Exploring the effect of alkyl end group on poly(L-lactide) oligo-esters. Synthesis and characterization

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Abstract Poly(L-lactide) (PLLA) oligo-esters with α-hydroxyl-ω-alkyl (alkyl = $-CH_2-[CH_2-CH_2]_n-CH_3$, where n = 1, 2, 4, 5, 6, 7, 8, 9, and 10) end groups were synthesized by ring-opening polymerization of L-lactide (L-LA) catalyzed by tin(II) 2-ethylhexanoate $Sn(Oct)_2$ in the presence of aliphatic alcohols as initiators ($HO-CH_2-[CH_2-CH_2]_m-CH_3$, where m = 1, 2, 4, 5, 6, 7, 8, 9, and 10). High yields (~ 62 to 71 %) and M_n(NMR) in the range of 2120-2450 Da (PLLA) were obtained. Effects of alkyl end groups on thermal properties of the oligo-esters were analyzed by DSC, TGA and SAXS. Glass transition temperature (T_g) gradually decreases with increase in the percent of $-CH_2-[CH_2-CH_2]_m-CH_3$ end group, as results alkyl end group provides most flexibility to PLLA. An important effect of alkyl end group on a double cold crystallization (T_{c1} and T_{c2}) was observed, and is directly related with the segregation phase between alkyl end group and PLLA. TGA analysis revealed that PLLA oligo-esters are more thermally stable with docosyl ($-C_{22}H_{45}$) respect to the butyl ($-C_4H_9$) end group, probably is due to steric hindrance of the end group (docosyl respect to butyl) toward intermolecular and intramolecular transesterification. SAXS analysis showed that alkyl end group as docosyl restricted the growth of lamellae thickness (D) due to steric hindrance. Characterization of hydroxyl and alkyl end groups in the PLLA oligo-esters was determined by MALDI-TOF, GPC, FT-IR and ^{1}H and ^{13}C NMR.

Keywords Poly(L-lactide)/Oligo-esters/Alkyl end group/Double cold crystallization/lamellae thickness/

Introduction

Poly(L-lactide) (PLLA) **1** is an important aliphatic polyester with degradable properties and potentials application in biomedical area [1]. Typically, PLLA is obtained by ring-opening polymerization (ROP) of L-lactide (L-LA) in presence of a catalyst as tin (II) 2-ethylhexanoate or tin octato $Sn(Oct)_2$ [1-3]. $Sn(Oct)_2$ is the most important catalyst in ROP of lactones because was approved by Food and Drugs Administration (FDA) as food additive [4].

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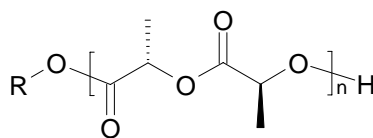
where R = H or alkyl

In ROP of lactones is common the use of initiators, for example: primary and secondary aliphatic alcohols (ROH) [2]. Initiator (ROH) can react with $Sn(Oct)_2$ and produce a tin alkoxide (Oct-Sn-OR) by transfer reaction [5,6], where tin alkoxide is active specie in the ROP of lactones as L-LA [6], as result a polyester with aliphatic (R) and hydroxyl (OH) end group can be obtained. A similar synthetic method was reported by Seppälä and coworkers [3] in the synthesis of PLLA with different hydroxyl end-groups.

PLLA with terminal groups α-hydroxyl-ω-alkyl has been used as: a) macroinitiator in the synthesis of diblock copolymers [7-9], b) compatibilizer within polymer blends

polyethylene/PLLA [10,11] and c) depressed factor in erosion surface of PLLA by enzymatic and hydrolytic degradation due to alkyl end group [12-14].

Recently, Abe and coworkers [12,13] studied the effect of alkyl end groups as dodecyl ($C_{12}H_{27}$) or tetracosyl ($C_{24}H_{49}$) on enzymatic [12,13] and nonenzymatic [13] degradation of the PLLA, they found that the alkyl end group affected the enzymatic degradation, end groups with carbon number bellow 11 and over 12 were homogeneously and heterogeneously degraded, respectively [13]. Contrary, the thermal properties of PLLA samples showed similar values and independent of the structure in the terminal alkyl group. In the two works previously reported [12,13], only high molecular weights were used for the study of PLLA with different alkyl end groups (M_n(GPC) = 106000 [12], and 73000 [13]). In a third work [14], the thermal properties of PLLA oligo-esters (M_n(GPC) = 7800-39000) with only a small alkyl end group as dodecyl ($C_{12}H_{27}$) were nearly identical respect to nonend-capped PLLA.

Hypothetically, the effect of one end group can be most important on PLLA oligo-ester (M_n(GPC) ~ 3500) that to polyester high molecular weights. However, the effect of linear alkyl end-group ($CH_3-[CH_2-CH_2]_m-CH_2-$) with systematic increase on PLLA oligo-esters never has been reported. In this work, a versatile synthesis of α-hydroxyl-ω-alkyl poly(L-lactide)s (PLLA)s is reported. In Scheme 1, different linear aliphatic alcohols ($HO-CH_2-[CH_2-CH_2]_m-CH_3$, where m = 1, 2, 4, 5, 6, 7, 8, 9, and 10) has been successfully used as initiators/chain transfer agents in each new reaction from ROP of L-lactide (L-LA) catalyzed by Sn(Oct)$_2$. The alkyl end group in PLLA was increased from butyl (C_4H_9) to docosyl ($C_{22}H_{45}$). α-Hydroxyl-ω-alkyl PLLA oligo-esters with M_n(GPC) =

3520-3600 [M_n(NMR) = 2120-2450] were obtained and characterized by ^{1}H and ^{13}C NMR, GPC, FT-IR and MALDI-TOF. The effects of the alkyl end group on PLLA oligo-esters were observed by DSC, TGA and SAXS.

Experimental

Materials

L-lactide (L-LA) [PURAC Biomaterials] was used without further purification. 1-butanol, 1-hexanol, 1-decanol, 1-dodecanol, 1-tetradecanol, 1-hexadecanol, 1-octadecanol, 1-eicosanol, 1-docosanol and tin (II) 2-ethylhexanoate [Sn(Oct)$_2$] were purchased from Aldrich and used without further purification.

Typical procedure for the synthesis of α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA10)

Polymerization was carried out in a 100 ml round-bottomed flask previously dried. L-lactide (L-LA, 40 mmol, 5.760 g), 1ml of a solution 0.123 M of tin(II) 2-ethylhexanoate Sn(Oct)$_2$ in toluene and 1-docosanol (4 mmol, 1.306 g) were charged and heated to reflux by stirring them in an oil bath at 170 °C for 2h (molar ratio LLA/Sn(Oct)$_2$ = 325 and L-LA/1-docosanol = 10). The oligo-ester obtained was precipitated from chloroform/methanol, recovered by filtration and dried under vacuum. The yield was calculated based on weight of monomer at the feed (yield = 69 %), M_n(NMR) = 2120, M_n(GPC) = 3600, M_w/M_n = 1.24. Other PLLA oligo-esters (PLLA1-9) were prepared and isolated in the same manner as described in the PLLA10. Molecular weight was monitored by ^{1}H NMR. IR (cm^{-1}): 2927 (ν_{as}, CH), 1757 (ν, C=O), 1457 (δ_s, CH), 1184 (ν_{as},

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C−(C=O)−O), 1091 (ν_{as}, O−C−C). ^{1}H NMR data for α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA10) (Figure 1): (300 MHz, CDCl$_3$, ppm) δ 5.18 (quartet, 1H, [C*H*], PLLA), 4.37 (quartet, 1H, [C*H*−OH], PLLA) 4.13 (octet, 2H, [C*H$_2$*O], docosyl), 1.60 (d, 3H, [C*H$_3$*], PLLA), 1.52 (d, 3H, [C*H$_3$*], PLLA), 1.50 (d, 3H, [C*H$_3$*], PLLA), 1.24 (s, 2H, [C*H$_2$*], docosyl), 0.87 (t, 3H, [C*H$_3$*], docosyl). ^{13}C NMR data for α-hydroxyl-ω-hexyl poly(L-lactide) (PLLA2) (Figure 2): (75 MHz, CDCl$_3$, ppm) δ 174.99 (g), 170.04 (q), 169.49 (j), 69.23 (h), 68.91 (k), 66.58 (m), 65.58 (f), 31.22 (c), 28.31 (e), 25.28 (d), 22.38 (b), 20.40 (p), 16.73 (i), 16.54 (l), 13.87 (a).

Characterization

^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Varian Unity *Plus* 300 (300 MHz ^{1}H and 75.47 MHz ^{13}C) and Bruker Avance 500 (500 MHz ^{1}H and 125 MHz ^{13}C). Chloroform-*d* (CDCl$_3$) was used as solvent. Spectra were referenced to the residual solvent protons at δ 7.26 for CDCl$_3$ in the ^{1}H NMR spectrum and the residual solvent carbons at δ 77.0 in the ^{13}C NMR spectrum. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) spectra were recorded in the linear mode by using a Voyager DE-PRO time-of-flight mass spectrometer (Applied Biosystems) equipped with a nitrogen laser emitting at 337 nm with a 3 ns pulse width and working in positive-ion mode and delayed extraction. A high acceleration voltage of 25 kV was employed. 2,5-Dihydroxybenzoic acid (DHB) at a concentration of 10 mg/ml in acetonitrile was used as matrix. Samples were dissolved in acetonitrile and mixed with the matrix at a molar ratio of approximately 1:100. FT-IR spectra were obtained with the attenuated total reflectance spectroscopy (ATR) technique on powder deposited over a diamond on zinc selenide

(ZnSe) crystal in a Perkin-Elmer Precisely Spectrum 100 FT-IR spectrometer. GPC measurements were determined using a Waters 244 gel permeation chromatograph equipped with a refractive index detector. A set of 104, 103 and 100 Å waters columns conditioned at 25 °C were used to elute samples at the flow rate of 1 ml/min HPLC-grade chloroform. Polystyrene standards (Polymer Laboratories) were used for calibration. Differential scanning calorimetry (DSC) was performed in a Mettler Toledo DSC822e instrument. Samples were sealed in aluminum pans. Two scans (25−180 °C and 0−180 °C) were performed with an initial heating rate of 10 °C/min and the fastest cooling rate of the instrument between runs under nitrogen purge. The melting points (T_m) and crystallizations temperatures (T_c) are given as the maximum and minimum of the endothermic and exothermic transition, respectively; and the data reported was taken from the second scan. The degree of crystallinity (x_i) for the PLLA homopolymer was calculated from the endothermic peak area ΔH_i by $x_i = \Delta H_i/\Delta H_i^0$, where ΔH_i^0 is the heat of fusion for perfect PLLA crystals (93 J/g) [11,15]. A thermal analysis (TA) Q500 instrument was used for TGA. Samples with weights between 10 and 30 mg were scanned in Hi-Resolution mode with an initial heating rate of 10 °C/min under flux of nitrogen. SAXS measurements were taken at beamline BM16 at the European Synchrotron Radiation Facility (Grenoble, France). Samples were placed in between aluminum foils within a Linkam hot stage and heated at 10°C/min while the SAXS spectra were recorded. Calibration of temperature gave a difference of approximately 7°C between the temperature reading at the hot stage display and the real temperature at the sample. Long period (L) and lamellae thickness (D) were calculated by $L = 2\pi/q_{max}$ and $D = L.x_i$, where q_{max} and x_i is the maximum scattering peak (by SAXS) and degree of crystallinity (by DSC), respectively.

Results and discussion

Synthesis and Characterization

Tin(II) 2-ethylhexanoate [Sn(Oct)$_2$] have been previously reported as catalyst for ring-opening polymerization (ROP) of lactones as L-lactide (L-LA) [1-3]. Storey and coworkers investigated the ROP of ε-caprolactone (CL) and L-LA by Sn(Oct)$_2$ [16] and stannous ethoxide Sn(OEt)$_2$ [17] as catalysts, respectively, in the case of Sn(Oct)$_2$ they found that 1-butanol is better initiator respect to ethylene glycol or 1,3-propanediol because a cyclic complex in the transfer reaction is not favored [16]. Usually, Sn(Oct)$_2$ in presence of an alcohol is one of the best catalyst in the synthesis of poly(L-lactide) (PLLA) due to control of molecular weight and an appropriate route for the obtention of end-funtionalized poly(L-lactide) (PLLA). In our case, ROP of the L-LA was carried out with Sn(Oct)$_2$ as catalyst and nine different aliphatic primary alcohols as initiators/transfer-agents (CH$_3$−[CH$_2$−CH$_2$]$_m$−CH$_2$−OH (ROH), where m = 1,2,4,5,6,7,8,9, and 10) with a L-LA/Sn(Oct)$_2$ and L-LA/ROH feed molar ratio of 325 and 10, respectively (Scheme 1). Moderate yields (62-71 %) were achieved at 170 °C for 2h. The value of theoretical degree of polymerization (DP) expected for all PLLA oligo-esters is 20. However, the DP obtained (by ^{1}H NMR) after purification is higher (DP$_{(NMR)}$ = 25-31). This result can be attributed to losses of oligomers in the recrystalization step. Nine different samples of poly(L-lactide) (PLLA1-10) were obtained by this route (Table 1). Unimodal distributions and moderate polydispersity (M_w/M_n = 1.23-1.33) were observed in all GPC chromatograms. Values of M_n(GPC) are higher than M_n(NMR). Overestimation of M_n obtained by GPC for PLLA is a common feature, since polystyrene standards are used in the construction of the calibration

curve, these different values were attributed to differences in hydrodynamic volume and molecular masses between polystyrene and PLLA [18-19]. In the case of oligo-esters as poly(L-lactide) or poly(ε-caprolactone) M_n values from the NMR analysis are close to the calculated theoretical M_n values [18-22]. Therefore, the absolute M_n was obtained from NMR analysis.

In Figure 1, ^{1}H NMR spectrum from α-hydroxyl-ω-docosyl PLLA (PLLA10) is showed, where methyne g [$-CH$(CH$_3$)–OH, δ 4.37, PLLA] and methyl a [CH_3-, δ 0.87, docosyl] end groups are clearly seen. Two methyl end groups at δ 1.52 (e) and 1.50 (h) for PLLA10 also can be observed. Other peaks in the spectrum were assigned to different methynes [$-CH$(CH$_3$)$-$O$-$] and methylenes [$-CH_2-$] in the main chain oligo-ester and end group, respectively. The peaks assignation is consistent with the observed in other PLLA oligomers spectra [23,24].

When 1-hexanol was used as initiator in the ROP of L-LA, ^{13}C NMR spectrum also shows evidence of the α-hydroxyl-ω-hexyl PLLA (PLLA6) end group (Figure 2). Terminal methyne close to hydroxyl m [$-CH$(CH$_3$)$-$OH, δ 66.58] and methyl within the hexyl terminated a [CH_3-(CH$_2$)$_5-$, δ 13.87] were observed. In carbonyl zone peaks three different signals can be distinguished: 1) ester carbonyl of the main chain j [$-C$(=O)$-$CH(CH$_3$)$-$O$-$, δ 169.49], 2) ester carbonyl of the hydroxyl end group q [$-C$(=O)$-$CH(CH$_3$)$-$OH, δ 170.04], and 3) ester carbonyl in the hexyl end group g [$-$CH(CH$_3$) $-C$(=O)$-$O$-$(CH$_2$)$_5-$CH$_3$, δ 174.99]. Peaks assignments for methynes and methyls were made comparing them with the ^{13}C NMR spectrum for PLLA reported by other authors [21,24,25]. Signals for methylenes were assigned using substituent additivity rules and literature data [26]. Carbon d appears with most difference between δ calculated and δ

NMR (Table 2), *d* is a double γ-carbon with respect to methyl and ester group, and produces a shift to the right due to steric compression of a *gauche* interaction [26]. A similar phenomenon was observed for carbon gamma (γ) in the main chain for the PCL [19].

MALDI-TOF spectrum for α-hydroxyl-ω-docosyl (PLLA) (PLLA10) is showed in the Figure 3a. Unimodal distribution similar to GPC is seen. A significant predominance of the linear PLLA10 oligo-ester was observed after analysis of signals. ^{1}H NMR confirmed this result. Tree type of signals can be observed in the view expansion of the zone between 1900 and 2125 uma (Figure 3b), two were assigned to α-hydroxyl-ω-docosyl (PLLA) (PLLA10) doped with sodium (A) and potassium (B) ions and a third signal correspond to α-hydroxyl-ω-(carboxylic acid) PLLA (HA-PLLA) (C). The presence of HA-PLLA is the result of an initiation by water or linear dilactide (with OH groups) as impurity [23].

FT-IR spectrum of PLLA10 showed typical bands at 2927 (CH, ν), 1757 (C=O, ν), 1457 (CH, δ), 1184 (−C−(C=O)−O−, ν), and 1091 cm^{-1} (−O−C−C−, ν) [26]. Usually, the band for C=O stretching vibration (1757 cm^{-1}) of PLLA is used as evidence of the formation of block copolymer in the PLLA-*b*-PCL [27,28].

Thermal properties: DSC and TGA

Thermal properties of poly(L-lactide) (PLLA) oligo-esters (PLLA1-10) were examined by dynamic scaning calorimetry (DSC) and thermogravimetric analysis (TGA). Effect of alkyl end group on thermal properties and crystalline nature of the PLLA was studied by DSC (Table 3). The thermal profile of α-hydroxyl-ω-butyl PLLA (PLLA1, Figure 4) reveals characteristics of glass transition temperature (T_g = 37 °C), crystallization

temperature (T_{c1} = 78 °C), and melting temperature (T_{m1} = 141 °C); a similar pattern to PLLA is observed in other synthesized [25,29] and commercials samples [29]. The values in melting point (T_m = 137-142 °C) and enthalpy of fusion (ΔH_m = 48-53 J/g) of PLLA samples are discrete, indicating similar crystallinity (x_i) in all oligo-esters. Hence, the alkyl terminal group in all samples does not affect the crystallinity (x_i) of PLLA. Different result was found by Abayasinghe et al for polyethylene-*b*-poly(L-lactide) (PE-*b*-PLLA) where the copolymer is more crystalline than homo-PLLA [11]. The effect of alkyl end group on T_g is plotted in Figure 5. T_g gradually decreases with an increase in the percent of alkyl $-CH_2-[CH_2-CH_2]_m-CH_3$ end group. The flexibility to PLLA is major due to the attachment of a big alkyl end group as docosyl $-CH_2-[CH_2-CH_2]_{10}-CH_3$. The contrary effect was reported by Frey and coworkers where the flexibility in hyperbranched polyglycerol was reduced by PLLA blocks [30].

In Figure 6, a new peak T_{C2} of cold crystallization exotherm for PLLA8-10 (11-15 % in weight of alkyl end group) with respect to PLLA1 (Figure 4) was observed. In based on comparison with T_{c1} of PLLA1 (Table 3, Figure 4) the first peak at 79 °C was assigned to PLLA homopolymer environment. The second peak at 52 °C (T_{c2}) was assigned to segments of PLLA $[-CO-CH(CH_3)-O-]_n$ close to the alkyl end group (octadecyl to docosyl). In the case of α-hydroxyl-ω-docosyl PLLA (PLLA10) (Figure 6c), where docosyl end group had 15 % in weight, a phases separated can be seen with two melting points, the first slightly at 38 °C attributed to docosyl end group and the second at 138 °C assigned to PLLA. The second peak of cold crystallization exotherm (T_{c2}) (Figure 6c) appears because lower energy is necessary in the crystallization process for PLLA chains close to alkyl end group, due to docosyl melted. To corroborate this idea, tree new different samples with

M_n(NMR) = 1040-1910 were synthesized (Table 4). In Figure 7, thermograms of PLLA with different M_n and percent in weight end group (% EG) are showed. It is possible see as the second melting point peak (T_{m2} = 37-47 °C) is most intense as the % EG is higher (17-31 %) and the T_{m1} attributed to PLLA decreased proportionally with the M_n(NMR) from 130 to 121 °C. Finally, in the Figure 7c a forceful segregation phases between docosyl (T_{m2} = 47) and PLLA (T_{m1} = 121) was observed. On the other hand, double cold crystallization (T_{c1} and T_{c2}) profile can be seen in the Figure 7a-b; however, the first peak of cold crystallization assigned to PLLA homopolymer environment (T_{c1} = 75-79 °C) was decreasing proportionally as the % EG has increased, even disappear with 31 %. To our knowledge, the phenomenon of double cold crystallization has never been observed in previous works from PLLA [12] or PE-*b*-PLLA [10,31,32]. Our evidence shows that: 1) when alkyl end group ($CH_3-[CH_2-CH_2]_n-CH_2-$) showed a percent in weight over 11 % in the PLLA, a double cold crystallization was induced in the PLLA oligo-ester, 2) the double cold crystallization of PLLA is directly related with the segregation phase between alkyl end group and PLLA, and 3) Based on the presence of a double cold crystallization in the thermograms is possible to affirm than that start segregation phases process is at % EG ≥ 11 for PLLA oligo-esters with M_n(NMR) = 2120-2450.

In the α-hydroxyl-ω-alkyl PLLA oligo-esters is expected that alkyl end group have an effect on thermal stability, and by thermogravimetric analysis (TGA) was observed, for example: Jamshidi [33] reported an increase in degradation temperature [detected by TGA] of the α-acetyl-ω-(carboxyl acid) PLLA (PLLA acetylated) respect to α-hydroxyl-ω-(carboxyl acid) PLLA. In our samples (Figure 8), thermogravimetric analysis (TGA) of PLLA oligo-esters showed only one inflection temperature for ω-butyl and ω-docosyl end

group at 215 and 223 °C, respectively. The difference in thermal degradation probably is due to steric hindrance of the end group (docosyl respect to butyl) toward intermolecular and intramolecular transesterification in the formation of monomer and cyclic oligomers.

Small-angle ray-x scattering (SAXS)

It is well-known that PLLA is a semicrystalline polyester with lamellar structure in its crystalline phase that can be detected by small-angle ray scattering (SAXS). With this idea, in the Figure 9 the SAXS curves for α-hydroxyl-ω-butyl poly(L-lactide) (PLLA 1) and α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA10) at different temperature are showed. In figure 9a, scattering of PLLA1 at lower temperature (27 °C) is not seen. Typically, scattering of PLLA commercial samples at room temperature has not been observed. However, when increasing temperature one scattering peak at $T = 80$ °C and $q_{max} = 0.54$ nm^{-1} is observed just after the beginning of the crystallization T_{c1}, based on q_{max} the long period ($L = 2\pi/q_{max}$) was calculated, $L = 11.6$ nm, indicating the distance center-to-center between lamellae. When the temperature was gradually increasing the maximum peak (q_{max}) is shifted toward higher value of L. Thus, lamellae growth in PLLA is proportional to the increase in L. Reaching a maximum peak at $T = 133$ °C with $q_{max} = 0.46$ nm^{-1} and $L = 13.6$ nm after its crystallization temperature ($T_{c1} = 78$ °C) and below the melting temperature ($T_m = 141$ °C); with higher temperature ($T > T_m$) the peak disappears totally when PLLA was melted and scattering is not seen. Therefore, any order after PLLA melting point is not observed. In the case of PLLA10 (Figure 9b) respect to PLLA1, one peak at 27 °C with $q_{max} = 1.01$ nm^{-1} ($L = 6.22$ nm) is observed. Scattering at 27 °C is induced by docosyl end group due to segregation phases between oligo-ester and aliphatic

terminal group. Similar patron was observed with octadecyl end group. When the temperature was raised, a maximum peak a $q_{max} = 0.63$ nm^{-1} ($T = 116$ °C) is observed. With this result, the maximum value of L for PLLA10 is 9.9 nm and respect to 13.6 nm of PLLA1, a decrease is seen. Based on L and crystallinity fraction (by DSC), the lamellae thickness (D) in both samples was calculated and a minor lamellae thickness in PLLA10 (D = 5.0 nm) respect to PLLA1 (D = 7.3 nm) was obtained. This result is explained in terms of the steric hindrance of docosyl end group toward lamellar growth.

Conclusion

Poly(L-lactide) (PLLA) oligo-esters were synthesized by ring-opening polymerization (ROP) of L-lactide (L-LA) catalyzed by tin(II) 2-ethylhexanoate $Sn(Oct)_2$ and using aliphatic alcohols $CH_3-[CH_2-CH_2]_m-CH_2-OH$ as initiators with a systematic sequence in the increase (m =1-10). Monofuntionality α-hydroxyl-ω-alkyl PLLA was found in all oligo-esters characterized. PLLA oligo-esters showed evidence of the effects of alkyl $CH_3-[CH_2-CH_2]_m-CH_2-$ end group on their thermal properties detected by DSC and TGA. Glass transition temperature (T_g) is gradually decreased with an increase in the percent of alkyl $-CH_2-[CH_2-CH_2]_m-CH_3$ end group, as results alkyl end group provides most flexibility to PLLA. The effect of the alkyl end group on crystallinity of PLLA was discrete. An important effect of alkyl end group on PLLA was observed with a double cold-crystallization (T_c) at higher values of percent in weight of end-group ($\geq$ 11 %) and directly related with the segregation phases between alkyl end group and PLLA. TGA analysis revealed that PLLA oligo-esters are more thermally stable with docosyl ($-C_{22}H_{45}$) respect to butyl ($-C_4H_9$) end group, probably is due to steric hindrance of the end group (docosyl respect to butyl) toward intermolecular and intramolecular transesterification. Lamellar growth in PLLA was sterically hindered by docosyl ($-CH_2-[CH_2-CH_2]_{10}-CH_3$) end-group with a decreasing value in the lamellae thickness (D).

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Scheme and Figure Captions
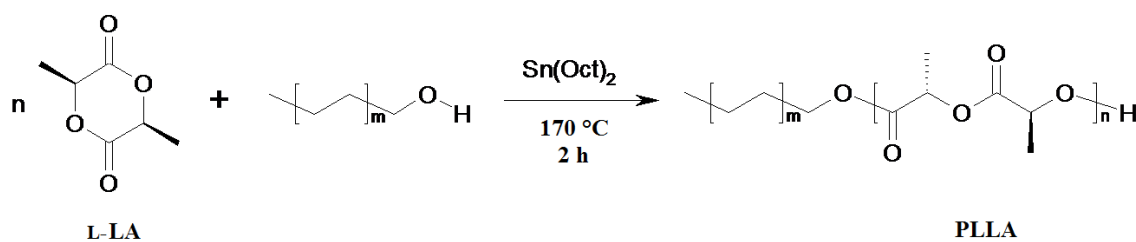
Scheme 1. Ring-opening polymerization (ROP) of L-lactide (LLA) catalyzed by tin(II) 2-ethylhexanoate $Sn(Oct)_2$ in presence of primary aliphatic alcohols as initiators (CH_3−[CH_2−CH_2]$_m$−CH_2−OH (ROH), where m = 1, 2,4,5,6,7,8,9, and 10).
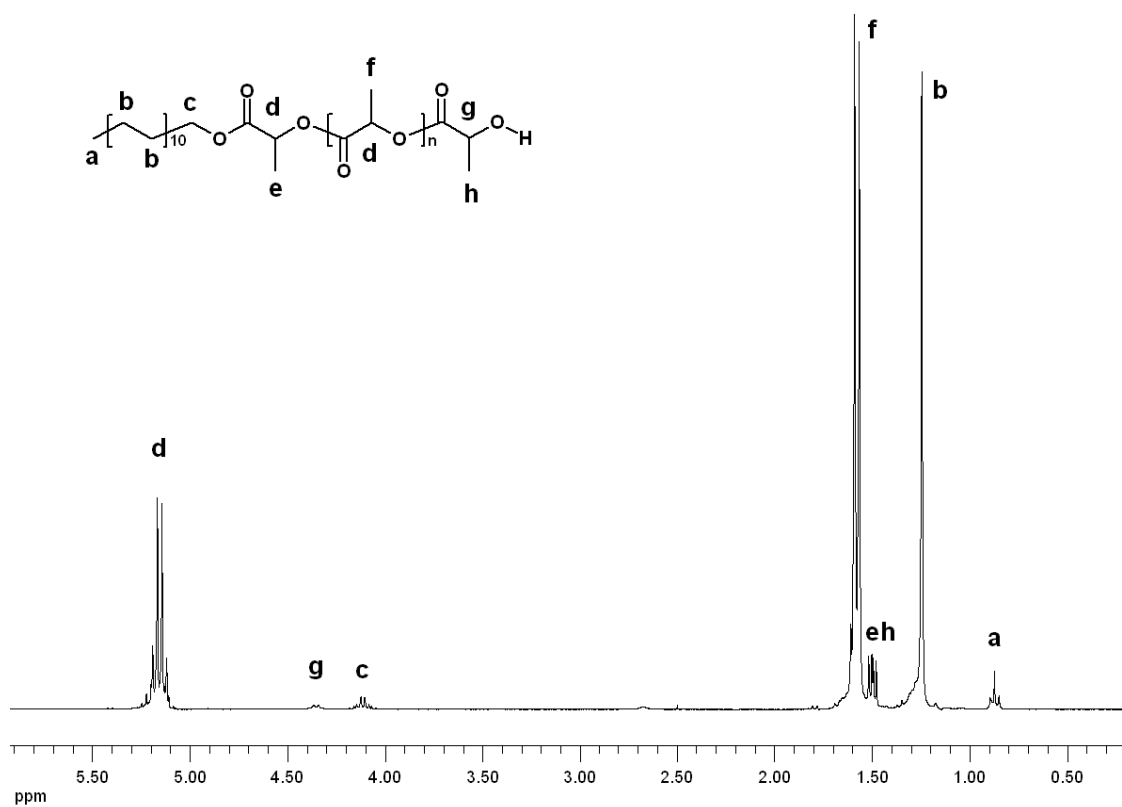
Figure 1. ^{1}H NMR (300 MHz) spectrum in CDCl$_3$ for the α-hydroxyl-ω-docosyl poly(L-lactide) [M_n(NMR) = 2120 (PLLA10, Table 1)].
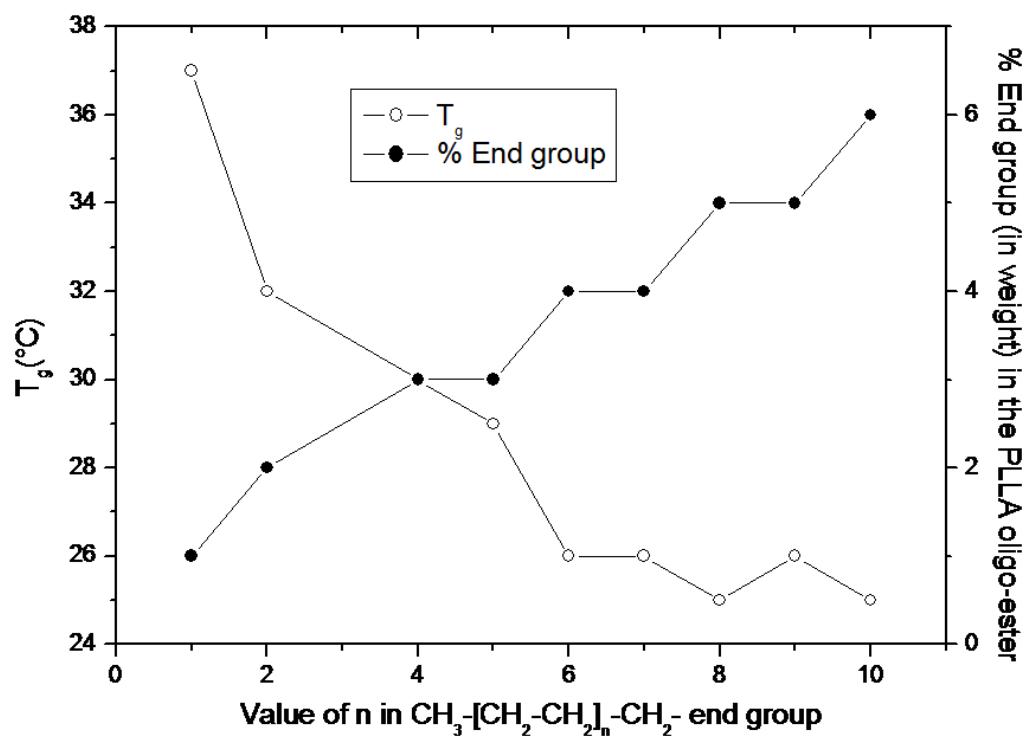
19
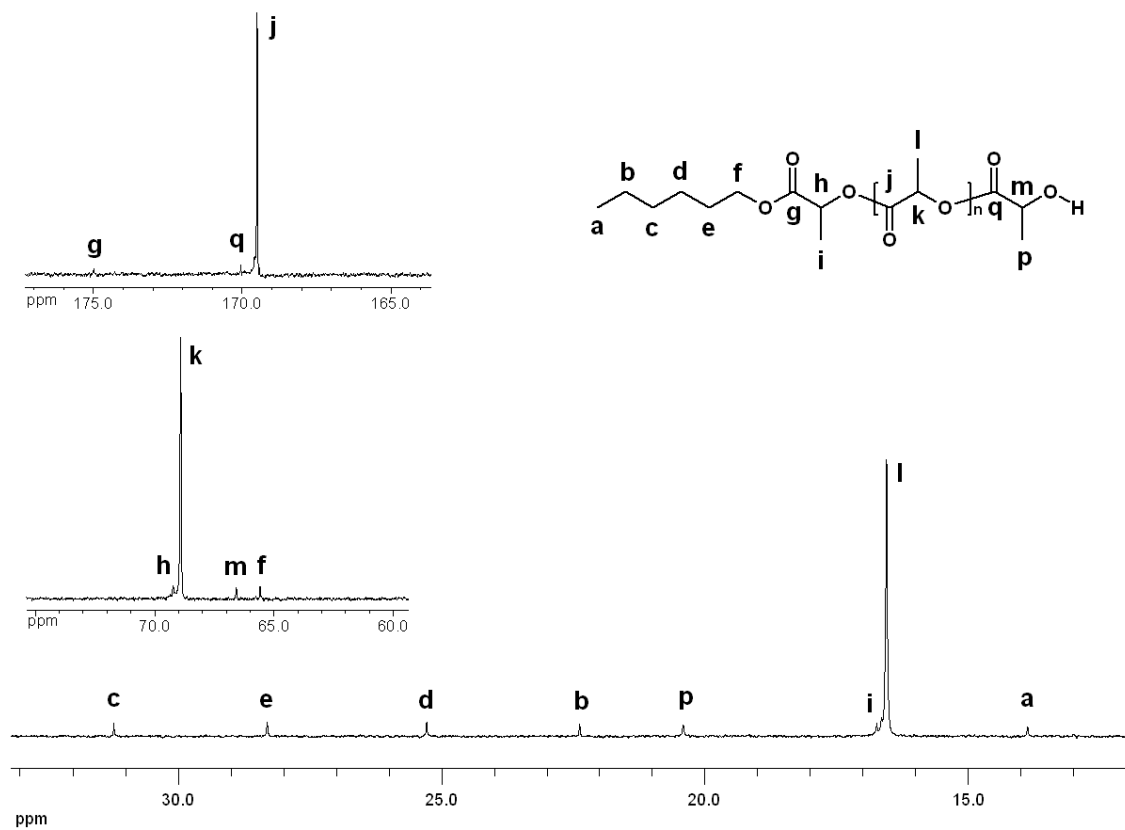
Figure 2. ^{13}C NMR (300 MHz) spectrum in CDCl$_3$ for the α-hydroxyl-ω-hexyl poly(L-lactide) [M_n(NMR) = 2260 (PLLA2, Table 1)].
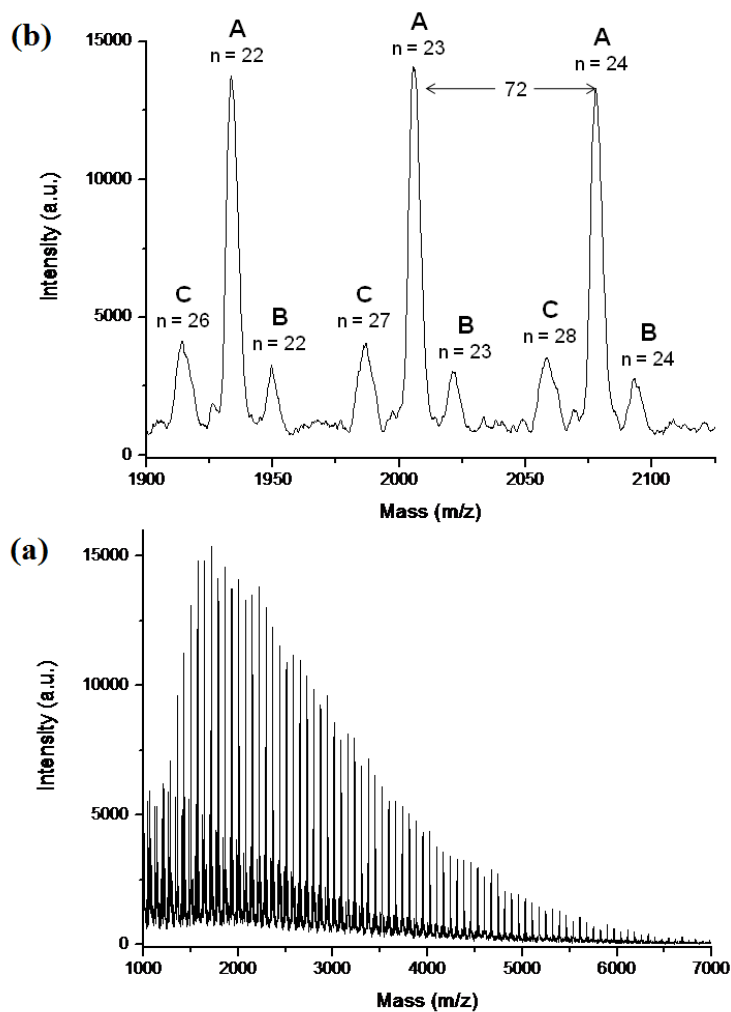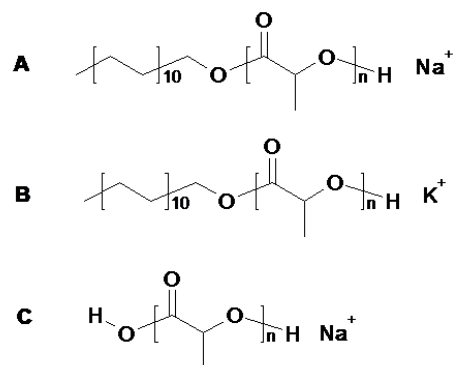
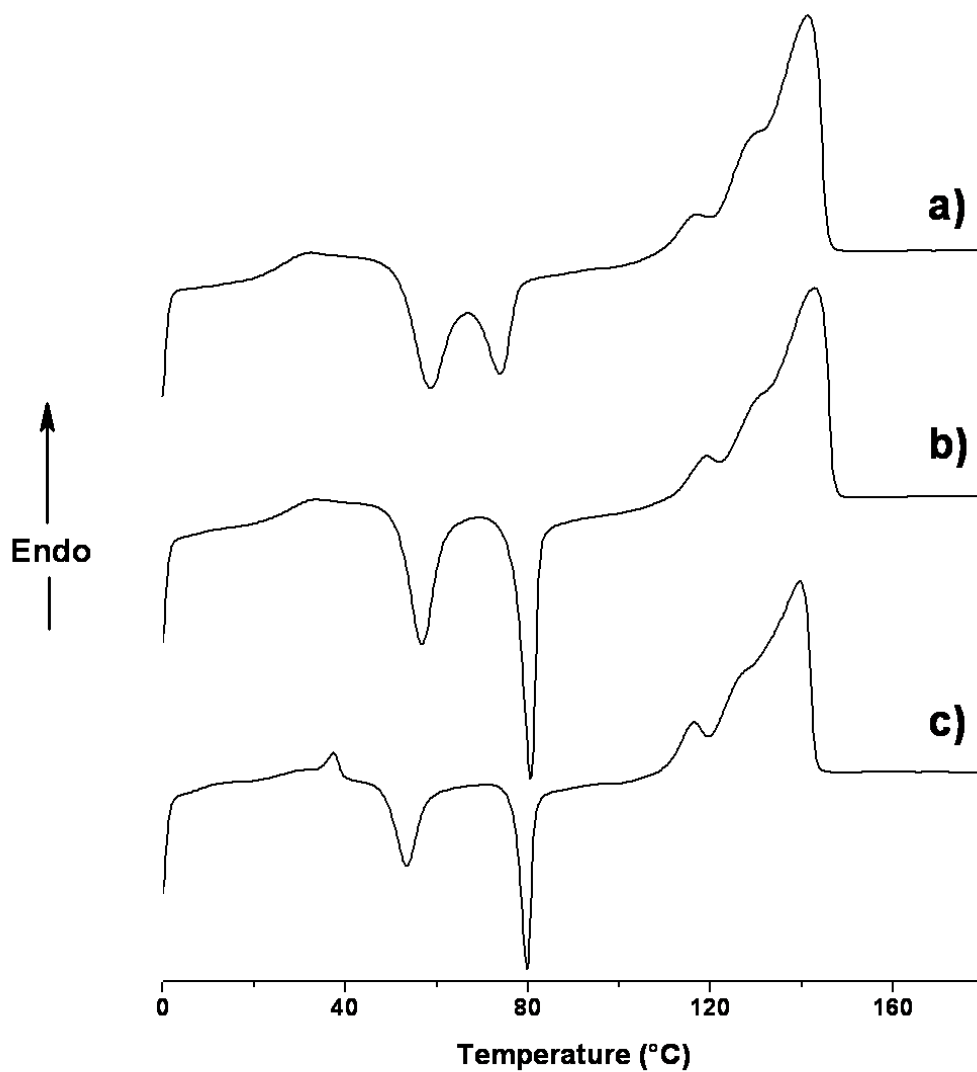**Figure 3.** MALDI-TOF spectrum of the (a) α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA10, Table 1). (b) Expanded view for the 1947-2303 m/z fragments.
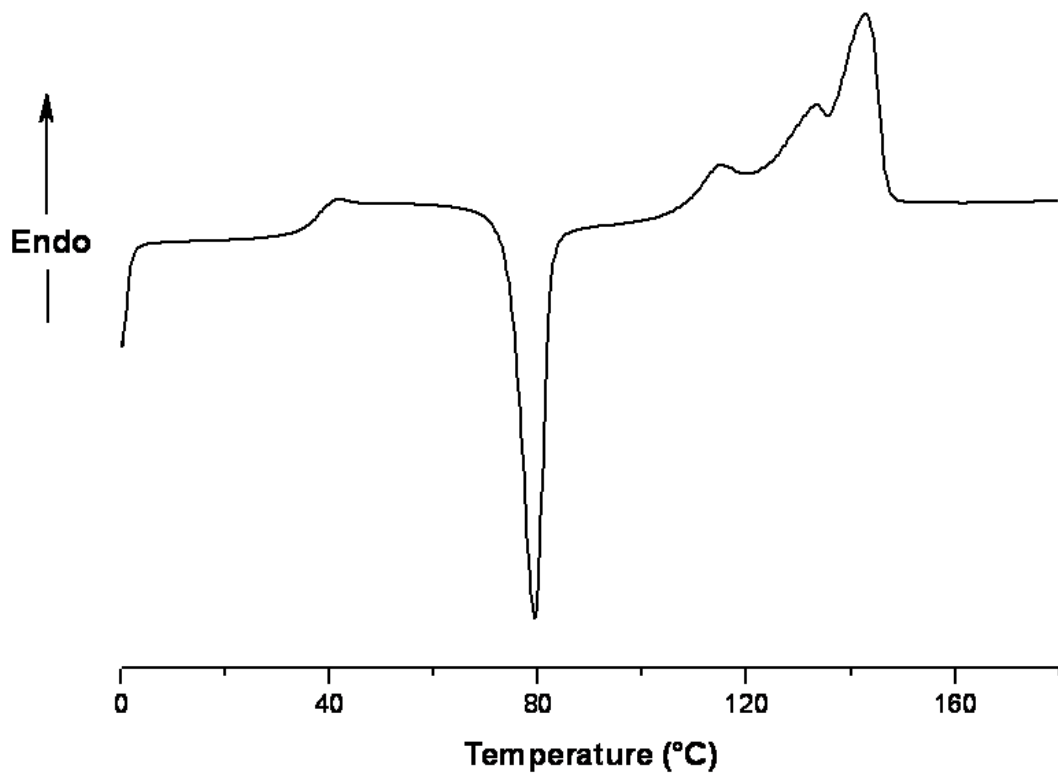
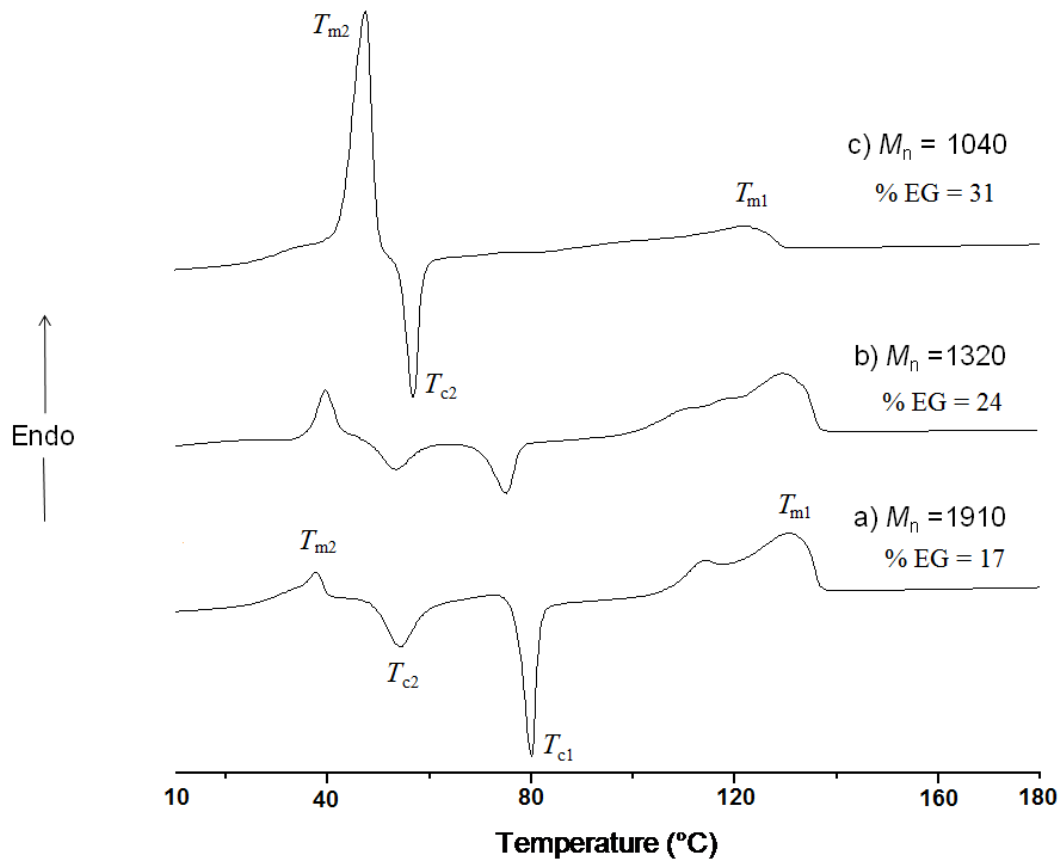**Figure 4.** DSC thermogram (second scan) of α-hydroxyl-ω-butyl poly(L-lactide) (PLLA1, Table 3).

**Figure 5.** Effect of alkyl end group on glass transition temperature (T_g) of poly(L-lactide) (PLLA).

Figure 6. DSC thermograms (second scan) of a) α-hydroxyl-ω-octadecyl poly(L-lactide) (PLLA8), b) α-hydroxyl-ω-eicosyl poly(L-lactide) (PLLA9) and c) α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA10, Table 3).
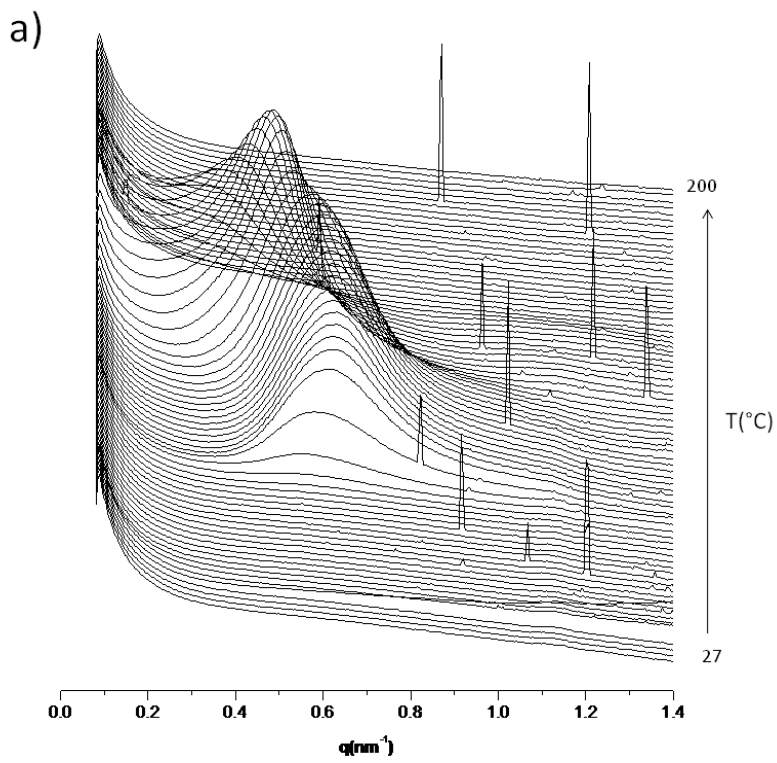
Figure 7. DSC thermograms (second scan) from α-hydroxyl-ω-docosyl poly(L-lactide) with different percent of end group (%EG) and M_n(NMR): a) 1910, b) 1320 and c) 1040.
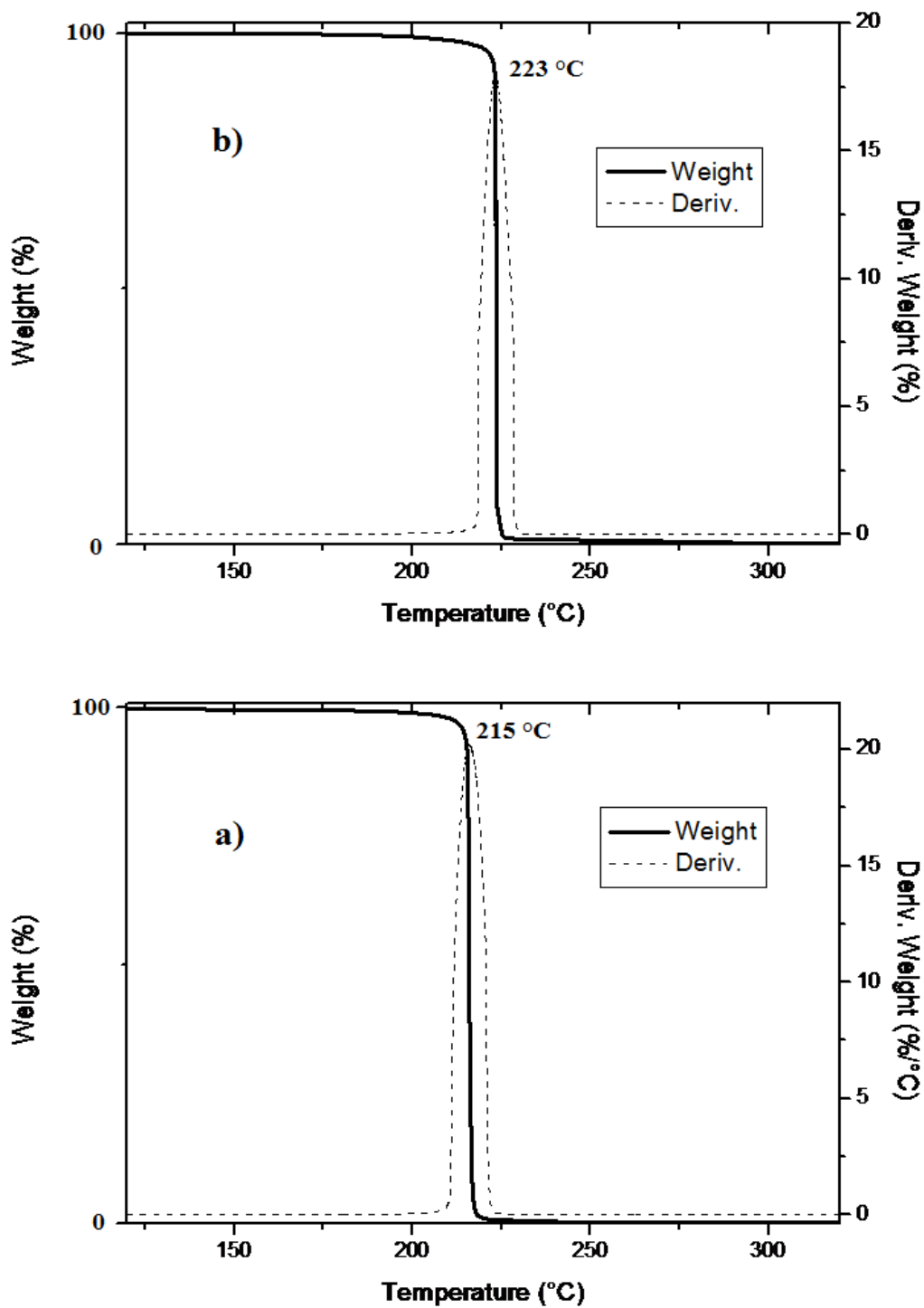
Figure 8. Thermal degradation of PLLA oligo-esters with different terminal group: (a) α-hydroxyl-ω-butyl and (b) α-hydroxyl-ω-docosyl.
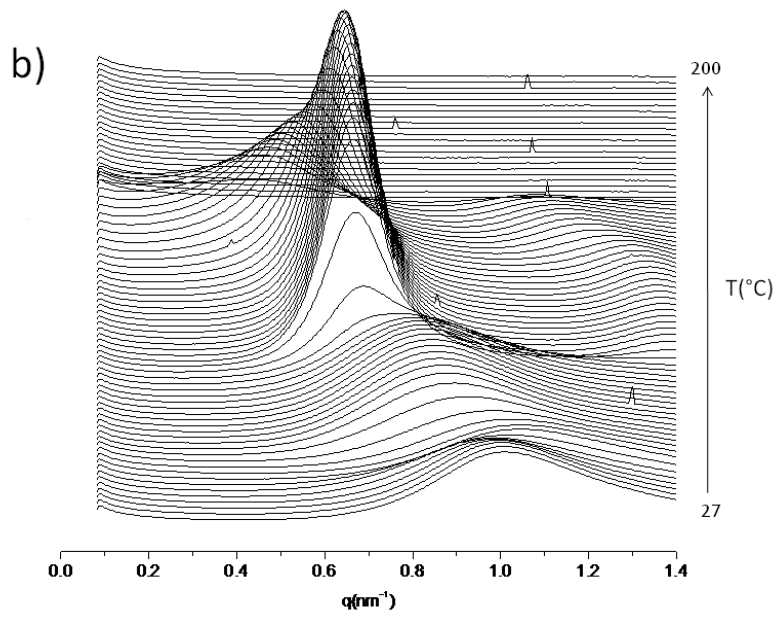
Figure 9. SAXS curves (Iq2 vs q) plotted during heating for: a) α-hydroxyl-ω-butyl PLLA and b) α-hydroxyl-ω-docosyl PLLA.

TABLES

Table 1. Ring-opening polymerization of L-lactide (LLA) using different alcohols $CH_3-[CH_2-CH_2]_n-CH_2-OH$ as initiators and tin (II) 2-ethylhexanoate $Sn(Oct)_2$ as catalyst.[a]

No.	Co-initiator	$[CH_2-CH_2]_n$ End group (n)	DP_{PLLA}[b,c]	$M_n(NMR)$[b,c]	$M_n(GPC)$[d]	M_w/M_n[d]	%EG in PLLA[b,e]	Yield[f] (%)
PLLA1	1-butanol	1	30	2230	3520	1.33	3	71
PLLA2	1-hexanol	2	30	2260	-	-	4	70
PLLA4	1-decanol	4	30	2310	-	-	6	66
PLLA5	1-dodecanol	5	31	2410	-	-	7	62
PLLA6	1-tetradecanol	6	29	2300	3550	1.23	9	66
PLLA7	1-hexadecanol	7	29	2330	-	-	10	69
PLLA8	1-octadecanol	8	29	2350	-	-	11	66
PLLA9	1-eicosanol	9	30	2450	-	-	12	66
PLLA10	1-docosanol	10	25	2120	3600	1.24	15	69

[a] Polymerization at 170 ºC for 2h with 40 mmol of LLA, a LLA/co-initiator molar ratio of 10 was used. [b] After recrystalization with chloroform/methanol. [c] Determined by ^1H NMR in $CDCl_3$. [d] Determined by gel permeation chromatography (GPC) using polystyrene standards. [e] Obtained from the equation % End group (% EG) = ($MW_{initiator}/M_n(NMR)$) × 100. [f] Respect to feed monomer.

Table 2. Chemical shift in the ^{13}C NMR spectrum for hexyl end group into α-hydroxyl-ω-hexyl poly(L-lactide) (PLLA2) [M_n(NMR) = 2260, Figure 2].[a]

Carbon	δ calcd[a]	δ NMR[b]
a	13.9	13.8
b	22.9	22.3
c	32.0	31.2
d	27.2	25.2
e	29.1	28.3
f	64.1	65.5

[a] Calculated by substituent additivity rules in the reference 20. [b] Determined by ^{13}C NMR in CDCl$_3$.

Table 3. Thermal properties of PLLA with different size of end group $(CH_3-[CH_2-CH_2]_n-CH_2-)$.[a]

No.	Co-initiator	%EG in PLLA[b]	T_g (°C)[c]	T_{c2} (°C)[c]	ΔH_{c2} (J/g)[c]	T_{c1} (°C)[c]	ΔH_{c1} (J/g)[c]	T_{m1} (°C)[c]	ΔH_{m1} (J/g)[c]	x_i (%)[c]
PLLA1	1-butanol	3	37	–	–	78	-34	141	51	54
PLLA2	1-hexanol	4	32	–	–	74	-31	139	48	51
PLLA4	1-decanol	6	30	–	–	71	-14	137	49	52
PLLA5	1-dodecanol	7	29	–	–	68	-26	139	53	56
PLLA6	1-tetradecanol	9	26	–	–	65	-26	138	50	53
PLLA7	1-hexadecanol	10	26	–	–	63	-29	140	49	52
PLLA8	1-octadecanol	11	25	58	–	73	-25	140	49	52
PLLA9	1-eicosanol	12	26	56	-12	79	-15	142	50	53
PLLA10	1-docosanol	15	25	52	- 8	79	-9	138	48	51

[a] After recrystalization with chloroform/methanol. [b] Obtained from the equation % End group (% EG) = $(MW_{initiator}/M_n(NMR)) \times 100$. [c] Obtained by DSC analysis.

Table 4. Effect of M_n on thermal properties of α-hydroxyl-ω-docosyl poly(L-lactide) (PLLA) (PLLA11-13).[a]

No.	M_n(NMR)[b]	% EG in PLLA[c]	T_{m2}[d] (°C)	ΔH_{m2}[d] (J/g)	T_{c2}[d] (°C)	ΔH_{c2}[d] (J/g)	T_{c1}[d] (°C)	ΔH_{c1}[d] (J/g)	T_{m1}[d] (°C)	ΔH_{m1}[d] (J/g)	x_i[d] (%)
PLLA11	1910	17	37	2.4	55	-13.4	79	-18.4	130	46.7	50
PLLA12	1320	24	39	6.7	53	-7.8	75	-8.8	129	44.3	47
PLLA13	1040	31	47	38.3	56	-17.0	-	-	121	24.6	26
PLLA14[e]	1920[e]	9	-	-	-	-	74	-30.8	126	46.9	50

[a] After recrystalization with chloroform/methanol. [b] Determined by ^{1}H NMR in CDCl₃. [c] Obtained from the equation % End group (% EG) = (MW$_{initiator}$/M_n(NMR)) × 100. [d] Obtained by DSC analysis. [e] α-hydroxyl-ω-dodecyl poly(L-lactide) (PLLA).