Blocky Poly(ε-caprolactone-*co*-butylene 2,5-furandicarboxylate) Copolyesters via Enzymatic Ring Opening Polymerization

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Abstract: Cyclic oligo(butylene 2,5-furandicarboxylate) and ε-caprolactone were copolymerized in bulk at 130-150 ºC by enzymatic ring opening polymerization using CALB as catalyst. Copolyesters within a wide range of compositions were thus synthesized with weight-average molecular weights between 20,000 and 50,000, the highest values being obtained for equimolar or nearly equimolar contents in the two components. The copolyesters consisted of a blocky distribution of the ε-oxycaproate (CL) and butylene furanoate (BF) units that could be further randomized by heating treatment. The thermal stability of these copolyesters was comparable to those of the parent homopolyesters (PBF and PCL), and they all showed crystallinity in more or less degree depending on composition. Their melting and glass-transition temperatures were ranging between those of PBF and PCL with values increasing almost linearly with the content in BF units. The ability of these copolyesters for crystallizing from the melt was evaluated by comparative isothermal crystallization and found to be favored by the presence of flexible ε-oxycaproate blocks. These copolyesters are essentially insensitive to hydrolysis in neutral aqueous medium but they became noticeably degraded by lipases in an extend that increased with the content in CL units.

Keywords: Furan-based polyesters, enzymatic polymerization, ring-opening polymerization, caprolactone copolyesters, FDCA, aliphatic-aromatic copolyesters, poly(butylene furanoate) copolyesters.

INTRODUCTION

ROP (Ring Opening Polymerization) is a well-recognized polymerization method suitable for preparing polymers from cyclic monomers that may be opened by either enthalpic or entropic driving forces.[1,2] Although this procedure has been used for the synthesis of a great diversity of polymers, its application to the preparation of

polyesters from lactones is by far the most widely known.[3,4] The milder reaction conditions required, the absence of volatile by-products, and the minimization of undesirable sub-products, are appreciated advantages of ROP over conventional polycondensation. Furthermore lipases seem to work particularly well as catalysts for the polymerization of lactones so that enzymatic Ring Opening Polymerization (*e*-ROP) is becoming a specialty of the method that reaches particular interest when green processing and sustainability are main synthesis concerns.[5-7]

Poly(alkylene furanoate)s, specifically poly(ethylene 2,5-furandicarboxylate) (PEF) and poly(butylene 2,5-furandicarboxylate) (PBF), are aromatic polyesters of renewable origin that are highly fashionable because of their potential for replacing poly(alkylene terephthalate)s (PET and PBT) in their industrial applications.[8,9] The exceptional relevance of 2,5-furandicarboxylic acid (FDCA) as monomer for the synthesis of bio-based polyesters has been splendidly shown by Sousa *et al*. in a recent review.[10] Polyfuranoates are semicrystalline polymers that display high melting and glass-transition temperatures and that have barrier properties even better than polyterephthalates. As it is characteristic of aromatic polyesters, PEF and PBF are highly resistant to hydrolysis and show very low biodegradability.[11,12] PEF and PBF are usually prepared by polycondensation of FDCA or its dimethyl ester (FDCA-Me_2) with ethylene glycol and 1,4-butanediol, respectively.[8] However the access to cyclic (alkylene 2,5-furandicarboxylate) oligomers (*c*$(EF)_n$ and *c*$(BF)_n$) recently afforded by chemical synthesis has opened the ROP route towards the preparation of these polyesters.[13,14] Additionally aromatic copolyesters made of butylene furanoate (BF) and butylene terephthalate (BT),[15] as well as aromatic-aliphatic copolyesters made from BF and butylene succinate (BS)[16] have been prepared by ROP in good yields with pretty high molecular weights. In these copolymerizations cyclic (butylene terephthalate) and (butylene succinate) oligomers were the respective comonomers of *c*$(BF)_n$, and tin octoate or/and supported lipases (CALB) were the catalysts used therein.

Poly(ε-caprolactone) (PCL) is a semicrystalline polyester of great interest in the biomedical field due to its excellent biocompatibility and exceptional biodegradability.[17,18] This polyester has however severe flaws derived from its low melting (~ 65 ºC) and its very low glass-transition (~-60 ºC) temperatures. PCL is invariably produced by ROP of ε-caprolactone by using either chemical or enzymatic methods. ROP copolymerization of CL with a wide variety of other cyclic monomers has been extensively examined with the purpose of designing PCL copolyesters with improved thermal and mechanical properties.[19-22] In this sense, the PCL copolyesters containing aromatic units and synthesized by ROP, as they are PCL-PHT[23] and PCL-PBT,[24] are particularly noteworthy in the present context. In these cases cyclic (hexamethylene terephthalate) (c(HT)$_n$) and cyclic (butylene terephthalate) (c(BT)$_n$) oligomers were copolymerized with CL at high temperature and in the presence of a tin catalyst to render random copolyesters with properties adjustable by composition.

In this paper we wish to report on copolyesters prepared by *e*-ROP of ε-caprolactone with cyclic butylene 2,5-furandicarboxylate oligomers. The approach followed in this work is again to design PCL copolyesters with improved properties but using a bio-based aromatic comonomer and applying a greener synthetic route. A series of copolyesters covering the almost full range of compositions are prepared and duly characterized, and their thermal properties and degradability evaluated as well. It should be mentioned that a set of PBF-PCL copolyesters with a similar chemical composition has been recently described by Zheng et al.[25] These copolyesters were prepared by a combination of polycondensation and ROP procedures and they have a microstructure made of soft and hard segments characteristic of thermoplastic elastomers.

EXPERIMENTAL

Materials

2,5-Furan dicarboxylic acid (FDCA, 98% purity) was obtained from Satachem (China). ε-Caprolactone (CL, 97%), 1,4-butanediol (BD, 99%), thionyl chloride ($SOCl_2$, 99%), di-azabicyclo[2.2.2] octane (DABCO, 99%), titanium (IV) butoxide (TBT, 97%) and lipase of porcine pancreas were purchased from Sigma-Aldrich Co. Lipase *Candida antarctica* (CALB) was a gift of Novozymes. Solvents used for reaction, isolation and purification were of high-purity grade and used as received with the exception of tetrahydrofurane (THF) that was dried on 3 Å molecular sieves. DABCO catalyst was purified by sublimation. CALB was dried in a vacuum desiccator at 50 ºC for 24 h previous to use.

Measurements

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-300 spectrometer at 25 °C, operating at 300.1 and 75.5 MHz, respectively. Samples were dissolved either in deuterated chloroform ($CDCl_3$) or in a 1:8 mixture of trifluoroacetic acid (TFA) and $CDCl_3$, and spectra were internally referenced to tetramethylsilane (TMS). About 10 and 50 mg of sample in 1 mL of solvent were used for ^{1}H and ^{13}C NMR, respectively. Sixty-four scans were recorded for ^{1}H and between 1,000 and 10,000 scans for ^{13}C NMR. High-performance liquid chromatography (HPLC) was performed at 25 °C in a Waters apparatus equipped with a UV detector of Applied Biosystems operating at a wavelength of 254 nm, and a Scharlau Science column (Si60, 5 μm; 250 x 4.6 mm). Cyclic oligomers (1 mg) were dissolved in chloroform (1 mL) and eluted with hexane:1,4-dioxane (70:30 v/v) at a flow rate of 1.0 $mL \cdot min^{-1}$. Molecular weight analysis was performed by GPC on a Waters equipment provided with RI and UV detectors. 100 μL of 0.1% (w/v) sample solution was injected and chromatographed with a flow of 0.5 $mL \cdot min^{-1}$. HR5E and HR2 Waters linear Styragel columns (7.8 mm x 300 mm, pore size 10^3-10^4 Å) packed with crosslinked polystyrene and protected with a

pre-column were used. Molar mass averages and distributions were calculated against PMMA standards.

Thermogravimetric analysis (TGA) of polymers was performed on a Mettler-Toledo TGA/DSC 1 Star System under a nitrogen flow of 20 mL·min^{-1} at a heating rate of 10 °C·min^{-1} and within a temperature range of 30-600 °C. The non-destructive thermal behaviour was examined by differential scanning calorimetry (DSC) within the 30-200 ºC range using a Perking-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. Melting temperature (T_m) was taken as the maximum of the endothermic peak appearing on the heating traces recorded from either polymer samples coming from synthesis or crystallized from the melt. Glass transition temperature (T_g) was taken as the inflection point of heating traces recorded at 20 °C·min^{-1} from melt-quenched samples. X-Ray diffraction patterns from powdered samples coming directly from synthesis were registered on a PANalytical X'Pert PRO MPD θ/θ diffractometer using the CuK_α radiation of wavelength 0.1542 nm. Micrographs were recorded using an Olimpus BX51 polarizing optical microscopy with a Linkam THMS 600 stage attached. For observation, 10 mg of sample were dissolved in 1 mL of 1,1,1,3,3-hexafluoro-2-propanol (HFIP) for PBF or chloroform for copolymers and PCL, and 0.2 mL aliquots of these solutions were slowly evaporated on a glass slide.

Synthesis of copolyesters

The cyclic oligomers *c*(BF)$_n$ used for copolymerization with CL were prepared by applying the high-dilution condensation method recently reported by us.[14] **¡Error! Marcador no definido.** Copolymerization of CL with *c*(BF)$_n$ was performed in bulk using CALB as catalyst. Briefly, mixtures of ε-caprolactone and *c*(BF)$_n$ with different compositions were placed in a three necked round bottom flask and heated at temperatures between 130 and 150 °C under a nitrogen atmosphere. Then 10% (w/w)

CALB was added to the reactants mixture and the reaction was left to proceed for 24 h. The reaction mixture was then cooled down to room temperature and a large volume of $CHCl_3$ was added to dissolve the polymer. After removing the enzyme by filtration, the solvent was evaporated under vacuum and the solid residue was dried for 24 h before analysis. PCL homopolyester was obtained from CL by the same procedure whereas the synthesis of PBF was performed by cyclopolymerization of $c(BF)_n$ catalyzed by TBT as previously described by us.[14]

Transesterification reactions in the copolyesters obtained by e-ROP were accomplished by subjecting them to heating in the presence of TBT. The selected copolyester and TBT (1 %-mole) were dissolved in $CHCl_3$ and the solution dried under vacuum to give a homogeneous residue that was heated at 200 °C for 24 h. After cooling, the treated product was dissolved in $CHCl_3$ and the solution filtered and evaporated to dryness. The residue was analyzed by ^{13}C NMR analysis to ascertain the degree of transesterification attained.

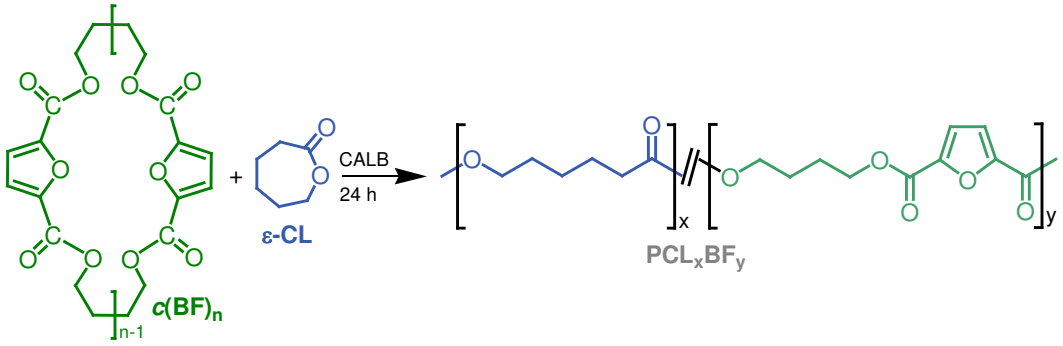
Hydrolytic and enzymatic biodegradation

Films for hydrolytic degradation and biodegradation studies were prepared from homopolyesters and copolyesters with a thickness of ~200 μm by casting from either HFIP or chloroform solution with a polymer concentration of 100 $g \cdot L^{-1}$. The films were cut into 10 mm-diameter, 20-30 mg-weight disks and dried under vacuum to constant weight. For hydrolytic degradation, samples were immersed in vials containing 10 mL of either citric acid buffer, pH 2.0 or sodium phosphate buffer, pH 7.4 at 37 °C. Enzymatic degradation assays were carried out at 37 °C in pH 7.4 buffered sodium phosphate solution with 10 mg of porcine pancreas lipase added. In this case the buffered solution was replaced every 72 h in order to maintain the enzyme activity. In both cases, the disks were withdrawn from the incubation medium at scheduled periods of time, washed carefully with distilled water, dried to constant weight, and finally analysed by GPC.

RESULTS AND DISCUSSION

Synthesis of PCL_xBF_y copolyesters by *e*-ROP

The method of synthesis used in this work for the preparation of copolyesters composed of 6-oxycaproate and butylene 2,5-furandicarboxylate units is based on the enzymatic ring opening polymerization (*e*-ROP) of mixtures of ε-caprolactone (CL) and a fraction of oligo(butylene 2,5-furandicarboxylate) cycles (*c*$(BF)_n$), as it is depicted in Scheme 1.



SCHEME 1. Enzymatic Ring Opening Polymerization (*e*-ROP) reaction leading to PCL_xBF_y copolyesters.

The oligomeric *c*$(BF)_n$ fraction was prepared by high dilution condensation of 1,4-butanediol and 2,5-furandicarboxylate dichloride according to a procedure recently described by us.[14] It consisted exclusively of cyclic species and was obtained in around 70% yield with a molar composition of approximately 60:30:10 in dimer, trimer and tetramer, respectively. It melts at 147 ºC and starts to decompose slightly above 275 ºC. This oligomeric fraction was used as it is, *i.e.* without separation of their different size components. A comparative kinetics study on the cyclopolymerization of individual *c*$(BF)_n$ species leading to PBF homopolyesters showed that although reactivity is higher for smaller cycle sizes, such differences are however not large enough as to warrant further fractionation.[14]

The polymerization reaction was carried out in bulk with both CL and *c*$(BF)_n$ in the molten state and the supported enzyme CALB suspended in the reaction mass. Reaction temperatures were set between 130 ºC, which is the minimum value required for melting the reactants, and 150 ºC, which is the maximum value compatible with enzyme activity. The capacity of CALB to retain polymerization catalytic activity at high temperatures has been reported in several occasions.[26-28] In this work an activity test has been carried out to confirm that such capacity is effective under the reaction conditions here used. Results are given in the SI document (Figure S1) which revealed that CALB retained about 80% of its initial activity after 24 h of reaction of a mixture of CL and *c*$(BF)_n$ at 150 ºC. CL:*c*$(BF)_n$ mixtures with molar ratios covering the whole range of compositions were assayed for producing a complete palette of PCL_xBF_y copolyesters. However copolyesters containing more than 80% of BF units as well as the PBF homopolyester could not be obtained by this procedure because of the too high melting temperature of these BF-enriched polyesters. In such cases the reaction mass became solid as soon as the polymer started to form which prevented further chain growing and attaining therefore acceptable molecular weights. The homopolyester PCL and the PCL_xBF_y copolyesters subjected to study in this work (Table 1) were prepared by *e*-ROP at 150 ºC and had M_w ranging between 50,000 for $PCL_{50}BF_{50}$ and 22,000 for $PCL_{20}BF_{80}$, and dispersities between 2.1 and 1.2. The PBF homopolyester used for reference had to be prepared by ROP at 250 ºC catalyzed by TBT and had a M_w of 65,000.

TABLE 1. Composition, Molecular Weight and Randomness of PCL_xBF_y Synthesized by *e*-ROP.

Polyester	Yield (%)	Composition[a] [CL]/[BF]		Molecular weight[b]		Microstructure[c]	
		Feed	Copolyester	M_w (g·mol^{-1})	$Đ$	n_{CL}	(B)
PCL	95	100/0	-	35,000	1.80	-	-
$PCL_{90}BF_{10}$	89	90/10	86/14	39,000	2.00	11.2 (6.6)	0.32 (0.50)
$PCL_{70}BF_{30}$	80	70/30	73/27	48,000	1.80	8.4 (3.2)	0.28 (0.36)
$PCL_{60}BF_{40}$	90	60/40	67/33	50,000	1.72	5.6 (5.5)	0.50 (0.55)
$PCL_{50}BF_{50}$	90	50/50	42/58	50,000	1.60	2.9 (1.3)	0.43 (0.66)
$PCL_{40}BF_{60}$	89	40/60	36/64	47,000	1.65	2.8 (n.d.)	0.44 (n.d.)
$PCL_{30}BF_{70}$	91	30/70	33/67	36,000	1.25	2.5 (1.5)	0.50 (0.70)
$PCL_{20}BF_{80}$	90	20/80	18/82	22,000	1.25	2.2 (1.3)	0.51 (0.58)
PBF	95	0/100	-	65,000	1.98	-	-

[a]Molar composition determined by ^{1}H NMR.
[b]Weight-average molecular mass and dispersity determined by GPC.
[c]Number average sequence lengths of CL units (n_{CL}) and degree of randomness (B) determined by ^{13}C NMR. In parenthesis, the values calculated for the copolyesters after heating treatment. n.d.: not determined.

Copolyesters composition and microstructure

The composition and microstructure of the whole series of PCL_xBF_y copolyesters obtained by *e*-ROP were determined by ^{1}H and ^{13}C NMR. These spectra are provided in the SI file associated to this paper (Figures S2 and S3) while the spectra registered from $PCL_{60}BF_{40}$ are presented in Figure 1 for illustration.

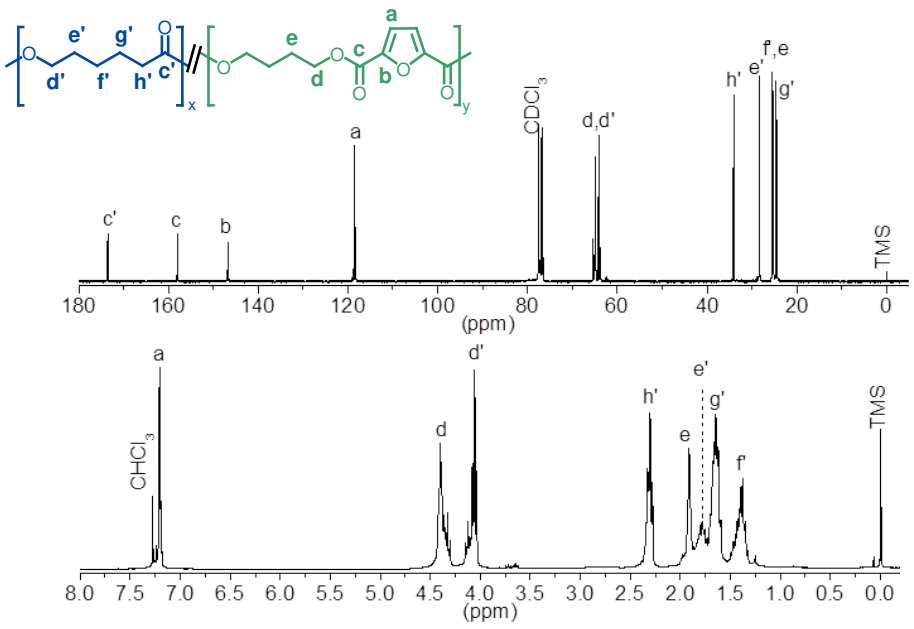


FIGURE 1. ^{13}C (top) and ^{1}H (bottom) NMR of $PCL_{60}BF_{40}$.

The molar composition of copolyesters in CL and BF units was determined by quantification of the ^{1}H NMR signals *d* and *d'* arising from the α-methylene of the ε-oxicaproate and oxybutylene units (Figure 1), respectively, and the resulting values are given in Table 1. A reasonable agreement between the CL:*c*$(BF)_n$ ratios found in the copolyesters and those used for their respective feeds was observed although differences became significant as the composition in the two units tended to equilibrate (about 15% for $PCL_{40}BF_{60}$ and $PCL_{50}BF_{50}$). Strikingly no apparent correspondence between the unbalancing sense and copolyester composition seems to exist.

The microstructure of the copolyesters was elucidated by NMR analysis on the basis of the ^{13}C NMR 24.5-24.6 ppm signal arising from the β-methylene of the ε-oxicaproate unit. This signal appears split into four peaks corresponding to the CLCLCL, CLCLB, FCLCL and FCLB triads present in the copolyesters (Figure 2a). The degree of randomness *B* was determined using the procedure reported by Tessier and Fradet[29] and later applied by us to copolymers made of cyclic oligo(hexamethylene terephthalate) with *p*-dioxanone,[30] which is based on the relative integration of the peak arising from homogeneous triad CL sequences. Equations 1 were used for determining the sequence lengths of BF (L_{BF}) and CL (L_{CL}),

$$L_{BF} = \frac{1}{1-a} \qquad L_{CL} = \frac{X_{CL}}{2X_{BF}(1-a)} \quad (\mathbf{eqs\ 1})$$

and the degree of randomness *B* is defined by equation 2. In these equations, x_{CL} and x_{BF} are the molar fractions of CL and BF units, respectively. *a* is a parameter specific for each composition that is calculated by means of equation 3 making use of the value of the triad fraction $F_{(CLCLCL)}$ obtained by integration of the corresponding ^{13}C NMR peak. The *B* values resulting from these calculations are listed in Table 1. These values are in the 0.28-0.51 range indicating that the microstructure of PCL_xBF_y prepared by *e*-ROP is in blocks with average homogeneous CL sequence lengths oscillating between 2 and 12 depending on composition.

$$\boldsymbol{B} = \frac{(1-a)(2X_{BF} + X_{CL})}{X_{CL}} \qquad (\mathbf{eq\ 2}) \qquad\qquad F(\mathrm{CLCLCL}) = \left(1 - \frac{2X_{BF}(1-a)}{X_{cL}}\right)^2 \qquad (\mathbf{eq\ 3})$$

As it is well known transesterification reactions usually take place in polyesters when they are heated at temperatures above their softening point and an appropriate catalyst is added. With the purpose of increasing the degree of randomness in the blocky PCL_xBF_y copolyesters prepared by *e*-ROP, samples were subjected to heating at 200 ºC in the presence of TBT for 24 h. As a consequence of this treatment slight changes in the copolyester compositions and molecular weights, which could be partially attributed to thermal degradation, were observed (for details see Table S1 in the SI file). The fact that the molecular weight slightly decreased instead of increasing with the heating treatment seems to indicate that no transesterification reactions implying chain ends occurred. However, this cannot be ascertained since no investigation of the occurrence of end groups has been performed. The ^{13}C NMR 24.5-24.6 ppm signal profiles registered from the heated copolyesters are compared with those obtained from the pristine samples in Fig. 2b. According to which should be expected for transesterification, a relative increasing of intensity of the peaks arising from triads other than CLCLCL became apparent after the heating treatment. The *B* values resulting for the heated copolyesters were found to range from 0.36 to 0.70, and the maximum length of the homogeneous CL sequences present in these copolyesters was now reduced to about six (Tables 1 and S1). Although a complete randomization has not been attained, microstructure differences are large enough as to deserve consideration regarding the thermal properties of the copolyesters. This issue will be discussed below.

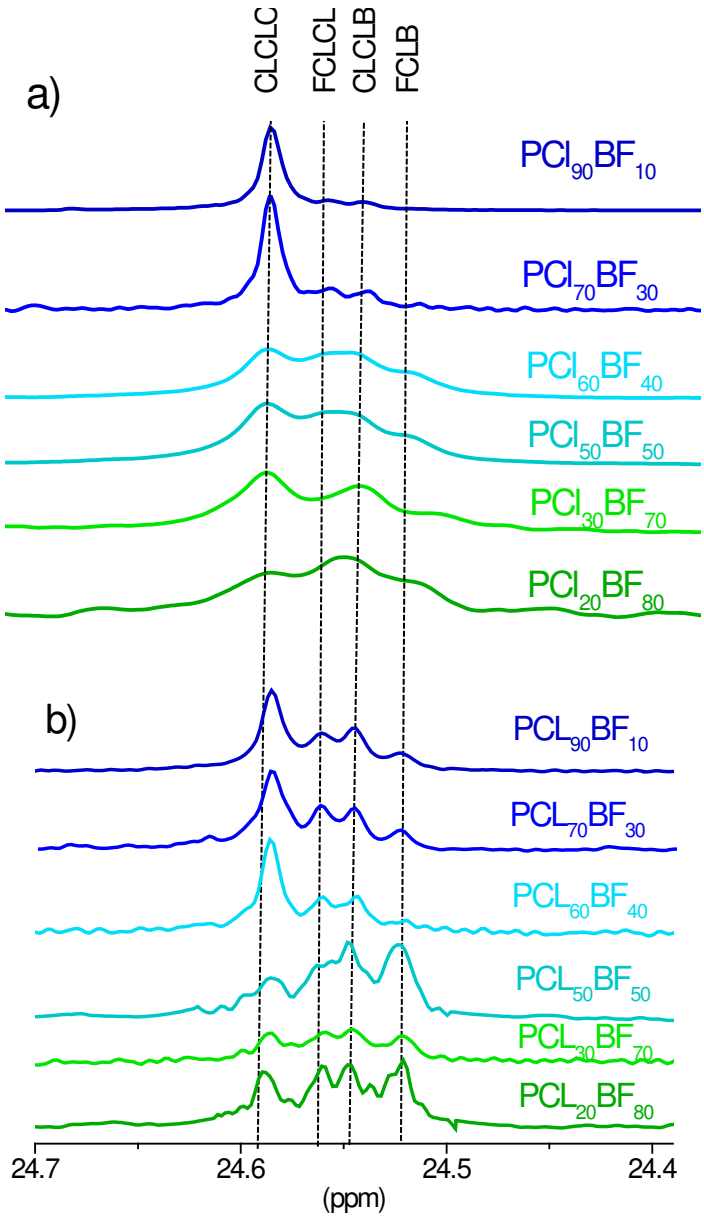


FIGURE 2. ^{13}C NMR spectra of the PCL_xBF_y copolyesters enlarged in the region 24.4-24.7 ppm. a) Before transesterification and b) after transesterification.

Thermal properties of PCL_xBF_y copolyesters

The thermal behavior of the PCL_xBF_y copolyesters obtained by *e*-ROP was examined by both TGA and DSC, and the most representative decomposition and phase transition parameters were measured by these techniques and listed in Table 2.

TABLE 2. Thermal Properties and Crystallizability of PCL_xBF_y Copolyesters Prepared *via e*-ROP.

Copolyester	TGA[a]			DSC[b]					Crystallization kinetics[c]			
					First heating		Second heating					
	$^{o}T_d$ (°C)	$^{max}T_d$ (°C)	R_w (%)	T_g (°C)	T_m (°C)	ΔH (J·mol^{-1})	T_m (°C)	ΔH (J·mol^{-1})	Tc (ºC)	n	ln$K$	$t_{1/2}$ (min)
PCL	345	401	10	-60	65	56	64	40	40	2.4	-2.59	2.4
									36	3.2	-1.75	0.4
$PCL_{90}BF_{10}$	330	384	11	-37	52	35	51	27	27	2.3	-4.23	4.7
									36	2.4	-4.94	2.4
$PCL_{70}BF_{30}$	332	392	7	-13	101	21	100	16	76	2.3	-4.44	5.6
$PCL_{60}BF_{40}$	342	390	6	-8	116	26	115	12	-	-	-	-
$PCL_{50}BF_{50}$	321	382	11	0	130	13	130	13	-	-	-	-
$PCL_{40}BF_{60}$	317	386	8	8	135	12	135	4	-	-	-	-
$PCL_{30}BF_{70}$	325	387	9	11	135	17	136	15	136	1.7	-1.65	2.0
$PCL_{20}BF_{80}$	323	388	8	19	148	33	152	32	128	2.4	-5.62	9.1
									136	2.4	-6.90	6.5
PBF	346	391	7	42	172	38	170	38	146	2.2	-4.42	10.3
									136	2.5	-5.33	6.7

[a]Thermogravimetric analysis under inert atmosphere. Thermal decomposition temperatures measured at 5% of weight lost ($^{o}T_d$) and at maximum weight loss rate ($^{max}T_d$). R_w: weight (%) remaining after heating at 600 ºC.
[b]DSC analysis for the first heating and for the second heating registered after cooling. The glass transition temperature (T_g) was measured at heating from samples quenched from the melt.
[c]Avrami parameters (n and K) and crystallization half-time ($t_{1/2}$) determined by isothermal crystallization at the indicated temperatures.

The TGA traces recorded for the whole copolyesters series are compared in Figure 3a and the derivative curves of a representative selection of them are depicted in Figure 3b. PCL and PBF homopolyesters have a very close behavior when subjected to heating at high temperatures under an inert atmosphere with onset and maximum rate decomposition temperatures differing in less than 3%. The values measured for the copolyesters are between those of the parent homopolyesters with $^{o}T_d$ and $^{max}T_d$ located within the 315-345 ºC 380-390 ºC ranges approximately. These results bring into evidence the high thermal resistance to heating of the PCL_xBF_y copolyesters and ensure their suitability for being processed by thermal methods.

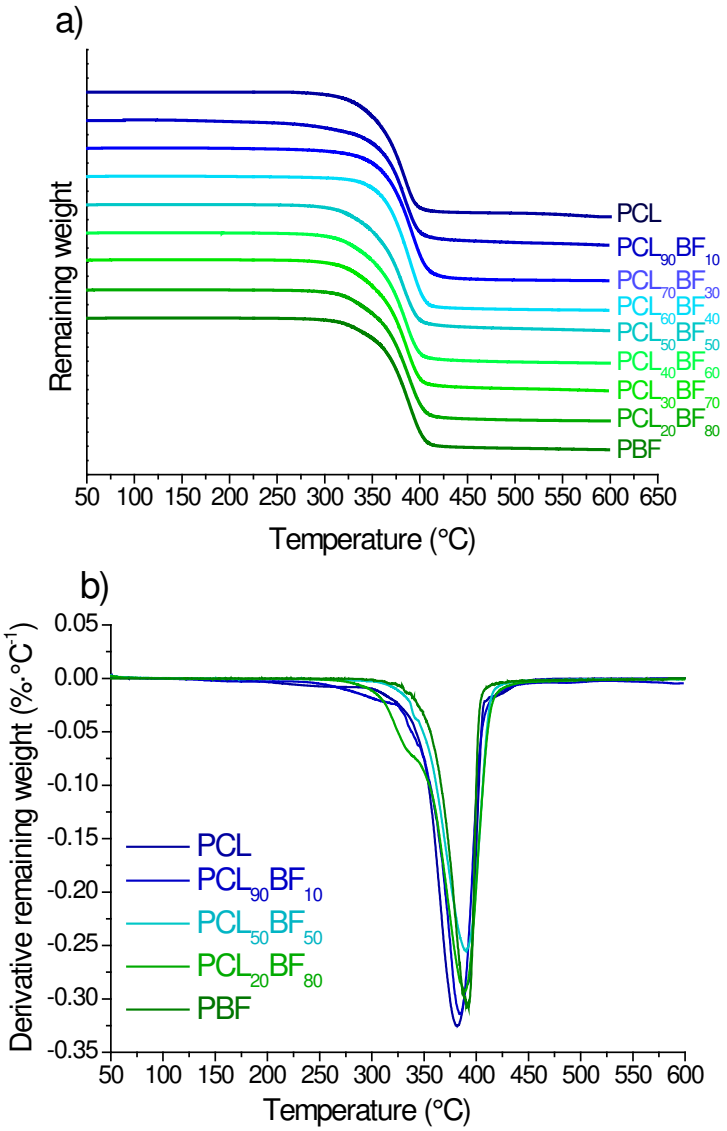


FIGURE 3. TGA traces of PCL_xBF_y copolyesters recorded under inert atmosphere (a) and the derivative curves of a selection of them (b).

The DSC traces recorded for the PCL_xBF_y series as well as for the two parent homopolyesters along the first heating-cooling-second heating cycle are shown in Figure 4. PCL and PBF are semicrystalline polyesters with T_m at 64-65 ºC and 170-172 ºC, respectively, and both were able to crystallize from the melt by almost reproducing the initial melting temperatures and developing a considerable crystallinity. All the copolyesters showed melting with enthalpy and temperature progressively decreasing from those of PBF as the content in CL increased (Figure 4a, first heating traces), and this behavior was shared by copolyesters that were crystallized from the melt (Figure

4c, second heating traces). With the exception of $PCL_{90}BF_{10}$, the melting observed in the copolyesters arises from the crystalline phase made of homogeneous BF sequences. It seems therefore that upon cooling, butylene 2,5-furandicarboxylate segments crystallized firstly preventing the crystallization of the ε-oxycaproate segments that became confined in between the initially formed PBF crystallites. This situation is only avoided for very low contents in BF (10% or less) because the BF sequences are then too short (less than four units) to be able to form stable crystallites. This interpretation is strongly supported by powder X-ray diffraction (XRD) which provided crystalline scattering profiles containing only characteristic PBF peaks[9,31] for polyesters with less than 90% of CL units (Figure S4 in the SI file). Furthermore polarizing optical microscopy (POM) of films crystallized from the melt showed crystalline morphologies consistent with their composition and texture changes taking place when 30% of BF units in the copolyester was reached (Figure S5 in the SI file).

On the other hand the glass-transition temperature of the copolyesters was observed to increase steadily along the whole -60-42 ºC interval limited by the values of PCL and PBF. DSC traces registered at faster heating rates from samples quenched from the melt are depicted in Figure 5. Apparently the insertion of the rigid BF units in the flexible chain of PCL largely restricts the mobility with the consequence of a very notable increase in T_g. Both T_m and T_g of PCL_xBF_y are plotted against the content in BF units in Figure 6. The trend observed for T_m is nearly linear for the whole series excluding $PCL_{90}BF_{10}$ which is highly reasonable since this copolyester is the only one containing crystallites made of PCL segments. The plot of T_g against the percentage content in BF units is also roughly linear with a moderate dispersion of values and an average positive slope of about 1 ºC·(BF-%)$^{-1}$. This result is particularly remarkable since it indicates that significant improvements in properties as rigidity, hardness and barrier may be achieved for PCL when moderate amounts of BF units are inserted in its chain.

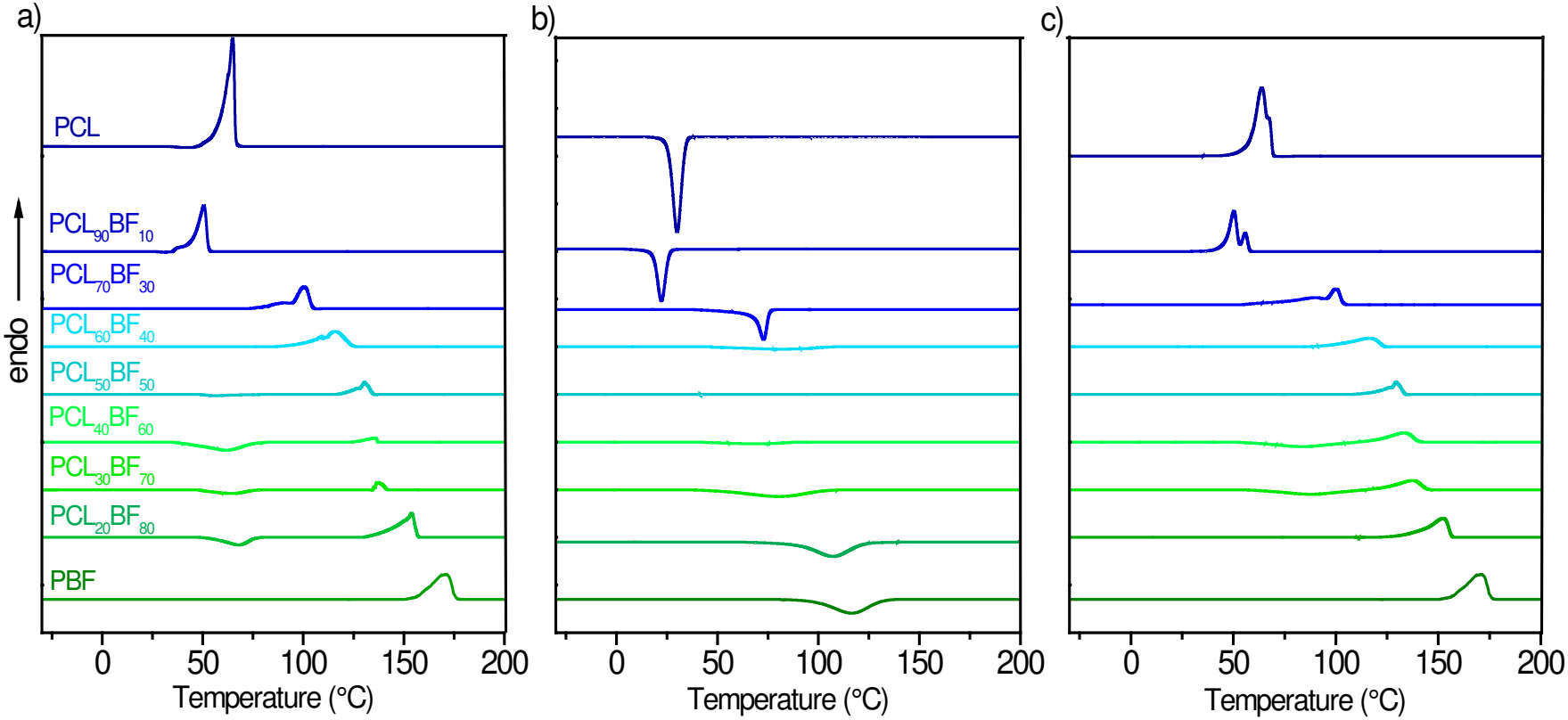


FIGURE. 4. DSC traces of PCL_xBF_y. a) First heating, b) cooling and c) second heating.

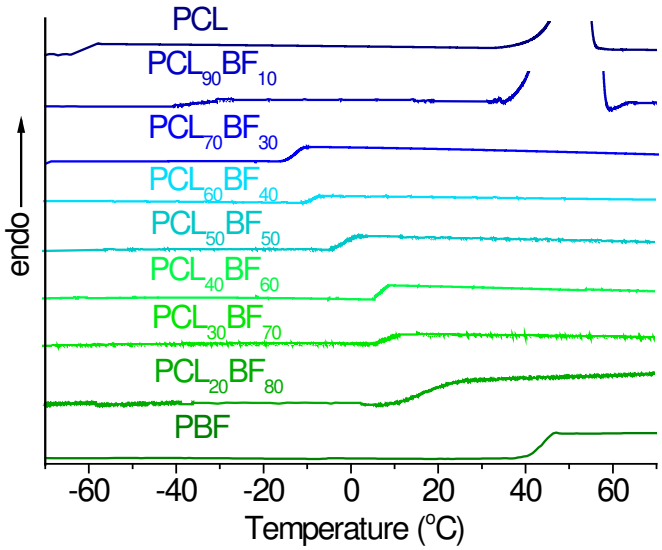


FIGURE. 5. DSC traces registered at a heating rate of 20 ºC· min^{-1} to show more clearly the inflections arising from T_g.

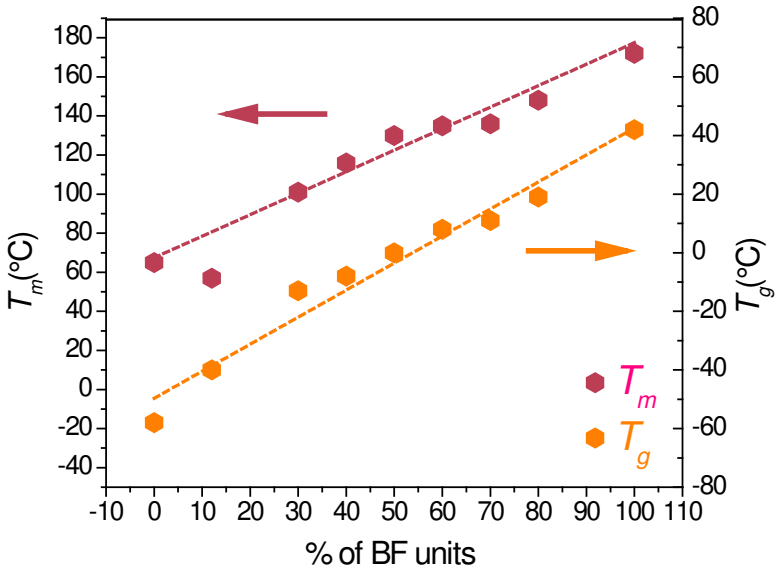


FIGURE. 6. Plots of T_m (a) and T_g (b) of PCL_xBF_y against the content of the polymer in BF-units.

Crystallizability

The ability for crystallizing upon cooling from the melt is a polymer property of high relevance as far as thermal processing is concerned. Both crystallization rate and crystallinity are the most significant parameters for a quantitative evaluation of polymer

"crystallizability". In order to appraise the effect of copolymerization on the crystallizability of the PCL_xBF_y system, a kinetics study of the isothermal crystallization of these polyesters has been carried out. Since crystallization temperature of PCL_xBF_y varies largely according to composition, the comparative study has to be limited to small groups of polyesters able to crystallize at the same temperature. The plots of relative crystallinity *vs* crystallization time for three different cases are shown in Figure 6. In Figure 6a, the homopolyesters and a selection of copolyesters with different composition are compared at different crystallization temperatures. According to what it is well known, PCL was observed to crystallize much faster than PBF, and in agreement whit this, crystallization rate of copolyesters was found to decrease for increasing contents in BF units. The observed behavior is not irrefutable however since it is obviously affected by differences in crystallization temperatures. In Figure 6b, the isothermal crystallization curves registered at 136 ºC for PBF and for two copolyesters containing different amounts of CL units are compared. This result certainty demonstrates the enhancing effect that the flexible ε-oxycaproate structure has on the crystallization rate of PBF. Reciprocally, the influence of the BF units on the crystallizability of PCL is evidenced in Figure 6c where the *X-t* curve of the homopolyester registered at 36 ºC is compared with that of the $PCL_{90}BF_{10}$ copolyester crystallizing at the same temperature. It is apparent therefore that the presence of the relative stiff furanoate units delays the crystallization of PCL.

Isothermal crystallization data were used for carrying out the Avrami kinetics analysis of all the compared polyesters. Double logarithmic plots of crystallinity *vs* time (see Figure. S6, SI file) were used for selecting the periods of time suitable for the analysis, and the Avrami parameters resulting for the homopolyesters and the selected copolyesters at different temperatures are listed in Table 2. Crystallization half times ($t_{1/2}$) oscillated between 0.4 min for the crystallization of PCL at 36 ºC and 10.3 min for PBF crystallized at 146 ºC. As it was already qualitatively deduced form the graphical

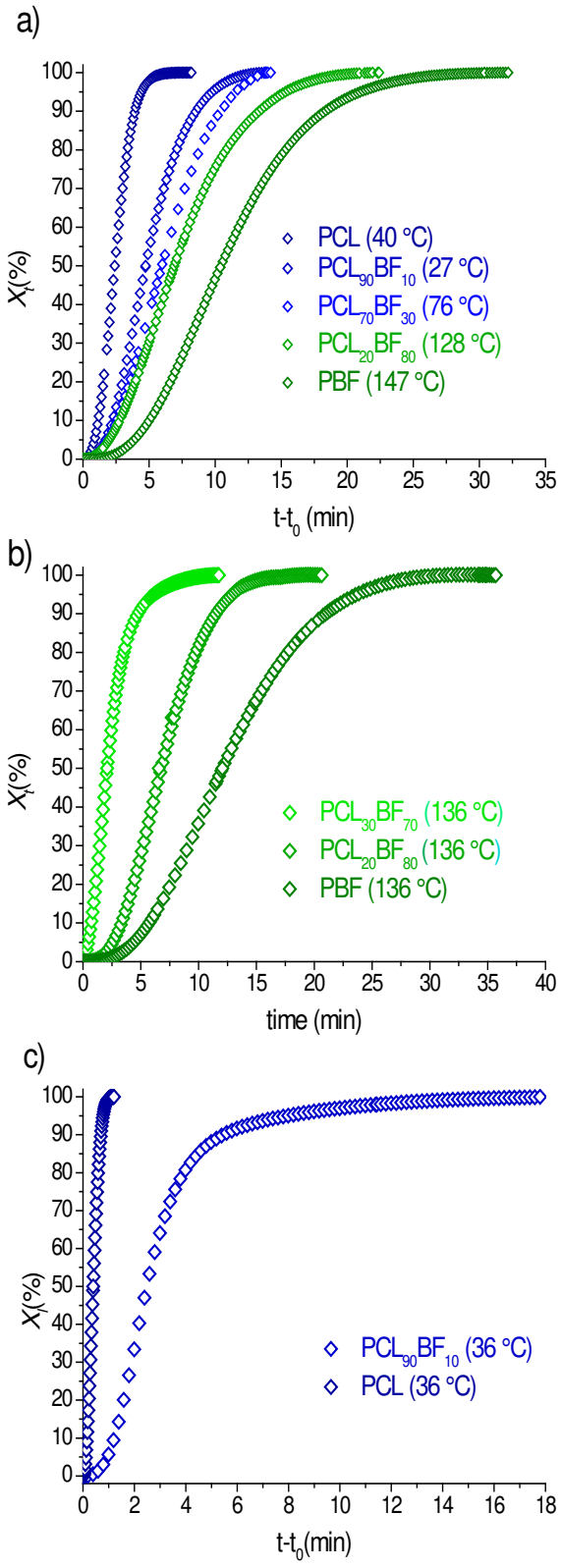


FIGURE 6. Crystallinity *vs* time plots for the isothermal crystallization of PCL_xBF_y copolyesters. a) A selection of polyesters crystallizing at different temperatures. b) BF-enriched polyesters with different contents in CL units crystallizing at the same temperature. c) PCL and PCL containing BF units crystalizing at the same temperature.

representations (Figure 6), $t_{1/2}$ of CL-enriched copolyesters increased with the presence of PBF and the opposite happened when the CL content increased in the BF-enriched copolyesters. It is worthy to note the effect of crystallization temperature on $t_{1/2}$ when comparison is made for the same polyester. In the case of homopolyesters crystallization rate decreased with temperature whereas the contrary effect was observed for copolyesters. It seems therefore that self-nucleation and chain mobility are the factors determining crystal growth for homopolyesters and copolyesters, respectively. This result is consistent with the blocky microstructure of the copolyesters since crystallization of the small blocks implies a topological rearrangement of the polymer chains that is favored by temperature, a requirement that is not needed by homopolyesters.

Since thermal properties of copolymers are largely affected by the chain microstructure, it is worthy of comment how this issue applies to PCL_xBF_y copolyesters. With this aim these copolyesters were analyzed by TGA and DSC after increasing their randomness degree by heating treatment (Table S1). The traces recorded from the whole series are depicted in the SI file (Figures S7 and S8), which revealed that differences in the T_d , T_m and T_g parameters with those obtained from the untreated copolyesters were not significant. On the contrary, the effect of the microstructure changes on crystallizability was much noticeable (Figure S9 in SI file). As expected, the crystallization rate of PCL_xBF_y decreased as the randomness of the copolyester increased, and this was applicable to copolyesters enriched in either CL or BF units, with crystallization halftimes becoming up to near eight times higher after the heating treatment (Table S2 in SI).

Hydrolytic degradation and biodegradation

The response of PCL to the action of water is well known. At temperatures close to ambient this polyester displays a high resistance to hydrolysis whereas it is rapidly degraded in the presence of lipases. On the contrary, PBF is quite resistant to the aqueous media both with and without enzymes added. The biodegradability of PCL-PBF copolyesters prepared by polycondensation has been explored by following by SEM the morphological changes taking place on the surface of samples incubated in water for four weeks.[25] This study reported that the copolyesters were eroded in an extent that increased with the content in CL units. In the present work a quantitative study of the degradability of PCL_xBF_y copolyesters has been carried out by following the decrease in both weight sample and polymer molecular weight along 40 days of incubation in water at 25 ºC with and without lipases added to the medium. A set of four copolyesters differing significantly in composition in addition to their two parent homopolyesters was selected for this study. Results are shown in Figure 7 where percentages of the remaining weight and the weight-average molecular weight are plotted against time. In the absence of lipases degradation was very scarce for all the examined polymers with practically no changes for PBF and maximum changes observed for PCL that were however of only about 2% and 4% for sample and molecular polymer losses, respectively (Figures 7a and 7a'). Conversely the observed response was much more pronounced when samples were incubated in the presence of porcine pancreas lipases so that ostensible differences were observed depending on composition (Figures 7b and 7b'). In full agreement with expectations, PBF remained unaltered whereas PCL degraded completely. The changes observed for copolyesters were more pronounced for higher contents in CL units with weight losses ranging from 20 and 40 % for $PCL_{30}BF_{70}$ and $PCL_{70}BF_{30}$, respectively. It becomes clear from our study that the hydrodegradability of PCL_xBF_y copolyesters under mild conditions is practically negligible whereas they become notably hydrolyzed in the presence of lipases. It is worth noting also that PBF may be made biodegradable by introducing in its chain moderate amounts of CL without practical alteration of their hydrolytic resistance.

CONCLUSIONS

The synthesis of cyclic (butylene 2,5-furandicarboxylate) oligomers, *c*$(BF)_n$, recently reported by us has prompted their use as monomers in Ring Opening Polymerizations leading to PBF homopolyesters and copolyesters. In the present work these cyclic oligomers have been copolymerized in bulk with ε-caprolactone by using CALB as catalyst. It is the first time that this synthesis is reported and that *c*$(BF)_n$ is copolymerized with a lactone of A-B type. The procedure avoids the use of both organic solvents and organometallic catalysts and leads therefore to polymers greener than those obtained by conventional polycondensation. Our results show that PCL-PBF copolyesters with a wide range of compositions and satisfactory molecular weights could be produced in high yields. Amazingly these copolyesters display a blocky distribution of the comonomers along the polymer chain which is in contrast with the random microstructure found for other PBF copolyesters prepared by this method. The copolyesters are semicrystalline with their T_m*'s* and T_g's oscillating between those of PCL and PBF. Copolyesters with minor contents in any of the two components are able to crystallize from the melt at a rate that decreases with the presence of stiff furanoate units. Furthermore, it is remarkable the notable increasing attained in the T_g of PCL when moderate amounts of furanoate units are incorporated in the chain for the relevance that this property has on the physical behavior of the polyester. On the other side, the influence of the presence of CL units on the biodegradability of PBF is more than remarkable given the strong reluctance of this polyester to be hydrolyzed under mild conditions. The overall conclusion is that a greener synthetic method has been developed for the preparation of PCL-PBF copolyesters free of metallic contaminants, and that these polymers display properties of interest for their potential use in packaging and biomedicine.

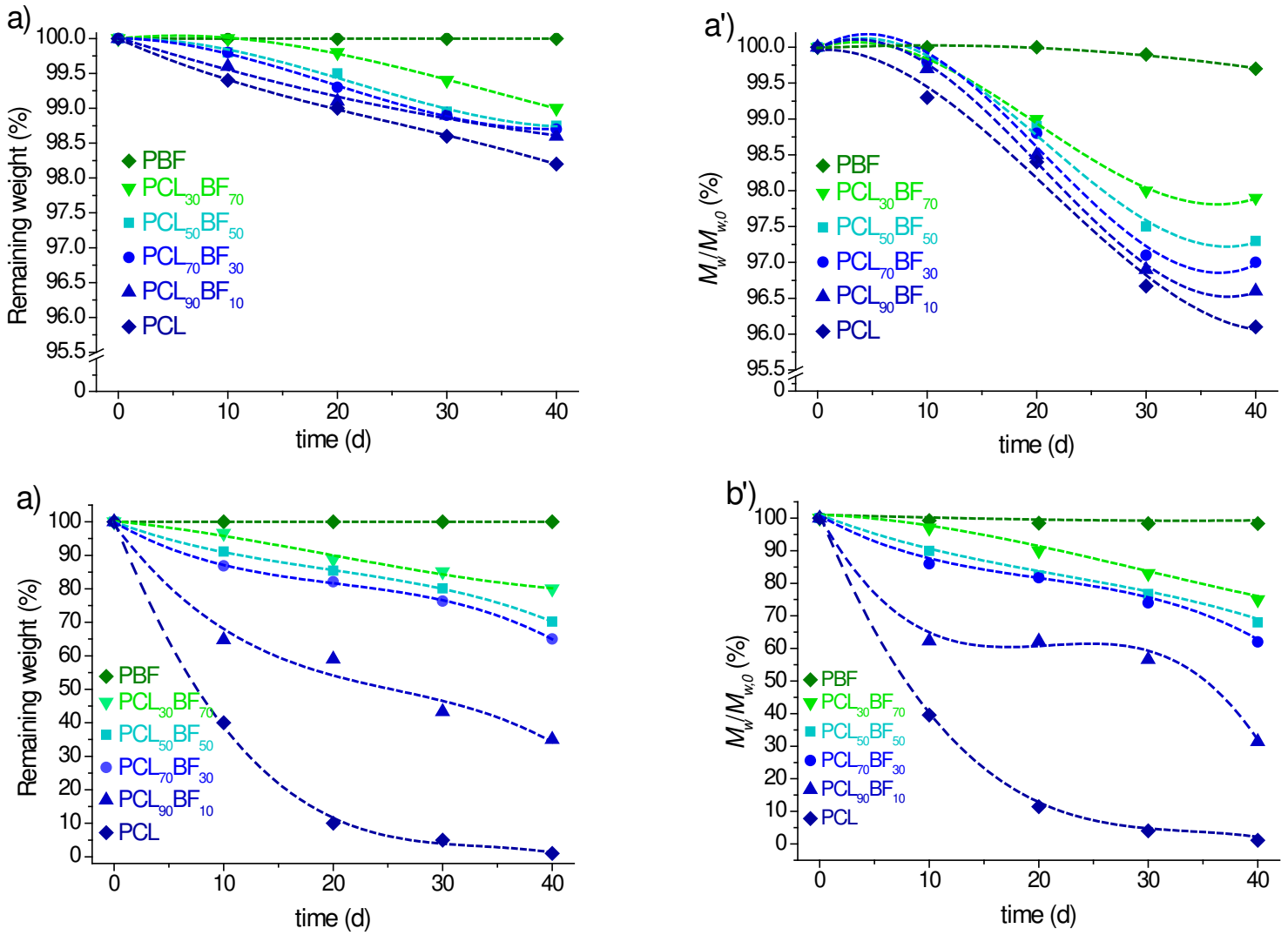


FIGURE 7. Degradation of PCL_xBF_y upon incubation in aqueous medium at pH 7.4 and 25 ºC followed by the decreasing in both weight and molecular weight with time a,a') In the absence of enzymes. b,b') With lipases added.

.**ACKNOWLEDGEMENTS**

Financial support for this research was afforded by MINECO with grants MAT-2012-38044-CO3-03 and MAT-2016-77345-CO3-03. J.C. Morales-Huerta thanks to CONACYT (Mexico) for the Ph.D. grant awarded. Authors are also thankful to Novozymes for providing the Novozym 435 that has been used throughout in this work.

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