

A Green Strategy for the Synthesis of Poly(ethylene succinate) and its Copolyesters via Enzymatic Ring Opening Polymerization

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Abstract:

Poly(ethylene succinate) (PES) with weight-average molecular weight above $60,000 \text{ g}\cdot\text{mol}^{-1}$ was efficiently obtained by enzymatic ring opening polymerization of cyclic oligo(ethylene succinate)s $\alpha(\text{ES})_n$, which in turn were prepared by lipase-catalysed cyclocondensation in solution of dimethyl succinate and ethylene glycol. The methodology was demonstrated to be also applicable to the synthesis of high molecular weight PES-copolyesters containing butylene succinate, ϵ -hydroxycaproate or L-lactate units with a random distribution.

Keywords: *Poly(ethylene succinate), enzymatic synthesis, ROP, cyclic oligoesters.*

1. Introduction

Sustainable polymers coming from renewable feedstocks and able to be biodegraded at convenient periods of time constitute nowadays a distinguished group of materials with high industrial potential and high interest in the biomedical field. [1,2] Among them, aliphatic polyesters of both AA-BB and A-B types, are by far the most studied and commercially used. [3,4] The easy accessibility to the bio-based blocks suitable for building these polyesters, their notable susceptibility to biodegradation, and their favourable basic properties, are good reasons accounting for their outstanding position.

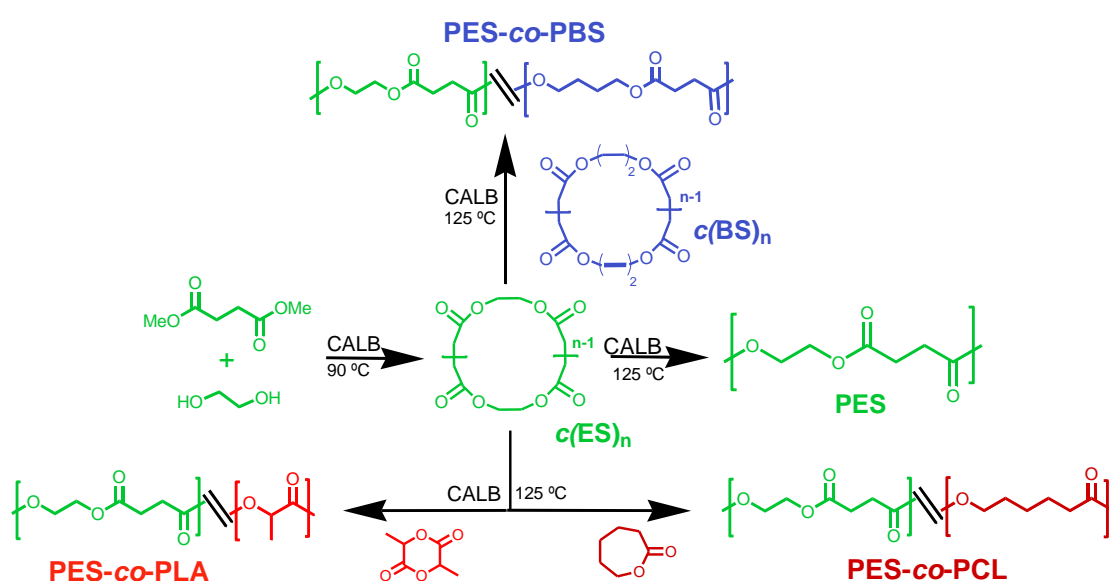
Ring opening polymerization (ROP) of strained lactones is the method of choice for the synthesis of poly(hydroxyalkanoate)s whereas poly(alkylene alkanedioate)s are preferably produced by polycondensation of alkanediols with dicarboxylic acids or their esters. [5,6] ROP usually takes place at milder conditions than polycondensation

with less generation of undesirable by-products. [7,8] Furthermore, the ROP reaction is efficiently catalysed by enzymes making feasible the preparation of metal-free polymers. [9-11] Additional advantages of ROP are the low viscosity of the reaction medium and the absence of volatiles therein produced. These features are largely appreciated when polymerization has to be performed *in situ* as it is the case of nanocomposite manufacture and reactive injection moulding.

In 2004, the US Department of Energy declared bio-based succinic acid (SA) as a high-potential chemical platform for the synthesis of compounds able to replace those currently in use but coming from fossil resources. [12] This is one of the main reasons explaining why poly(alkylene succinate)s, and in particular poly(butylene succinate) (PBS) and poly(ethylene succinate) (PES), are ahead of bio-based polyesters of AA-BB type. [13] The industrial synthesis of PBS is currently performed by polycondensation of SA (or its dimethyl ester, DMS) with 1,4-butanediol (BDO) assisted by tin or titanium organometallic catalysts. In 2006 Matsamura et al. [14,15] reported the synthesis of PBS by enzymatically catalysed ROP (*e*-ROP) of cyclic di(butylene succinate). This dilactone may be isolated in large amounts as a subproduct of the polycondensation process industrially used for the manufacture of PBS. [16] PES is also commercially accessible although it has not achieved production at the ton-scale yet. The synthesis of PES is carried out by reaction of succinic acid either with ethylene glycol or ethylene oxide. PES is more biodegradable than PBS, melts slightly above 100 °C, and displays fair mechanical properties. [17-19] This polyester is currently under vigorous investigation addressed to create PES-copolyesters suitable for new demanding biomaterial applications. [20-22]

The polycondensation methods usually provide polyesters with moderate molecular weights and they all require the concourse of organometallic catalysts. In this communication we wish to report on a new strategy for the synthesis of PES that

combines the enzymatic production of cyclic oligo(ethylene succinate)s, $c(ES)_n$, with their enzymatic polymerization to render polymers with high molecular weight and absent of metallic impurities. It is the first time that the synthesis of $c(ES)_n$ and its use for the preparation of PES is reported. This procedure has been found to be readily extensible to the preparation of random PES-copolyesters by enzymatic copolymerization of $c(ES)_n$ with other cyclic esters either commercially available or easily accessible by synthesis. The proposed strategy is depicted in Scheme 1.



Scheme 1. Route to PES homopolymer and copolymers by e-ROP.

Experimental

A detailed account of the materials and measuring methods used in this work is provided in the Electronic Supplementary Information (ESI) associated with this communication. Novozyme 435 (lipase B *Candida antarctica*, CALB, 40%) was a kind gift of Novozymes. According to the information provided by Novozymes Data Sheet, the nominal activity of Novozyme 435 is >10,000 PLU/g. PLU is the amount of enzyme activity which generates 1 μmol of propyl laurate per minute under defined

standard conditions. This enzyme was chosen for this work since it has been reported to render very high molecular weight PBS.[14] Furthermore Novozyme 435 is known to display remarkable stability and catalytic efficiency, as well as a broad substrate specificity compared to other lipases.[23]

The cyclic oligomers $c(ES)_n$ were synthesized by applying the methodology recently reported by us for the preparation of their butylene succinate analogues $c(BS)_n$. [20] Briefly, a three-necked round bottom flask was charged with 250 mL of toluene, 4.97 mmol (0.73 g) of DMS, 4.97 mmol(0.31 g) of EG and CALB (100% w/w of the total monomer concentration), and the mixture was left to react for 48 h at 90 °C under a nitrogen flow. 4 Å molecular sieves were placed at the top of the flask in order to absorb the remained methanol. The reaction mixture was then diluted with 70 mL of $CHCl_3$ and the enzyme was removed by filtration. The residue recovered upon solvent evaporation was subjected to flash chromatography to eliminate the acyclic species and to render the $c(ES)_n$ mixture in approximately 70% yield. 1H NMR (δ ppm, $CDCl_3$, 300 MHz): 4.30 (m, 4H), 2.68 (m, 4H). ^{13}C NMR (δ ppm, $CDCl_3$, 75.5 MHz): 172.62, 172.05, 171.55, 62.48, 62.33, 62.15, 29.33, 28.96, 28.80.

Polymerization of $c(ES)_n$ was performed by ROP using $Sn(Oct)_2$ and CALB catalysts. For the first case, $c(ES)_n$ and 1% (w/w) of tin catalyst were placed in a three-necked round bottom flask and dissolved in $CHCl_3$. Then, the solvent was evaporated and the mixture left to react at 125 °C for 24 h under a nitrogen atmosphere. For *e*-ROP the oligomeric fraction was mixed with CALB and the reaction left to proceed under the same conditions as before. The temperature chosen for polymerization is certainly high provided that it is enzymatically catalysed. Nevertheless, the capacity of Novozyme 435 to retain its enzymatic activity at temperatures up to 150 °C has been reported by different authors.[24-26] For following the reaction progress, aliquots of the reaction mass were removed at

progressive periods of time and analysed by GPC. Copolyesters $coP(ES_{52}BS_{48})$, $coP(ES_{49}CL_{51})$ and $coP(ES_{72}LA_{28})$ were prepared applying the same procedure to comonomeric pairs of $c(ES)_n$ and $c(BS)_n$, CL or LA in a 50:50 molar ratio.

Results and discussion

Graphical data obtained in the characterization of the cyclic $c(ES)_n$ mixture are shown in Fig. 1, and a detailed account of numerical data is provided in the ESI file. The NMR spectra (Fig. 1a) were in full agreement with the constitution expected for the $c(ES)_n$ mixture, and they did not show any signal indicative of the presence of linear oligomers. The MALDI-TOF spectrum (Fig. 1b) contained the m/z signal sequence arising from the 144 molar mass attributable to the ethylene succinate. MALDI-TOF results could be reasonably attributed to the trimer and tetramer species. A comparison of these results with those reported for $c(BS)_n$ is given in Table 1. The two fractions were obtained in similar yields although the $c(ES)_n$ appears to be more homogenous with trimer and tetramer species being clearly predominant in this fraction. The fact that the $c(BS)_n$ fraction is composed of smaller cycle sizes (dimer and trimer) is fully reasonable by taking into account the longer length of the butylene unit.

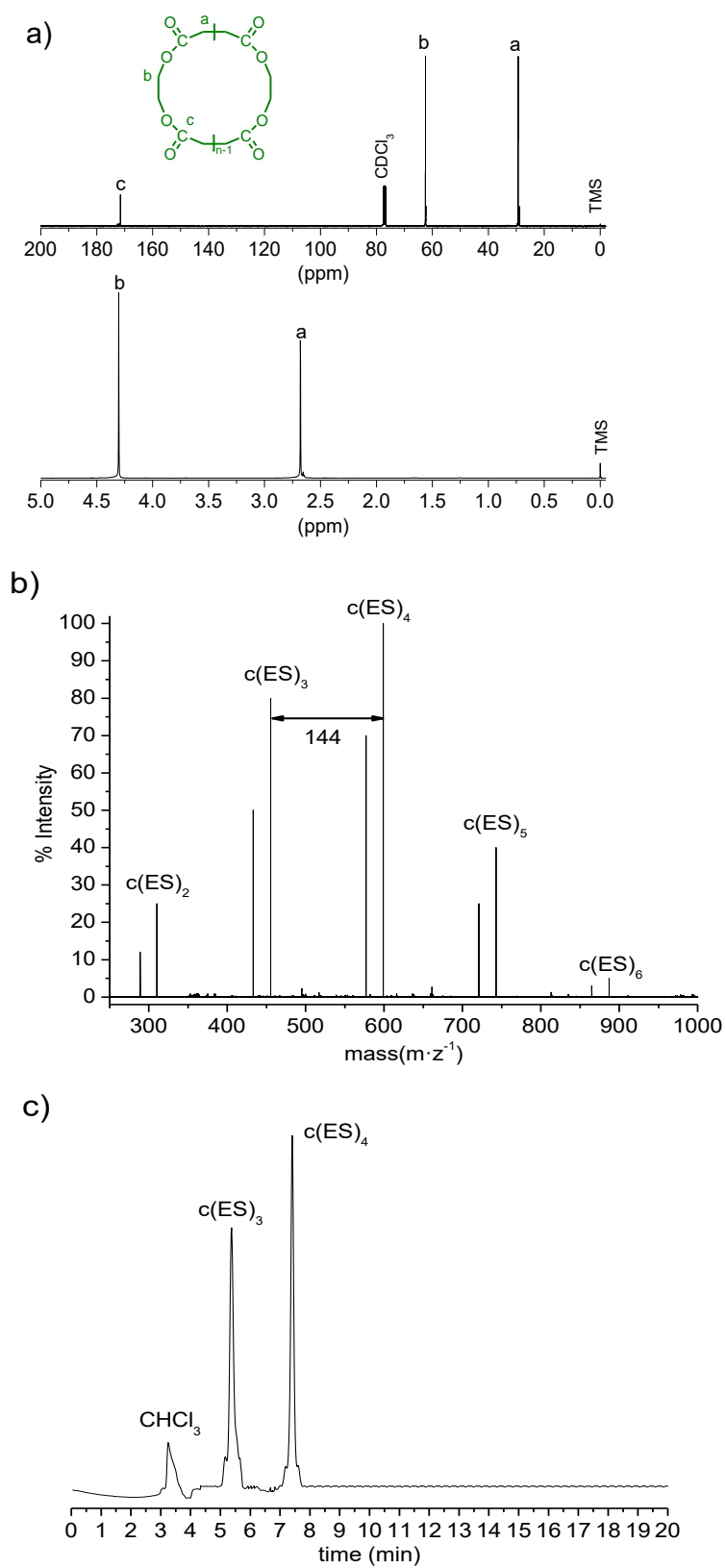


Fig. 1 Characterization of $c(ES)_n$. a) ^{13}C (top) and ^1H (bottom) NMR; b) MALDI-TOF; c) HPLC.

Table 1
Alkylene Succinate Cyclic Oligomers $c(ES)_n$ and $c(BS)_n$.

	Precursors	Yield ^a (%)	Composition ^b (\bar{n} : 2/3/4/ \geq 5)	T_m^c (°C)	$T_{d,5\%}^c$ (°C)	T_{max}^c (°C)
$c(ES)_n$	DMS+ EG	70	0/~45/~55/<10	100	200	300/400
$c(BS)_n$	DMS+ BD	70	~50/~40/~10/<10	105	266	340/400

^a Yields obtained after removing the linear species by chromatography.

^b Oligomeric composition determined by HPLC.

^c Melting and decomposition temperatures (onset and maximum rate) determined by DSC and TGA.

Thermal properties of $c(ES)_n$ and $c(BS)_n$ are not very different. Both fractions melt around 100 °C and display the same thermal decomposition pattern although $c(ES)_n$ starts to lose weight almost 50 °C lower than $c(BS)_n$. The TGA traces of $c(ES)_n$ show two weight falls centred around 250 °C and 400 °C which are made to correspond to partial volatilization of the cycles and decomposition of the polymer formed *in situ* upon heating, respectively. Comparison of GPC and NMR data recorded from $c(ES)_n$ before and after being heated at 200 °C gave support to this interpretation (see Fig.SI-1 in ESI).

e-ROP of $c(ES)_n$ was performed in the bulk at 125 °C with 40% of CALB added to the molten cycles. The evolution of the polymerization reaction was followed by GPC of aliquots drawn at scheduled times which revealed a continuous increasing of the average molecular weight of the formed polymer with time. Data recorded from these measurements are plotted in Fig. 2 which shows an exponential chain growing at the earlier stages that becomes asymptotic after one day of reaction to finally attains a molecular weight about 65,000 g·mol⁻¹ with a \bar{D} of 1.7. For comparison, $c(ES)_n$ was polymerized under the same conditions but replacing the enzyme by 1% of tin dioctanoate. The M_w - t profile resulting in this case was also asymptotic but the finally attained M_w was around 50,000 g·mol⁻¹. A parallel polymerization assay performed at 125 °C in the absence of catalyst revealed that ROP of $c(ES)_n$ induced

exclusively by heating, progressed linearly with a small slope to produce a PES with $M_w \sim 10,000 \text{ g}\cdot\text{mol}^{-1}$ after 24 h of reaction.

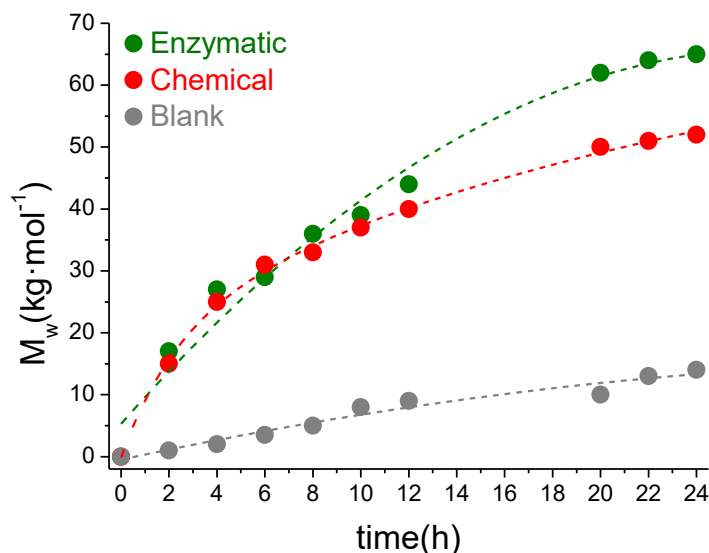


Fig. 2 Evolution of M_w of PES generated in the ROP of $c(\text{ES})_n$ at $125 \text{ }^\circ\text{C}$ using CALB, $\text{Sn}(\text{Oct})_2$ and in the absence of catalyst.

The great attention that nowadays is receiving the development of aliphatic copolyesters containing alkylene succinate units has encouraged us to explore the feasibility of *e*-ROP for preparing such copolyesters from the $c(\text{ES})_n$ fraction. With such purpose polymerization experiments of equimolar mixtures of $c(\text{ES})_n$ and several selected lactones were carried out for 24 h under the same reaction conditions that were used for the synthesis of the homopolyester. $c(\text{BS})_n$ synthesized by enzymatic cyclocondensation and displaying the features indicated in Table 1 (detailed characterization data are provided in Fig. SI-2 in the ESI file), commercial L-lactide (LA) and commercial ϵ -caprolactone (CL), were the cyclic comonomers of choice. Preliminary results obtained in these copolymerization experiments are compared in Table 2, and the ^1H NMR spectra registered from PES and the three copolyesters are depicted in Fig. 3. A close examination of these spectra allowed ascertaining the

chemical constitution expected for the polyesters and determining their comonomeric compositions which were found to be very close to those used in their respective feeds for the copolyesters containing butylene succinate and ϵ -hydroxycaproate units. The lower content in LA units found for *coPES*₇₂LA₂₈ is attributed to partial sublimation of L-lactide taking place during the course of the reaction. On the other hand, the analysis of the signals multiplicity appearing in the ¹³C NMR spectra (see Fig. SI-3 in ESI for details) strongly suggested that the comonomeric units are randomly distributed along the polymer chain for the all three prepared copolyesters.

Table 2
PES copolyesters prepared by e-ROP.

	Yield (%)	M_w^b (g·mol ⁻¹)	\mathcal{D}	$^oT_{d, 5\%}^c$ (°C)	$^{\max}T_d^c$ (°C)	T_g^d (°C)	T_m^d (°C)	ΔH_m^d (J·mol ⁻¹)
PES	90	65,000	1.7	310	385	-12	100	55
<i>coPES</i> ₅₂ BS ₄₈	85	60,000	1.9	300	400	-28	49	20
<i>coPES</i> ₄₉ CL ₅₁	80	60,000	1.8	295	401	-31	40	18
<i>coPES</i> ₇₂ LA ₂₈	76	50,000	1.8	332	390	-5	67	19

^aComposition of copolyesters measured by ¹H NMR.

^bMolecular weight measured by GPC.

^cDecomposition temperatures (onset and maximum rate) determined by TGA.

^dGlass-transition and melting temperatures and melting enthalpy determined by DSC.

GPC measurements revealed that the molecular weights and dispersities of the PES-copolyesters were comparable to that obtained for the homopolyester. Finally, an exploratory estimation of the more substantial thermal properties of *coPES*₅₂BS₄₈ carried out by TGA and DSC (Figs. SI-4 and SI-5 in ESI) brought into evidence the good coincidence of its thermal degradation and reversible transition parameters with those previously reported for similar copolyesters prepared by chemical methods.^{21,22} Although the values measured for the copolyesters made from caprolactone and L-lactide could not be contrasted in the same way because these copolyesters have not been described so far in the accessible literature, the behaviour observed for both

coPES₄₉CL₅₁ and coPES₇₂LA₂₈ is in agreement with what one should be expected from their comonomeric constitution and composition.

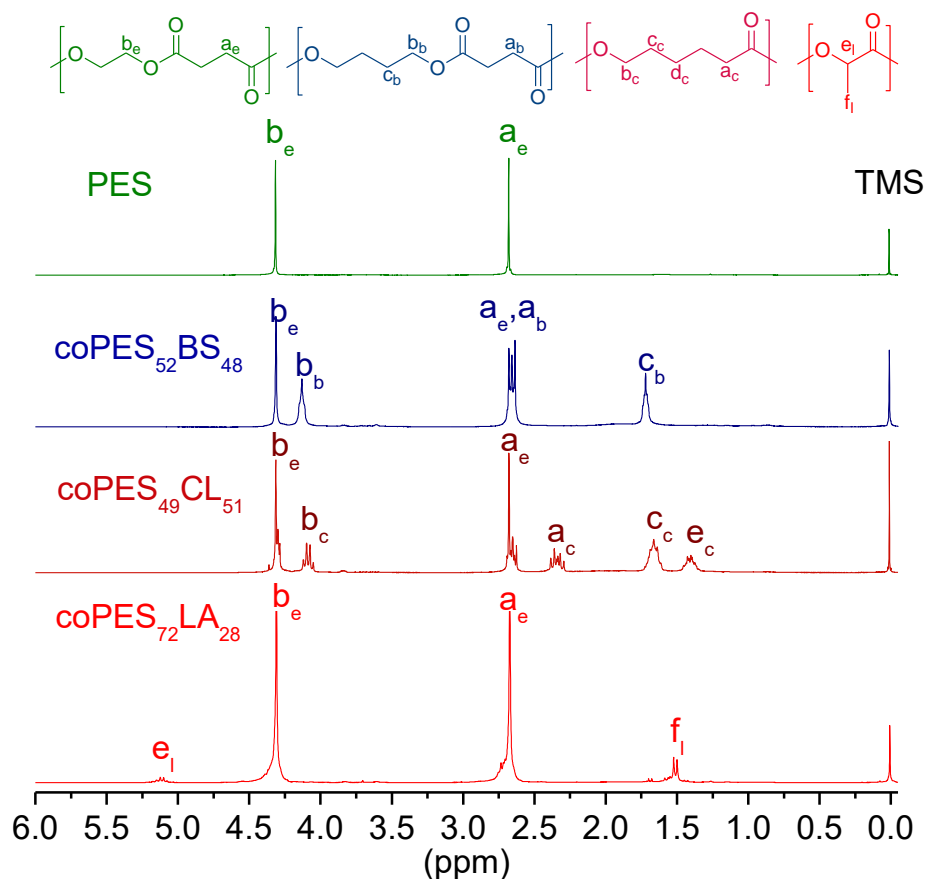


Fig. 3. ¹H NMR of PES, coPES₅₂BS₄₈, coPES₄₉CL₅₁ and coPES₇₂LA₂₈.

Conclusions

Ring opening polymerization catalysed by lipase has been demonstrated to be a convenient method for the preparation of both PES homopolyester and aliphatic copolyesters containing ethylene succinate units. The oligo(ethylene succinate)s cycles required for e-ROP could be efficiently prepared by enzymatic cyclization of two potentially bio-based compounds, *i.e.* ethylene glycol and dimethyl succinate.

Since organometallic catalysts are fully avoided through the whole process, free-metal polymers could be prepared. The polymerization reaction of $\epsilon(\text{ES})_n$ took place faster in the presence of lipase than when catalysed by organometallic compounds. Noteworthy the polymers resulting by e-ROP had molecular weights high enough as to make unnecessary the application of additional treatments (either post-polycondensation or use of extenders) for increasing chain lengths. Cyclic esters including both AA-BB and A-B types with different ring strains were successfully used as comonomers of $\epsilon(\text{ES})_n$ for the synthesis of PES copolyesters by e-ROP. The results attained in this piece of work demonstrate the suitability of the enzymatic route as a green alternative for the synthesis of PES homo- and co-polyesters, in particular when these materials are intended to be used in biomedical applications.

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