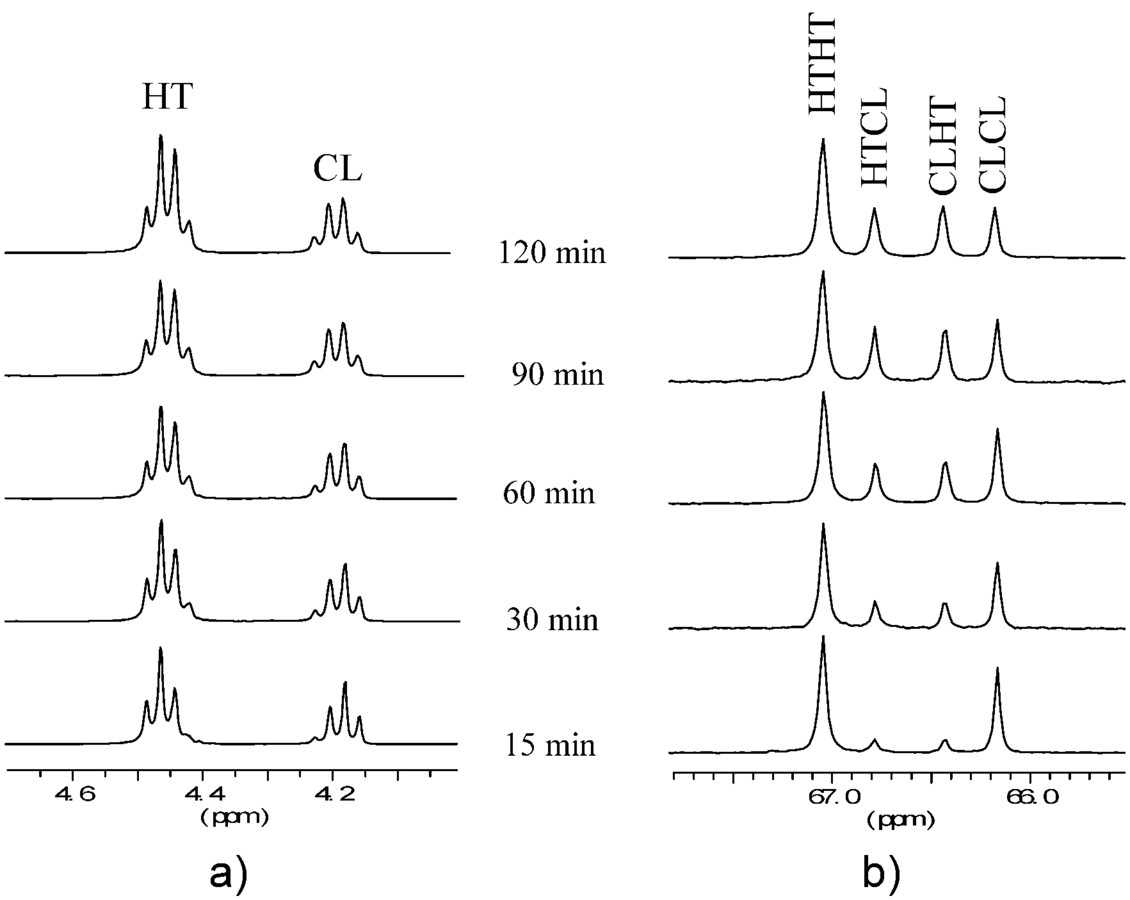

Figure 3. Evolution of the ^{1}H (a) and ^{13}C NMR (b) signals arising from the α-CH_2 of the hexamethylene and pentamethylene segments of *co*PHT$_{50}$CL$_{50}$ with the progress of the polymerization reaction.

Table 3. Composition, Average Sequence Lengths and Randomness ofcoPHT$_x$CL$_y$Copolyesters

		composition[a]		dyad content[b] (mol %)			number average sequence length[c]		randomness[c]
copolyester	*t* (min)	x_{HT}	x_{CL}	HTHT	HTCL+CLHT	CLCL	n_{HT}	n_{CL}	*R*
*co*PHT$_{90}$CL$_{10}$	15	89.4	10.6	85.9	8.5	5.6	21.27	2.31	0.48
	120	90.6	9.4	79.7	17.2	3.1	10.26	1.36	0.83
*co*PHT$_{80}$CL$_{20}$	15	78.8	21.2	76.5	16.7	6.8	10.15	1.81	0.65
	120	79.8	20.2	67.5	31.0	1.5	5.34	1.09	1.10
*co*PHT$_{70}$CL$_{30}$	15	75.3	24.7	70.4	17.4	12.2	9.07	2.39	0.53
	120	67.3	32.7	54.9	39.4	5.7	3.80	1.29	1.04
*co*PHT$_{50}$CL$_{50}$	15	47.4	52.6	39.2	17.6	43.2	5.47	5.92	0.35
	30	48.3	51.7	31.0	37.1	31.9	2.67	2.73	0.74
	60	46.3	52.7	27.8	41.8	30.4	2.33	2.45	0.83
	90	52.9	47.1	35.9	36.7	27.4	2.24	1.94	0.96
	120	51.5	48.5	31.4	47.6	20.0	2.29	1.82	0.98
*co*PHT$_{30}$CL$_{70}$	15	29.4	70.6	22.7	13.0	64.3	4.48	10.90	0.32
	120	28.7	71.3	13.1	43.0	43.9	1.61	3.05	0.95
*co*PHT$_{10}$CL$_{90}$	15	10.2	89.8	5.6	7.3	87.1	2.51	24.73	0.44
	30	14.5	85.5	8.6	16.7	74.7	2.02	9.97	0.59
	60	10.4	89.6	5.9	13.5	80.6	1.87	13.98	0.61
	90	12.9	87.1	6.5	21.4	72.1	1.60	7.71	0.75
	120	10.2	89.8	4.5	17.8	77.7	1.51	9.75	0.76

[a] Determined from signals observed in ^{1}H NMR spectra. [b] Determined from the α-methylene signals in the hexamethylene segments of HT and CL units. Observed in the ^{13}C NMR spectra. [c] Calculated by applying the statistical approach reported in ref 29.

tion of the monomers mixture; approximately 0.6 mmol of TBT catalyst per mol of DMT was added. Transesterification was carried out under a low nitrogen flow for a period of 5 h with formation of methanol. The temperature was then raised to 275 °C and the pressure reduced to 0.5−1 mbar, and the polycondensation reaction was allowed to proceed isothermally under these conditions for 120 min. The reaction mixture was then cooled to room temperature, and atmospheric pressure was recovered with a nitrogen flow to prevent degradation. The solid mass was dissolved in chloroform, and the polymer precipitated with cold diethyl ether, collected by filtration, and washed thoroughly with cold diethyl ether. All samples were dried at 60 °C under reduced pressure for a minimum of 24 h before use. (33.6 g, 84% yield). δ(H) (CDCl$_3$, 300 MHz): 1.56 (m, 4H), 1.83 (q, 4H), 4.36 (t, 4H), 8.09 (s, 4H). δ(^{13}C) (CDCl$_3$, 75.5 MHz): 25.7, 28.6, 65.3, 129.5, 134.1, 165.8.

Synthesis of Cyclic Oligomers by Cyclo-Depolymerization of PHT. The cyclic oligomers were produced by depolymerization of PHT according to the following procedure: PHT (4.96 g, 20 mmol previously dried overnight in a vacuum oven at 60 °C) and DCB (200 mL) containing 3 mol % DBTO were introduced into a 250 mL round-bottom flask equipped with a condenser. This mixture was stirred vigorously, and the cyclo-depolymerization reaction was

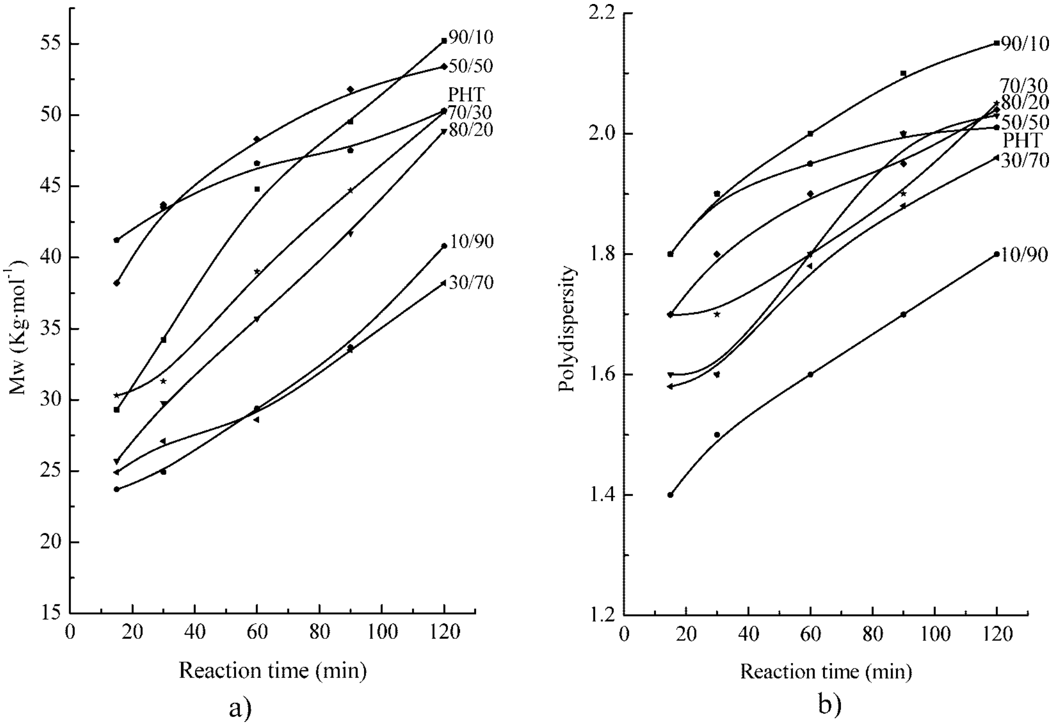

Figure 4. Evolution of the weight-average molecular weight (a) and polydispersity (b) of the resulting copolymer as a function of reaction time for the different *co*PHT$_x$CL$_y$ copolyesters.

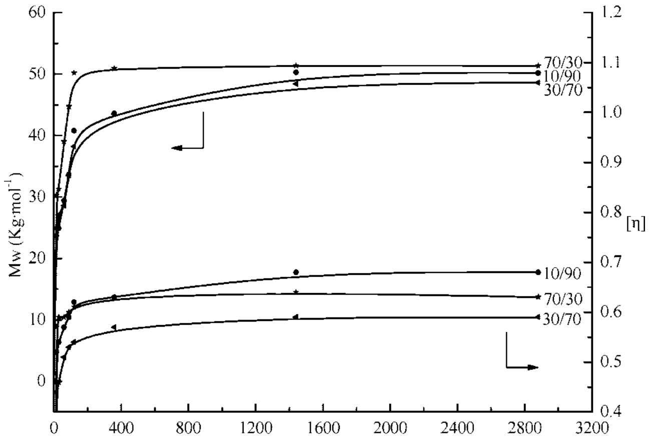

Figure 5. Effect of long reaction times on intrinsic viscosity and weight average molecular weight of the different *co*PHT$_x$CL$_y$ copolyesters.

allowed to proceed under reflux temperature of 180 °C for 4 days. The mixture was cooled to room temperature and then filtered. The DCB was rapidly evaporated off under vacuum at 50 °C to dryness, and the recovered solid (4.2 g, 85% yield, crude cyclic product) was dissolved in chloroform and precipitated with cold diethyl ether. The precipitated solid was recovered by filtration and reprecipitated from dichloromethane with diethyl ether (2.19 g, 44% weight). This fraction $c(\mathrm{HT})_{6-7}$ was dried at 50 °C under reduced pressure for 48 h before characterization. δ(H) ($CDCl_3$, 300 MHz): 1.54 (m, 4H), 1.82 (q, 4H), 4.36 (t, 4H), 8.08 (s, 4H). $\delta(^{13}C)$ ($CDCl_3$, 75.5 MHz): 25.7, 28.6, 65.3, 129.5, 134.1, 165.8.

Synthesis of PHT by Ring-Opening Polymerization of c(HT)$_{6-7}$. The $c(\mathrm{HT})_{6-7}$ fraction (0.2 g, 0.8 mmol) and Sb_2O_3 catalyst (1.17 mg, 0.5 mol %) were introduced into a vial and mixed by dissolving them in DCM and then slowly evaporated the solvent under vigorous stirring. The residue was dried at 50 °C under reduced pressure for 24 h. The dried mixture was introduced into a two-necked round-bottom flask equipped with a nitrogen inlet/outlet. The flask was purged with nitrogen to remove all traces of moisture and residual air and immersed into a bath containing an eutectic mixture of molten sodium nitrite, sodium nitrate, and potassium nitrate at 200 °C. Polymerization was carried out at this temperature for a period of 20 min under a nitrogen atmosphere. Finally, the reaction mixture was quenched in an ice−water bath, and atmospheric pressure was recovered using nitrogen to prevent degradation. The resulting polymer was dissolved in chloroform, precipitated with cold diethyl ether, and dried at 50 °C under reduced pressure for 48 h before characterization (0.18 g, 92% yield). δ(H) ($CDCl_3$, 300 MHz): 1.54 (m, 4H), 1.82 (q, 4H), 4.35 (t, 4H), 8.08 (s, 4H). $\delta(^{13}C)$ ($CDCl_3$, 75.5 MHz): 25.7, 28.6, 65.3, 129.5, 134.1, 165.8.

Synthesis of Poly(hexamethylene terephthalate-co-caprolactone) Copolyesters (PHT$_x$CL$_y$) by Ring-Opening Polymerization. A mixture of cyclic oligomers $c(\mathrm{HT})_{6-7}$ and ϵ-caprolactone (CL) with the selected composition ratio, and Sb_2O_3 (0.5 mol %), was prepared as described above and introduced into a two-necked round-bottom flask equipped with a nitrogen inlet/outlet. The flask was purged with nitrogen to remove all traces of moisture and residual air, and immersed in a salt bath at a temperature range of 175−180 °C. The reaction was carried out at a selected temperature within this range under circulating nitrogen atmosphere for the scheduled period of time (from 15 to 120 min). The final reaction mixture was quenched in an ice−water bath, and atmospheric pressure was recovered using nitrogen to prevent degradation. The resulting copolymers were obtained in over 90% yield and were characterized without any further purification.

Hydrolytic and Enzymatic Degradation. For hydrolytic and enzymatic degradation studies amorphous 0.2-mm-thick films of polyesters were prepared by melt-compression followed by quenching into ice-cold water. The films were then cut into 10-mm diameter disks with a weight in the 60−80 mg range, which were dried under vacuum for 48 h. The hydrolytic degradation was performed by incubation in saline phosphate pH 7.4 and carbonate pH 10.2 buffers. Discs were placed into vials containing 10 mL of buffered solutions, which were sealed to avoid evaporation of the fluids and stored in a heat chamber at either 37 °C for pH 7.4 or 80 °C for pH 10.2 solutions. The enzymatic degradation was carried out in phosphate buffered saline solution (pH 7.4, 37 °C) using lipase from *P. fluorescens* (0.1 mg·mL^{-1}). At the end of the scheduled

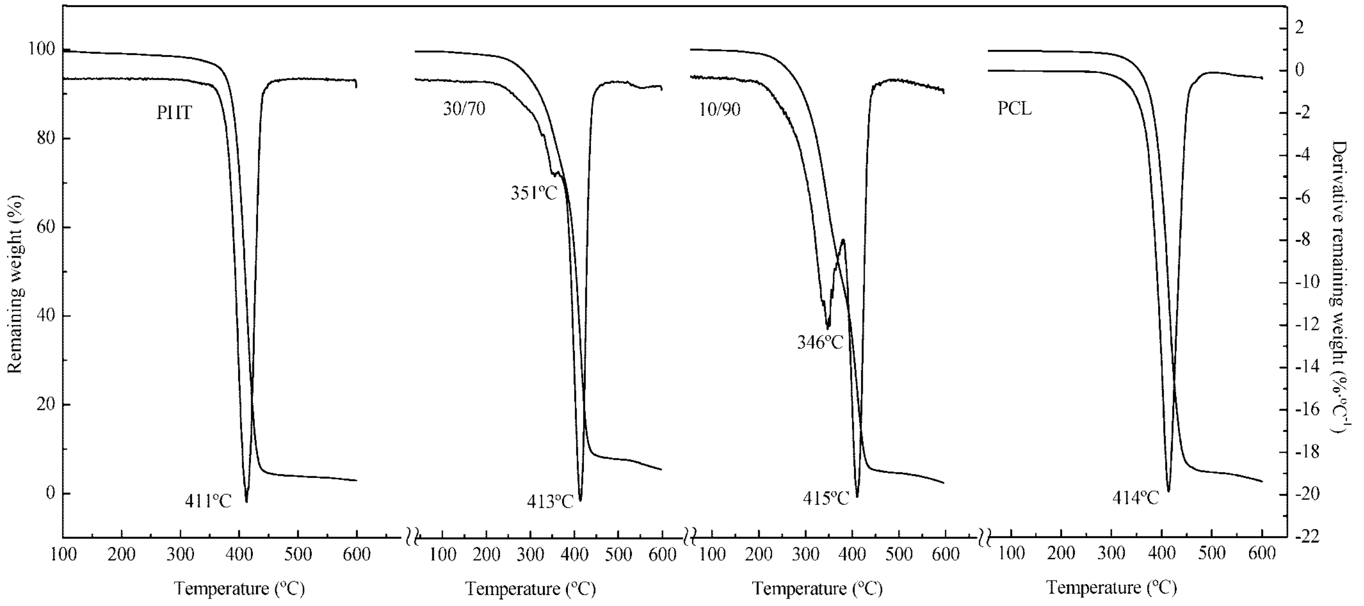

Figure 6. Comparison of TGA traces of *co*PHT$_x$CL$_y$ copolymers having the indicated compositions with those of the parent homopolymers PHT and PCL.

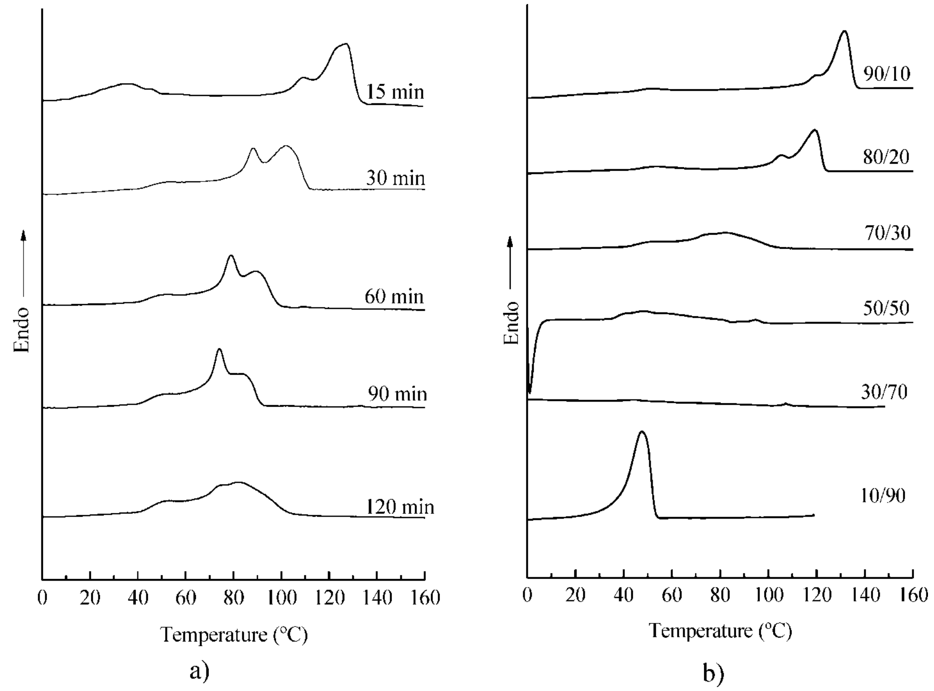

Figure 7. Compared DSC heating thermograms recorded from the molten samples of *co*PHT$_x$CL$_y$. (a) *co*PHT$_{70}$CL$_{30}$ generated at the indicated reaction times. (b) *co*PHT$_x$CL$_y$ with the indicated compositions and generated at 120 min of reaction.

incubation periods, the disks were withdrawn from the incubation medium, washed thoroughly with distilled water and dried to be then subjected to weighting and GPC analysis. All experiments were made in triplicate.

Results and Discussion

Polymerization and Cyclo-Depolymerization of PHT. The synthesis strategy followed in this work for the preparation of PHT homopolyester and *co*PHT$_x$CL$_y$ copolyesters by ring-opening polymerization is shown in Scheme 1. This scheme includes the polycondensation and depolymerization processes employed for yielding the cyclic hexamethylene terephthalate oligomers used in such polymerizations. The polyester PHT used as raw material for the production of *c*(HT)$_n$ cyclic oligomers was prepared by melt polycondensation of HD and DMT. This reaction was performed according to Quintana et al.,[28] the resulting polyester being obtained in 84% yield with a weight-average molecular weight of ≈63 000 and a polydispersity near 2. Details of reaction conditions and characteristics of the produced PHT are given in Table 1.

Cyclo-depolymerization of PHT was carried out in dilute solution by following the method optimized by Brunelle et al.[16] for the preparation of cyclic butylene terephthalate oligomers from poly(butylene terephthalate), which is based on the use of active tin catalysts. Characterization of the depolymerization product was performed by NMR and combined HPLC and MALDI−TOF spectroscopy. As it is illustrated in Figure 1, end-groups analysis by NMR evidenced that the crude product consisted mainly of cyclic compounds accompanied by a small amount of linear oligomers. The HPLC and MALDI−TOF

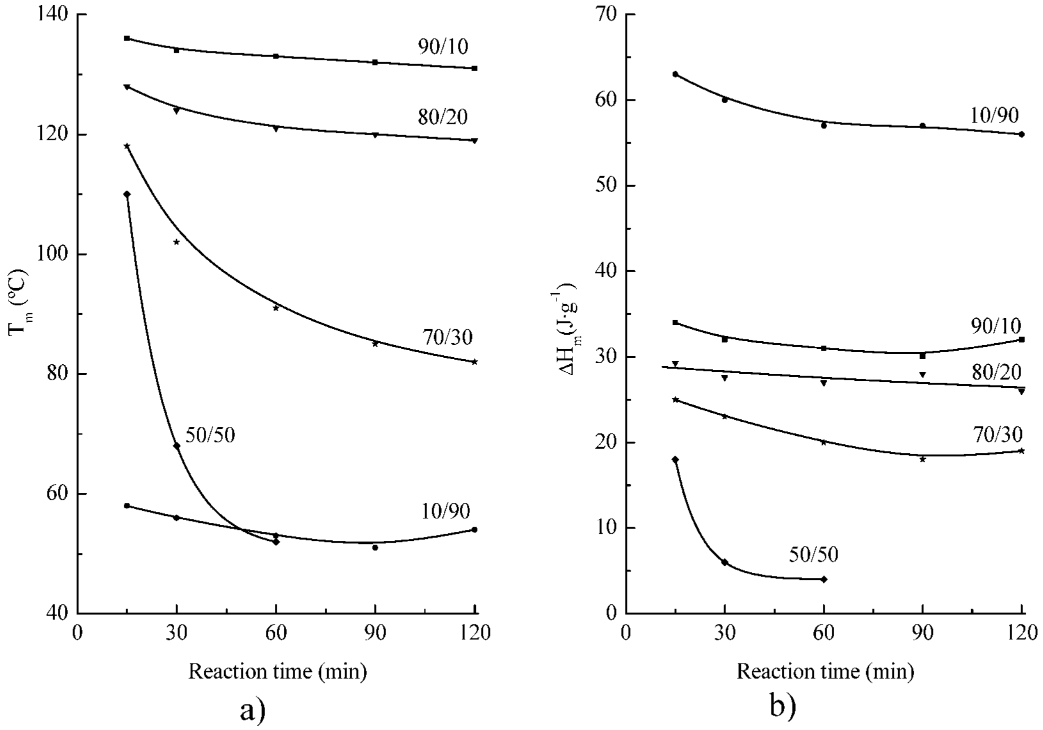

Figure 8. Evolution of the melting temperature (a) and enthalpy (b), for semicrystalline coPHT$_x$CL$_y$ copolymers as a function of reaction time.

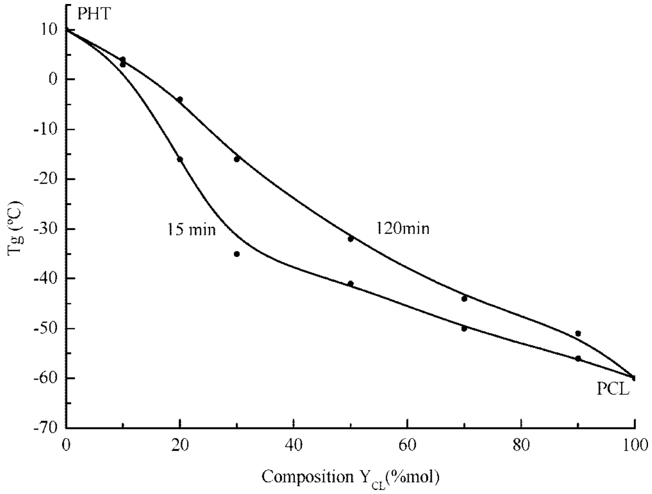

Figure 9. Influence of composition and reaction time on the glass transition temperature (T_g) of coPHT$_x$CL$_y$ copolymers.

analysis (Figure 2a) revealed that the product is essentially a mixture of cyclic oligomers ranging from 2 to 9; the dimer is the main component (42.7%) followed by the trimer and tetramer (26.5 and 13.9%, respectively) and the larger cycles amount to about 18% of the mixture. After repeated precipitation from halogenated solvents with ether, the acyclic components could be completely removed, as was certified by the disappearance from the ^{1}H NMR spectrum of the peak at 3.79 ppm arising from CH_2OH end groups (Figure 1). As it is shown in Figure 2b, the MALDI−TOF analysis of this isolated fraction revealed detectable oligomer sizes ranging from 2 to 9, but the HPLC chromatogram showed only six measurable peaks whereas no additional peak was observed for longer elution times. After fractionation, separated collection, and individual analysis by MALDI, the six peaks observed by HPLC could be made to correspond to c(CH)$_n$ for $n = 2-7$, in increasing order of elution time. Quantification of peak areas in the chromatogram indicated that this fraction consisted essentially of a mixture of c(CH)$_6$ (61%) and c(CH)$_7$ (30%); the other accompanying cycles of smaller size amount to less than 9% of the total. This hexamer and heptamer enriched fraction, c(CH)$_{6-7}$, was selected for the polymerization and copolymerization studies described below.

Ring-opening polymerization of c(HT)$_{6-7}$ was performed in the bulk at a temperature near to 200 °C and using either Sb_2O_3 or TBT. Details of reaction conditions and results are given in Table 1, together with molecular-size and thermal data of the resulting polymers. The reaction yields and characteristics of the PHTs obtained with each catalyst were very similar; the observed slight differences were within the range of experimental error. Although the polymer size was found to increase slightly with reaction time, the PHT resulting after 120 min still had a molecular weight rather lower than that of the PHT obtained by polycondensation. Such difference in polymer size could account for the slight differences in T_g and T_m, as well as in thermal stability, observed between the two polyesters.

Ring-Opening Copolymerization of Hexamethylene Terephthalate Cyclic Oligomers and ϵ-Caprolactone. Ring-opening copolymerization of c(HT)$_n$ with CL was carried out in the manner described above for the preparation of PHT homopolyester. Mixtures of the two comonomers with HT/CL molar ratios ranging between 10/90 and 90/10 were polymerized at 175 °C in the presence of Sb_2O_3. HT and CL contents, microstructure, and molecular size of the copolymers that were generated at increasing reaction times from 15 to 120 min were determined at intervals of 15 or 30 min for each feed composition assayed. Polymerization results and characteristics of the copolymers produced at the initial and end reaction times are given in Table 2. The HT/CL contents were precisely determined by NMR which revealed that the composition of the resulting copolymer is in excellent agreement with the initial feed composition in every case. Such close correspondence is essentially maintained over the whole range of reaction times applied (the small fluctuations observed are very likely due to inaccuracy in the experimental measurements). The evolution of the copolymer microstructure with reaction time was monitored via the changes observed for the ^{1}H and ^{13}C NMR signals arising from the

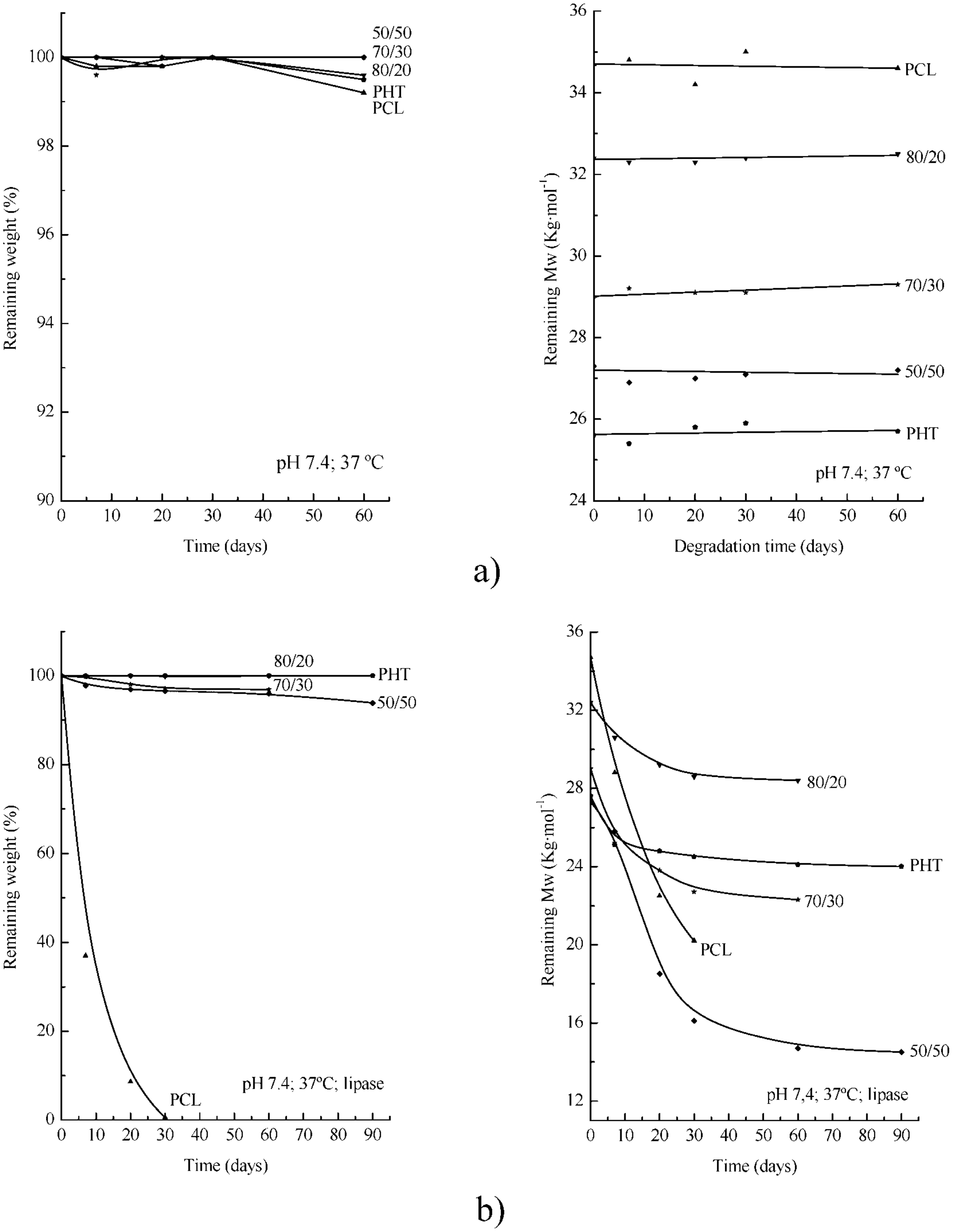

Figure 10. Comparison of hydrolytic degradation of *co*PHT$_{80}$CL$_{20}$, *co*PHT$_{70}$CL$_{30}$, and *co*PHT$_{50}$CL$_{50}$ copolymers with that of the parent homopolymers PHT and PCL at 37 °C and pH 7.4, without or with lipase (a and b). The remaining weight and weight-average molecular weights of the residual incubated polymer are plotted against incubation time.

α-CH$_2$ of the hexamethylene and pentamethylene segments of HT and CL units, respectively, as illustrated in Figure 3 for the case of PHT$_{50}$CL$_{50}$. By comparison of the intensities of the respective peaks, it could be inferred that the contents of HTHT and CLCL dyads decrease in parallel with the increase in the contents of HTCL and CLHT dyads as the reaction time increases. A detailed account of the NMR analysis results is provided in Table 3, where experimental copolymer compositions and dyad contents are given for each copolymer prepared at each reaction time. The average lengths of the homogeneous sequences consisting of HT or CL units, and the degree of randomness of the resulting copolymers, were calculated according to Randall.[29] These results reveal that a blocky microstructure is generated at short reaction times, and evolves to a nearly random distribution as the reaction proceeds. Such behavior is common to the whole series, although the degree of randomness finally achieved is lower for copolymers with higher comonomer ratio values. As is well documented for both aliphatic and aromatic polyesters, the randomization observed must result from the occurrence of both intra- and intermolecular transesterification reactions taking place between (HT) and (CL) homogeneous chain segments at the high temperatures applied for the reaction. Since the Bernoulli statistics define a theoretical value of $R = 1$ for a fully random copolymer,[30–32] it can be concluded that *co*PHT$_x$CL$_y$, with contents in the two comonomers higher than 10% (which have R values between 0.95 and 1.1) must have a nearly random microstructure. It should be noted, however, that the R values determined here refer to the

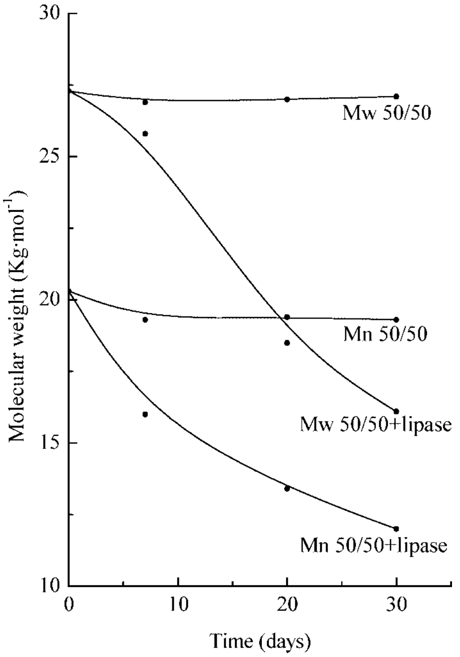

Figure 11. Influence of the presence of lipase on the evolution of number and weight-average molecular weights of *co*PHT$_{50}$CL$_{50}$ copolymer subjected to hydrolysis under simulated physiological conditions.

copolymer microstructure but not to the preference of the comonomers for incorporating into the growing polymer chain. If the oligomeric nature of *c*(HT)$_{6-7}$ is taken into account, a hexamethylene terephthalate unit (HT)$_n$ consisting of 6.2 units on average should be assumed for theoretical calculations. This would lead to much lower *R* values for the random copolymer. The conclusion deriving from such consideration is that the randomization process caused by transesterification starts to operate from the earliest reaction times.

The evolution of M_w and polydispersity (PD) of *co*PHT$_x$CL$_y$ copolymers with reaction time is plotted in Figure 4. As expected, the common behavior of the whole series is that both polymer size and PD increase with reaction time, displaying an ascendant profile which is more or less steady and pronounced depending on copolymer composition. Since polymerization yields are very high from the beginning of the reaction, the increase observed in polymer size should be interpreted as being mainly due to the occurrence of esterification reactions taking place between chain ends. What is clearly seen in these plots is that the copolymer chain is still growing at the end of the period of time selected for the study. In order to know the effect of longer reaction times on the molecular size of the forming copolymer, some additional experiments were carried out, lengthening the reaction time up to 48 h. The evolution of the weight-average molecular weight and intrinsic viscosity of the resulting copolymer with reaction time is plotted in Figure 5 for three selected compositions. The results coming from this study revealed that the increase in molecular size practically ceased after approximately 3 h of reaction, the increment observed with respect to copolymers obtained at 120 min being nonsignificant.

Thermal Properties of co-PHT$_x$CL$_y$ Copolymers. The thermal data of copolyesters recorded by DSC and TGA analysis are compared in Table 2, where the corresponding data for the parent homopolymers PHT and PCL obtained by ring-opening polymerization are also included for comparison. PHT decomposition takes place in a single step, initiated above 350 °C, and attains the maximum rate at 411 °C, leaving 5% of residue. PCL decomposes following a very similar pattern, with the maximum decomposition rate at 414 °C and leaving only 3% of residue. Such decomposition patterns agree with the occurrence of an unzipping depolymerization mechanism reaction proceeding with the generation of cyclic monomer or oligomers. The thermal stability of *co*PHT$_x$CL$_y$ is close to that of the parent homopolymers, and shows a decomposition profile over approximately the same range of temperatures. Whereas the influence of microstructure on thermal decomposition is almost negligible for the whole series of *co*PHT$_x$CL$_y$, copolymers enriched in CL, i.e., *co*PHT$_{30}$CL$_{70}$ and *co*PHT$_{10}$CL$_{90}$, display a more complex decomposition process (Figure 6). In these two cases, the common decomposition step of the whole series is preceded by another one, taking place at around 350 °C. Such behavior can be explained if the two-step decomposition mechanism proposed by Dubois et al.[33,34] for the thermal degradation of end-capped PCL is assumed to operate here. According to such mechanism, the ester groups of the CL segments present in these copolymers would undergo thermal breaking to generate volatile compounds, which would account for the weight loss observed at lower temperatures. At higher temperatures, decomposition continues through a back-biting mechanism according to the same profile that is observed for the other members of the series, as well as for the parent homopolymers.

Conversely, the crystallization-fusion behavior of *co*PHT$_x$CL$_y$ appears to be extremely sensitive to composition and microstructure. This is the logical consequence of the large differences in T$_m$ and crystallizability existing between PHT and PCL. A collection of DSC traces representative of the behavior of the copolyester series is shown in Figure 7, and values for the characteristic thermal parameters of the copolyesters obtained at initial and final reaction times are compared in Table 2. All copolymers obtained at 15 min of reaction exhibit endothermic peaks indicative of melting, whatever their composition. This melting peak, which is usually multiple (as is common in polyesters), moves with the CL content of the copolymer from a value close to the T_m of PHT (~140 °C) down to the T_m of PCL (~60 °C). On the other hand, the copolymers obtained at 120 min of reaction time display lower crystallinity, the *co*PHT$_{50}$CL$_{50}$ and *co*PHT$_{30}$CL$_{70}$ copolymers showing no melting peak. The DSC traces obtained by cooling from the melt revealed that these copolymers are able to crystallize at undercoolings that are more pronounced as the microstructure becomes more randomized. The evolution of copolymer melting temperature and enthalpy as a function of polymerization time is shown in Figure 8 for those cases in which crystallinity becomes observable. In copolymers with extreme ratios in HT/CL units (90/10 and 10/90), the decay of T_m and ΔH_m with reaction time is slight, due to the meager effect that randomization has on crystallization for such compositions, i.e., regardless of the microstructure of the copolymer, homogeneous segments are long enough to form crystallites with stable size. In contrast, both melting temperature and enthalpy decrease drastically for copolymers containing moderate amounts of both units, i.e., 70/30, 50/50, and 30/70. In these cases, the homogeneous segments left after randomization do not attain the length required to generate stable crystals. The effect of composition and microstructure on T_g is also noticeable, the values for the copolymers obtained at short and long reaction times being listed in Table 2. In addition, a graphical representation of these data is depicted in Figure 9. In this plots it can be clearly observed that the T_g decreases from 3 to −56 °C, approaching the PHT and PCL T_g values, as the CL content increases from 10% to 90%. On the other hand, randomness gives rise to an increase in T_g for most of the copolymers, this effect being more noticeable as the composition in the two comonomers becomes more balanced. It should be noted that a single T_g is observed in all the

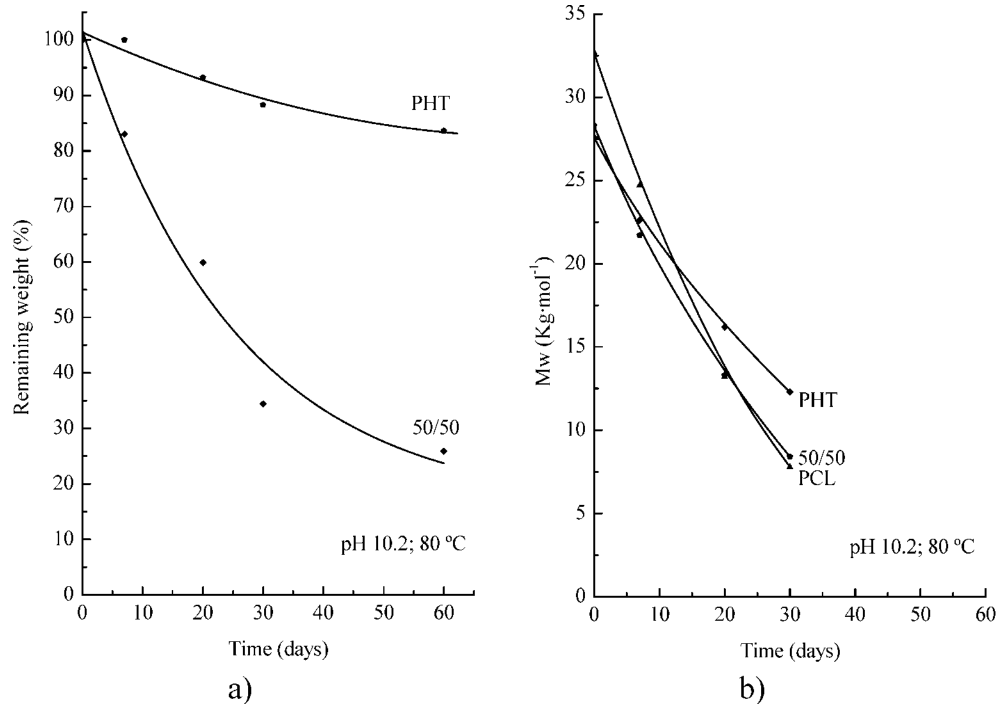

Figure 12. Comparison of hydrolytic degradation of *co*PHT$_{50}$CL$_{50}$ copolymer and PHT and PCL at 80 °C and pH 10.2. The remaining weight and the weight-average molecular weight of the residual incubated polymers (a and b) are plotted against incubation time.

copolymers, despite the fact that a second T_g should be observable in the case of copolymers containing long homogeneous segments of either unit.

Hydrolytic Degradation of coPHT$_x$CL$_y$ Copolymers. The difficulty in hydrolyzing aromatic polyesters and PCL under mild conditions is well-known.[35,36] On the other hand, PCL is known to be highly susceptible to hydrolysis under physiological conditions in the presence of lipase, a property that makes this polyester of exceptional interest as a biodegradable material.[20] The effect of inserting caprolactone units in the PHT chain on the hydrolytic degradability of the polyester was examined as the final part of this work. To investigate this issue, *co*PHT$_x$CL$_y$ copolymers containing at least 20 mol % of CL and obtained at short reaction times, therefore having a blocky microstructure, were subjected to degradation assays under a variety of conditions. Degradation results obtained for *co*PHT$_{80}$CL$_{20}$, *co*PHT$_{70}$CL$_{30}$, and *co*PHT$_{50}$CL$_{50}$, as well as for the parent homopolymers PHT and PCL, upon incubation in aqueous pH 7.4 buffer at 37 °C with and without lipase, are presented in Figure 10. The changes taking place in both sample weight and weight-average molecular weight of the polymer were followed as a function of incubation time. According to the invariance observed for these parameters, it was concluded that there was no significant degradation in any of the assayed polymers when incubated in the absence of enzyme. The results obtained in the presence of lipase were much more positive. A noticeable decay in M_w was observed for all the polymers, the decrease being more pronounced for higher contents in CL. Thus, *co*PHT$_{50}$CL$_{50}$ displayed a degradation profile similar to that of PCL, with a reduction of approximately 50% in molecular size after incubation for two months. The fact that almost no weight loss was observed for PHT and copolymers, whereas PCL practically disappeared after 30 days of incubation, is interpreted as being due to the nonsolubility of the degraded fragments containing aromatic units. This is a well-known effect that has been reported on numerous occasions.[37–39] The evolution of the polydispersity of *co*PHT$_{50}$CL$_{50}$ with enzymatic degradation can be evaluated in Figure 11, where variations taking place in both number and weight average molecular weights with time are compared. Apparently, degradation causes no significant change in polydispersity, the initial value of 1.4 being practically retained throughout the process.

To finish this study, and in order to estimate the resistance of these copolymers to hydrolysis in the absence of lipase, the *co*PHT$_{50}$CL$_{50}$ copolymer, as well as PHT and PCL homopolymers, were incubated at 80 °C in water at pH 10.2. Results are compared in Figure 12, which clearly reveals that under such conditions, the influence of the CL units on the degradability of the polyester chain is more noticeable than under physiological conditions. In fact, the decrease in molecular weight with incubation time is seen to be greater for the copolymer than for PHT, and comparable to that taking place for PCL. Even more remarkable is the weight that is lost upon incubation, particularly if compared with the near invariance observed for PHT. Nevertheless, differences in water solubility at this temperature between degraded segments consisting of fully aromatic polyester chains and those containing CL units should be taken into account for a correct interpretation of these results.

Conclusions

Cyclo-depolymerization of PHT in solution was a reliable procedure for producing cyclic hexamethylene terephthalate oligomers. An hexamer and heptamer enriched fraction practically exempted of acyclic compounds could be prepared by selective precipitation of the crude depolymerization product. Ring-opening polymerization of this cyclic fraction catalyzed by Sb_2O_3 afforded PHT homopolymers with characteristics and properties practically undistinguishable from those displayed by the polyester prepared by polycondensation.

Ring-opening copolymerization of the hexamer and heptamer enriched fraction and ϵ-caprolactone took place in very short reaction times, affording copolymers in high yields and with compositions very close to those of the respective feeds used for copolymerization. Transesterification reactions were found to occur simultaneously to the ring-opening reaction from the beginning of the polymerization. As a result, the distribution of the HT and CL units in the copolymer chain became more homogeneous as the reaction proceeded, so that the initial blocky microstructure was almost randomized at the end of the polymerization process. The thermal properties and crystallinity of these copolyesters were dependent on both composition and microstructure. The opolyesters showed T_{g} and T_{m} values intermediate between those of the two parent homopolymers PHT and PCL, and they could not be crystallized when the contents in HT and CL units were comparable and the microstructure was random.

The copolyesters containing more than 10 mol % of CL were readily degraded under simulated physiological conditions in the presence of lipase, but they were apparently inert in the absence of enzyme. Contrarily to PHT and other copolyesters with lower CL content, the 50/50 copolyester underwent extensive hydrolysis upon incubation at pH 10.2 and 80 °C.

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