Titanium-catalyzed transesterification as a route to the synthesis of fully biobased poly(3-hydroxybutyurate-*co*-butylene dicarboxylate) copolyesters, from their homopolyesters

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ABSTRACT

Fully biobased poly(3-hydroxybutyrate-*co*-butylene adipate) (poly(HB-*co*-BA)) and poly(3-hydroxybutyrate-*co*-butylene succinate) (poly(HB-*co*-BS)) copolyesters were synthesized by transesterification between small chain length PHB and poly(butylene dicarboxylate)s (PBS or PBA) with different molar masses, different HB/BA (or HB/BS) molar ratios, in solution or in bulk, using titanium (IV) isopropoxide (TTIP) as an effective catalyst. All synthesized copolyesters were fully characterized by different chemical and physicochemical techniques including NMR, SEC, FTIR, WAXS, DSC and TGA. The influence of (i) the reaction process (ii) the nature of poly(butylene dicarboxylate) used, (iii) the molar masses of the starting homopolymers, (iv) the reaction temperature, (v) the catalyst amount and (vi) the HB/BS (or HB/BA) molar ratio on the transesterification reaction and copolyester properties were investigated. The transesterification in bulk with 1 mol.% of TTIP at 175 °C from low molar mass starting homopolyesters permitted to quickly obtain random copolyesters with final composition similar to the feeds and without thermal degradation. Random poly(HB-co-BA) copolyesters were amorphous at room temperature, whereas poly(HB-*co*-BS) copolyesters melted at temperatures higher than 40 °C. Poly(HB-*co*-BS) copolyesters exhibited only a PBS crystalline phase, except for copolyesters with a low degree of randomness and a significant HB content. The melting and crystallization temperatures as well as their respective enthalpies decreased with the randomization and the HB content.

1. Introduction

Polyhydroxyalkanoates (PHA) are a family of biopolymers synthesized by several bacteria as intracellular carbon and energy storage granules. A wide variety of prokaryotic organisms can accumulate PHA from 30 to 80% of their cellular dry weight. PHAs can be produced from various renewable resources by fermentation, to develop environmentally friendly materials consistent with a more sustainable development. PHAs are biodegradable but exhibit also biocompatibility in contact with living tissues, suitable for biomedical applications, *e.g.*, tissue engineering [1,2]. Poly[(*R*)-3-hydroxybutyrate] (PHB) is commercially available and it is one of the most prominent PHAs. However, its application as a thermoplastic material is rather limited, mainly due to its high melting temperature (T_m) of approx. 175 °C, high glass transition temperature (T_g) of approx. 4 °C, high crystallinity (X_c) (approx. 60%) and high thermal sensitivity [2]. Indeed, PHB possesses a low thermal stability with a degradation initiation close to the T_m [1] and decomposes easily by random cis-elimination chain scission at temperatures above 150 °C, thus limiting its usage [3–5].

Different approaches have been tested to overcome the above drawbacks and then obtain efficient PHB-based materials such as (i)

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the elaboration of multiphase systems, *e.g.*, by blending with other polymers [6–8] or plasticizers [9], or (ii) the bio- or chemosynthesis of 3-hydroxybutyrate (HB)-based copolymers. Bacterial syntheses with varying substrates and strains have allowed the (bio) synthesis of random copolyesters based on HB units [10–12]. Varying the chemical structure of the co-monomeric unit and its amount in the copolymer afford copolyesters with a wide range of T_m, X_c and behaviors. Moreover, block copolyesters based on HB segments were successfully bioproduced with improved properties over random copolyesters [10]. However, despite their important and varied potential applications, studies of such macromolecular architectures still remain limited, mainly because of their lacks of availability in large quantities and their costs.

The chemosynthesis of PHA-based copolymers required first the production of controlled PHA oligomers. These oligomers can be synthesized by anionic- [13,14], chemical- [15,16] and enzymatic [17,18] ring-opening polymerization (ROP) of lactones, or by the enzymatic [19] and chemical [20,21] esterification of hydroxyacids. PHA molar mass reduction with functionalization to obtain hydroxyl-terminated PHA (PHA-diol) oligomers can be performed by either organometallic- [22] and acid-catalyzed [23] alcoholysis or sodium borohydrate reduction [24,25]. From PHA oligomers, different tailored materials can be obtained including block poly (ester-urethane)s, block poly(ester-ether)s and block or random copolyesters based on PHB blocks with others blocks, such as poly(ε-caprolactone) (PCL), poly(ethylene glycol) (PEG) or poly(butylene adipate) (PBA) [26,27]. PHB-based block copolyesters were synthesized *via* the chemical [28,29] or enzymatic [30] ROP of ε-CL and lactide initiated from PHB-diol oligomers. PEG-PHB-PEG triblock copolymers can be obtained by chain-end esterification [31]. Micro-block and random poly(HB-*co*-CL) and poly(HB-*co*-BA) copolyesters with different compositions have also been synthesized by acid-catalyzed transesterification in solution [32,33].

In a recent study [34], lipase-catalyzed synthesis of biobased micro-block and random copolyesters from PHB-diol oligomers and poly(butylene succinate) (PBS), a well-known biobased, biodegradable and biocompatible aliphatic polyester suitable for packaging and biomedical applications [35–37], has been investigated. More than lipases, organometallic catalysts have been widely used to synthesize high molar mass aliphatic (co)polyesters from diacid and diol building blocks [38–40]. Recently, poly(lactic acid) and poly (3-hydroxybutyrate-*co*-3-hydroxyvalerate) have been slightly transesterified by zinc acetate to improve the compatibility of the blend [41]. However, the efficiency of the transesterification was not analyzed. Whilst these metal-based catalysts showed a remarkable transesterification capacity, especially for titanium-based catalysts [42], to the best of our knowledge, no organometallic transesterification between PHB and PBS or PBA has been reported so far.

The aim of this study was, thus, to synthesize poly(HB-*co*-BA) and poly(HB-*co*-BS) copolyesters by two different transesterification processes (solution or bulk) from PHB and PBA or PBS with titanium (IV) isopropoxide (TTIP) as an effective catalyst. Impallomeni et al. demonstrated that the transesterification between two homopolyesters occurred at a correct rate only when homopolyesters molar mass are not too high [32,33]. Then, small chain length PHB, and PBA or PBS with limited molar masses, were used. The effect of (i) the catalytic process, (ii) the temperature, (iii) the catalyst amount, (iv) the starting homopolyesters molar masses, (v) the HB/BS molar ratio and others factors on the architecture of the synthesized copolyesters were studied. The macromolecular architectures (*e.g.*, composition and sequence distribution) of the resulting copolyesters were determined by NMR, FTIR and SEC. The crystalline structure, thermal stability and thermal properties of the corresponding architectures were studied by WAXS, TGA and DSC, respectively. Finally, the bulk transesterification pathway has been compared to the enzymatic one which had been previously described [34].
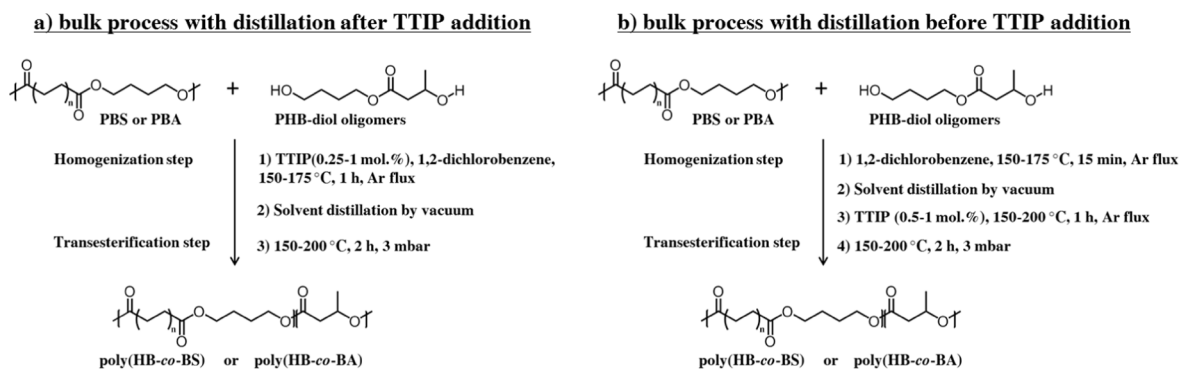
2. Experimental part

2.1. Materials

Small chain length poly[(R)-3-hydroxybutyrate] (PHB) of different molar masses (M_n: 4000, 7000 and 15,000 g/mol, as determined by SEC) were synthesized by tin-catalyzed alcoholysis of high molar mass PHB with 1,4-butanediol, according to a protocol based on previous reports [22] and detailed in the supporting information SI.1. Poly(butylene adipate) (PBA) and poly (butylene succinate) (PBS) with different molar masses were synthesized according to a protocol based on previous reports [38–40] and also detailed in the supporting information SI.2. PBA of M_n = 8000 and 20,000 g/mol and PBS of 10,800 and 28,000 g/mol (from SEC determinations) were used. Before the reaction, small chain length PHB, PBA and PBS were dried at 40 °C under vacuum in an oven for 16 h. Titanium (IV) isopropoxide (TTIP) (98 + %) was supplied by Acros. Anhydrous 1,2-dichlorobenzene (99%) and chloroform were supplied by Sigma-Aldrich. Petroleum ether was supplied from Fisher. All solvents for the analytical methods were of analytical grade, and used without further purifications.

2.2. Titanium-catalyzed transesterification in solution

In a round-bottom reactor, dried small chain length PHB and PBA (or PBS) were dissolved in a small amount of anhydrous 1,2-dichlorobenzene (~1.5 mL/g of homopolyester) at 150–175 °C under an argon atmosphere. After 15 min, the proper amount of TTIP (from a 20 wt.% solution of TTIP in 1,2-dichlorobenzene) was added into the reaction mixture. The reaction continued for 4 h at atmospheric pressure under argon. At the end of the reaction, the mixture was precipitated into a large volume of vigorously stirred cold petroleum ether and the copolyester was recovered by filtration. The copolyester was then purified by first a dissolution step in a minimum of chloroform, and then a second precipitation step into a large volume of vigorously stirred cold petroleum ether followed by a filtration. The recovered final product was dried under reduced pressure in an oven at 50 °C for 24 h.

a) bulk process with distillation after TTIP addition

b) bulk process with distillation before TTIP addition

Scheme 1. Bulk transesterification process with distillation (a) after and (b) before TTIP addition in the reaction mixture.

2.3. Titanium-catalyzed transesterification in bulk

After a first step leading to the homogenization of dried PHB and PBA (or PBS) in anhydrous 1,2-dichlorobenzene (~1 mL/g of homopolyester) at 150–175 °C under an argon atmosphere, two possibilities have been studied to add the catalyst: before the solvent removal ("distillation after TTIP introduction") and after the solvent removal ("distillation before TTIP introduction).

In the case of bulk transesterifications with distillation after TTIP introduction (Scheme 1a), after 1 h of reaction with TTIP under an argon flux, the solvent (~1 mL/g of homopolyester) was distilled off the reaction mixture by vacuum and the transesterification proceeded under reduced pressure (~3 mbar) for 2 h. At the end of the reaction, the reaction mixture was dissolved in a minimum of chloroform, precipitated into a large volume of vigorously stirred cold petroleum ether and recovered by filtration. The final product was dried under reduced pressure in an oven at 50 °C for 24 h.

In the case of Scheme 1b (distillation before TTIP introduction), after an homogenization step of 15 min, the solvent was distilled off the reaction mixture and the proper amount of TTIP (from a 20 wt.% solution of TTIP in 1,2-dichlorobenzene) was added into the reaction mixture. The reaction mixture was then stirred for 1 h under an argon atmosphere. After 1 h, the pressure was decreased, resulting in the removal of the residual solvent. The transesterification was performed under reduced pressure (~3 mbar) for 2 h. The copolyester recovery was performed as previously stated.

2.4. General methods and analysis

^{1}H- and ^{13}C-NMR spectra of polyesters were obtained with a Bruker 400 MHz spectrometer. CDCl$_3$ was used as solvent to prepare solutions with concentrations of 8–10 and 30–50 mg/mL for ^{1}H-NMR and ^{13}C-NMR, respectively. The number of scans was set to 128 for ^{1}H-NMR and at least 4000 for ^{13}C-NMR. Calibration of the spectra was performed using the CDCl$_3$ peak (δ_H = 7.26 ppm, δ_C = 77.16 ppm).

The number-average molar mass (M$_n$), the mass-average molar mass (M$_w$) and the dispersity (Đ) of the polyesters samples were determined in chloroform by size exclusion chromatography (SEC), using a Shimadzu liquid chromatograph. PLGel Mixed-C and PLGeL 100 Å columns and refractive index detector were used. Chloroform was used as eluent at a flow rate of 0.8 ml/min. The apparatus was calibrated with linear polystyrene standards from 162 to 1,650,000 g/mol.

Infrared spectroscopy (IR) was performed with a Nicolet 380 Fourier transformed infrared spectrometer (Thermo Electron Corporation) used in reflection mode and equipped with an ATR diamond module (FTIR-ATR). The FTIR-ATR spectra were collected at a resolution of 4 cm^{-1} and with 64 scans per run.

Differential scanning calorimetry (DSC) was performed using a TA Instrument Q200 under nitrogen (flow rate of 50 mL/min), calibrated with high purity standards. Samples of 2–3 mg were sealed in aluminum pans. A three-step procedure with a 10 °C/min ramp was applied that involved: (i) heating from room temperature to 180 °C and holding for 3 min to erase the thermal history, (ii) cooling to -80 °C and holding for 3 min and (iii) heating (second heating) from −80 to 180 °C. The crystallinity (X$_c$) was calculated according to Eq. (1),

$$X_c(\%) = \frac{\Delta H_m}{\Delta H_m^0} \times 100$$

(1)

where ΔH_m is the melting enthalpy and ΔH_m^0 is the melting enthalpy of a 100% pure crystalline polyester.

Thermal degradations were studied by thermogravimetric analyses (TGA). Measurements were conducted under helium atmosphere (flow rate of 25 mL/min) using a Hi-Res TGA Q5000 apparatus from TA Instruments. Samples (1–3 mg) were heated from room temperature up to 600 °C at a rate of 20 °C/min.

Wide angle X-ray Scattering (WAXS) data were recorded on a Siemens D5000 diffractometer using Cu K$_\alpha$ radiation (1.5406 Å) at 25–30 °C in the range of 2θ = 14–34° at 0.4° min^{-1}. Analyses are performed on compressed-molded sheets.

Table 1
Copolyesters obtained from organometallic transesterification of PHB and PBA.

Sample	Experimental conditions								Yield	¹H NMR		SEC		¹³C-NMR		
	Feed HB/BA	$M_{n,PBA}$	$M_{n,PHB}$	Reaction type	Temp.[a]	Time	Pressure	TTIP amount		Exp. HB/BA[b]	Therm. degrad.[c]	M_n	Đ	L_{BA}	L_{HB}	R
	mol.%	kg/mol	kg/mol		°C	h	mbar	mol.%	wt.%	mol.%	mol.%	kg/mol				
Copo-BA-1	1/1	20.0	7.0	Solution	150	4	1000	1	91	0.92/1	0	6.1	1.7	43	19	0.07
Copo-BA-2	1/1	8.0	4.0	Bulk	210	2	3	1	79	0.89/1	8	8.7	2.0	3.3	1.4	0.99
Copo-BA-3	2/1	8.0	4.0	Bulk	175	2	3	1	81	1.89/1	1	8.5	1.9	2.1	2.0	0.96
Copo-BA-4	2/1	8.0	4.0	Solution	175	4	1000	10	74	1.84/1	6	2.6	1.5	2.2	1.9	0.98

[a] Reaction temperature.
[b] Experimental HB/BS molar ratio determined by ¹H-NMR.
[c] Percentage of PHB thermal degradation calculated using ¹H-NMR.

3. Results and discussion

3.1. Organometallic synthesis of poly(HB-co-BA) copolyesters in bulk and solution

Titanium-catalyzed syntheses of poly(3-hydroxybutyrate-*co*-butylene adipate) (poly(HB-*co*-BA)) copolyesters with different HB/BA molar ratios were carried out in bulk (with "distillation before TTIP addition") or in solution, from PBA of two different molar masses (M_n = 8000 or 20,000 g/mol) and from small chain length PHB of two different molar masses (M_n of 4000 or 7000 g/mol). M_n and Đ of the corresponding copolyesters were determined by SEC and presented in Table 1. M_n between 2600 and 8700 g/mol were obtained with Đ of approx. 1.5–2.0. Copolyesters were recovered with a high yield (~75–90 wt.%).

Reactions in solution led to the synthesis of copolyesters with lower M_n than ones synthesized *via* the reaction in bulk. The decrease of M_n for reactions in solution was higher when the reaction was performed at higher temperature, with a higher catalyst amount and using initial homopolyesters of lower molar mass as observed for Copo-BA-4 compared to Copo-BA-1. One can suppose that the decrease of M_n for Copo-BA-4 was due to the PHB thermal degradation by random β-scissions, creating crotonyl end-groups which are non-reactive end-groups [3–5]. On the other side, the reaction in bulk permitted to obtain copolyesters with higher molar masses. Moreover, one can observe that M_n values seemed not influenced by the feed HB/BA ratio. This latest result was very interesting to synthesize copolyesters with high HB content since Impallomeni et al. reported a decrease of M_w with the HB content for the acid-catalyzed transesterification in solution [33]. However, since the previous statement was based on only two samples, it should be taken with caution.

The chemical structures of synthesized poly(HB-*co*-BA) copolyesters and their corresponding homopolyesters (PBA and PHB-diol) were verified by ¹H-, ¹³C-NMR and FTIR. The ¹H-NMR spectrum of poly(HB-*co*-BA) is presented in Fig. 1a, whereas spectra of their corresponding homopolyesters are found in Fig. SI.1a with a complete peak assignment in SI.3. ¹H chemical shifts at δ = 1.28, 2.45–2.65 and 5.25 ppm were assigned to −O−CH(C$\underline{H}_3$)−CH$_2$−CO−, −O−CH(CH$_3$)−C$\underline{H}_2$−CO− and −O−C$\underline{H}$(CH$_3$)−CH$_2$−CO− protons from HB repetitive units, respectively. ¹H chemical shifts at δ = 1.69 and 4.09 ppm were ascribed to −O−CH$_2$−C$\underline{H}_2$− and −O−C$\underline{H}_2$−CH$_2$− protons from 1,4-BDO repetitive units, whereas the ones at δ = 1.65 and 2.32 ppm were ascribed to −CO−CH$_2$−C$\underline{H}_2$− and −CO−C$\underline{H}_2$−CH$_2$− protons from adipate repetitive units, respectively. Moreover, the primary (HO−⊕ C$\underline{H}_2$−CH$_2$−) and secondary (HO−C$\underline{H}$(CH$_3$)−CH$_2$−) hydroxyl terminal groups signals were observed at respectively δ = 3.67 and 1.20 ppm, at tiny intensities, in agreement with the relatively high molar mass of the samples. Furthermore, the presence of crotonyl end-groups (Scheme SI.3) from PHB degradation was verified by ¹H chemical shifts at δ = 1.87, 5.82 and 6.96 ppm ascribed to C$\underline{H}_3$−CH=CH−CO−, CH$_3$−C$\underline{H}$=CH−CO− and CH$_3$−CH=C$\underline{H}$−CO− protons, respectively [3]. The intensity of crotonyl, end-groups
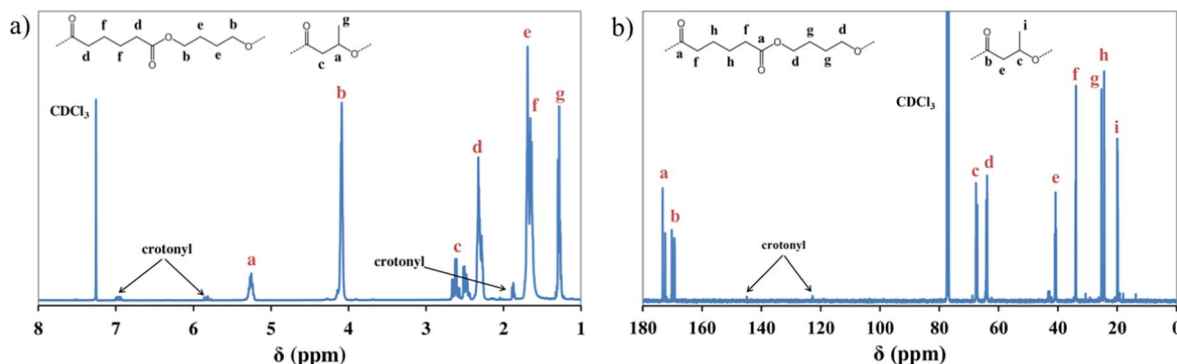

Fig. 1. (a) ¹H- and (b) ¹³C-NMR spectra of Copo-BA-2 in CDCl₃.

was calculated using relative intensities of protons at δ = 6.96 and 5.25 ppm assigned to crotonyl and HB groups, respectively. The presence of PHB thermal degradation was observed at different intensities in copolyesters, except for Copo-BA-1. Whereas the thermal degradation of Copo-BA-3 was very low (*i.e.*, 1 mol.%), Copo-BA-2 and Copo-BA-4 exhibited significant amount of crotonyl end-groups. The high amount of PHB thermal degradation in Copo-BA-2 was due to the high reaction temperature, whereas the one in Copo-BA-4 was surely due to the too high amount of catalyst.

The final molar composition in BA (χ_{BA}) and HB (χ_{HB}) segments in poly(HB-*co*-BA) copolyesters was calculated from ^{1}H-NMR spectra using relative intensities of protons in α of ester functions in 1,4-BDO (δ = 4.12 ppm) and HB (δ = 5.25 ppm) segments, respectively. In this calculation, since the primary hydroxyl end-groups (OH−CH$_2$−CH$_2$−CH$_2$−C$\underline{H}_2$−O) exhibited also a signal at 4.12 ppm and was, thus, overlapped with the one of the 1,4-BDO repetitive unit, the contribution of the primary hydroxyl end-groups in the intensity of the signal at 4.12 ppm assigned mainly to the 1,4-BDO repetitive unit should be removed. χ_{HB} was determined according to Eq. (2),

$$\chi_{HB} = \frac{I_{5.25}}{\frac{I_{4.12} - I_{3.67}}{4} + I_{5.25}} \times 100 \tag{2}$$

Final HB and BA contents in the chains are presented in Table 1. All synthesized copolyesters presented a HB/BA molar ratio close to the initial feed one.

To investigate further the structure of poly(HB-*co*-BA) copolyesters, ^{13}C-NMR was performed. The ^{13}C-NMR spectrum of poly(HB-*co*-BA) is presented in Fig. 1b, whereas spectra of the corresponding homopolyesters are found in Fig. SI.2a. ^{13}C chemical shifts at δ = 24.4 and 33.9 ppm were ascribed to CO−CH$_2$−C$\underline{H}_2$− and CO−C$\underline{H}_2$−CH$_2$ - carbons from adipate repeating units, whereas ones at δ = 25.3 and 64.0 ppm were ascribed to O−CH$_2$−C$\underline{H}_2$− and O−C$\underline{H}_2$−CH$_2$− carbons from 1,4-BDO repeating units, respectively. ^{13}C chemical shifts at δ = 20.0, 40.8 and 67.2–67.8 ppm were assigned to −O−CH(C$\underline{H}_3$)−CH$_2$−CO−, −O−CH(CH$_3$)−C$\underline{H}_2$−CO− and −O−C$\underline{H}$(CH$_3$)−CH$_2$−CO− carbons from HB repeating units, respectively. Finally, four doublets of ^{13}C chemical shifts were observed at δ = 169–173 ppm assigned to carbonyl carbons from HB and adipate repetitive units. Characteristics signals of PHB thermal degradation were observed at δ = 120–150 ppm. Moreover, due to the high sensibility of ^{13}C-NMR to small differences in the chemical environment, the different triad structures (B-A-B, HB-A-B, B-A-HB, HB-A-HB, A-HB-B, HB-HB-B, A-HB-HB and HB-HB-HB) were observed on the ^{13}C-NMR spectra presented in Fig. 2, with HB, B and A as the HB, 1,4-BDO and adipate segments, respectively. The splitting of signals assigned to PHB (δ = 169 ppm) or PBA (δ = 173.3 ppm) permitted the determination of the average sequence length of HB and BA units (L$_{HB}$ and L$_{BA}$, respectively) and the degree of randomness (R) using Eqs. (3)–(5) [33],

$$L_{BA} = 1 + \frac{2 \times (I_{B-A-B} + I_{HB-A-B})}{I_{A-HB-B} + I_{HB-HB-B} + I_{B-A-HB} + I_{HB-A-HB}} \tag{3}$$

$$L_{HB} = 1 + \frac{2 \times (I_{A-HB-HB} + I_{HB-HB-HB})}{I_{A-HB-B} + I_{HB-HB-B} + I_{B-A-HB} + I_{HB-A-HB}} \tag{4}$$

$$R = \frac{1}{L_{HB}} + \frac{1}{L_{BA}} \tag{5}$$

where I$_{B-A-B}$, I$_{HB-A-B}$, I$_{B-A-HB}$, I$_{HB-A-HB}$, I$_{A-HB-B}$, I$_{HB-HB-B}$, I$_{A-HB-HB}$ and I$_{HB-HB-HB}$ are integration of peaks assigned to carbonyl carbons (δ ~ 169–173 ppm).

Results are listed in Table 1. For a mixture of homopolymers R is equal to 0, the values between 0 and 1 are obtained for block copolymers, whereas R is equal to 1 for fully random copolymers and R = 2 for strictly alternating distribution. According to the
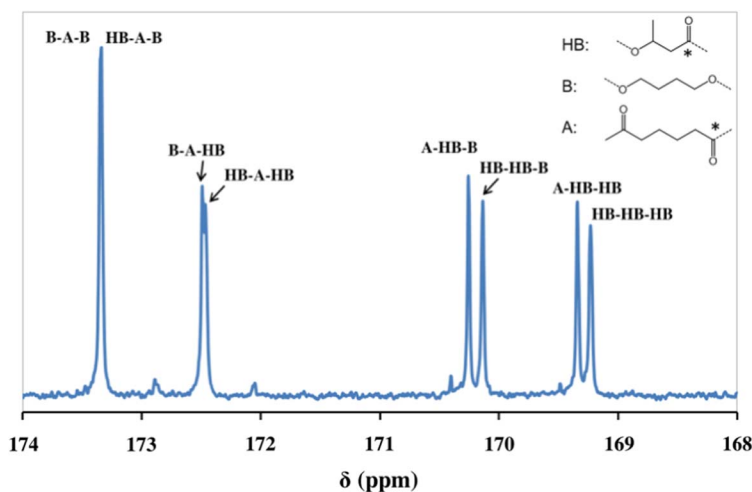

Fig. 2. ^{13}C-NMR spectra of poly(HB-*co*-BA) copolyester in CDCl$_3$ centered on carbonyl peaks and chemical structures corresponding to abbreviations.
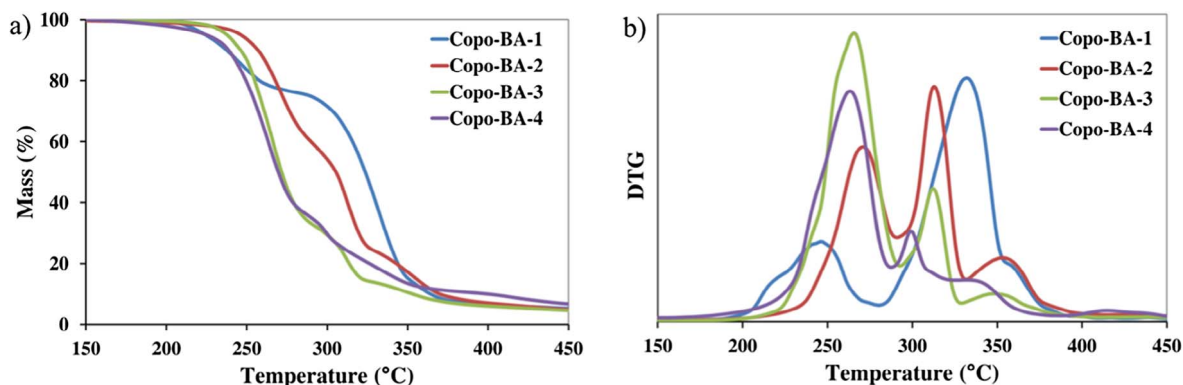
Fig. 3. (a) Mass loss and (b) their DTG curves of poly(HB-*co*-BA) copolyesters degradation under helium.

copolyester, L_{HB} and L_{BA} varied between 1.4 and 43. The transesterification in solution of Copo-BA-1 was not performed at a significant extent (*i.e.* $L_{BA} = 43$, $L_{HB} = 19$ and $R = 0.07$) contrary to Copo-BA-4 which had a random structure (*i.e.* $L_{BA} = 2$, $L_{HB} = 2$ and $R = 0.98$). This result can be due to (i) the lower amount of catalyst used, (ii) the lower reaction temperature and (iii) the use of starting materials with higher molar masses, which has been reported to prevent the transesterification reaction [33]. The two copolyesters synthesized in bulk exhibited a random distribution sequence, between HB and BA segments, as it was expected using a titanium-based organometallic catalyst [38,43].

FTIR spectra of poly(HB-*co*-BA) copolyesters are presented in Fig. SI.3a. Characteristic vibration bands were observed in the poly (HB-*co*-BA) spectrum at 2955 (C−H asymmetrical stretching), 2855 (C−H symmetrical stretching), 1720 (C=O stretching of ester moieties), 1370 (symmetric deformation of the −CH$_2$− groups), 1160 (C−O−C stretching of ester moities), 1055 (O−C−C vibration in 1,4-BDO), 955 (C−O symmetric stretching) and 735 cm^{-1} (−CH$_2$− of the adipate in-plane bending) [38,44].

TGA traces of poly(HB-*co*-BA) copolyesters are shown in Fig. 3 with their corresponding derivatives (DTG) curves. Main data are summarized in Table SI.1. Under helium, all copolyesters degraded in two or three main steps which involve competitive mechanisms. First, Copo-BA-1, Copo-BA-2 and Copo-BA-3 showed a good thermal stability without mass losses before 180–200 °C. For its part, Copo-BA-4 showed a mass loss starting at already 150 °C due to its lower molar mass, as demonstrated by Chrissafis et al. [39], and maybe some residual solvent. First, a small mass loss was recorded at approx. 200–230 °C for Copo-BA-1 to 3 and 150–220 °C for Copo-BA-4 attributed to the degradation of low molar mass chains along with the cyclization at the chain-ends and backbiting reactions (Scheme SI.3) [39,45]. Copo-BA-1 exhibited a two-step degradation profile with DTG maximums at 245 and 345 °C corresponding to HB and BA segments thermal degradation, respectively. The thermal degradation temperatures of the two blocks were in agreement with the thermal degradation temperatures of their respective homopolyesters (Fig. SI.4). All three other copolyesters with random structures (Copo-BA-2 to 4) exhibited a three-step degradation profile between 200 and 400 °C with three maximum degradation rates ($T_{deg,max}$) determined from the DTG curves at approx. 265, 315 and 355 °C. The first temperature was assigned to HB segments, whereas the two others were ascribed to the BA thermal degradation. In total, degradations led to a substantial mass loss of approx. 90–94% mostly by β-(cis-elimination) and α-hydrogen bond scissions (Scheme SI.3) [3,46]. After 450 °C, no mass loss was observed and a small amount of ash (~4 wt.%) was recovered at 500 °C.

The crystalline structure of poly(HB-*co*-BA) copolyesters was studied by WAXS. WAXS patterns of Copo-BA-1 and Copo-BA-2 are presented in Fig. 4 and compared to PHB and PBA patterns. Copo-BA-2 exhibited similar patterns as Copo-BA-3 and Copo-BA-4 (data not shown). No crystalline structures were observed in these three copolyesters. However, Copo-BA-1 exhibited a mixture of both PHB and PBA crystalline phases. Small diffraction signals at $2\theta = 13.6$ and $17.1°$ assigned to the (0 2 0) and (1 1 0) planes in the WAXS patterns, were attributed to PHB crystals [47], whereas signals at $2\theta = 21.7$, 22.5 and 24.1° were assigned to the PBA β-form crystals
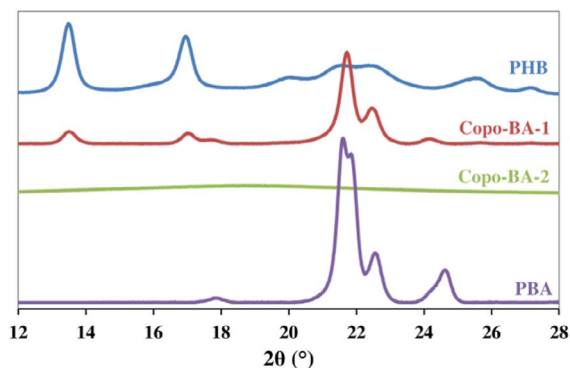

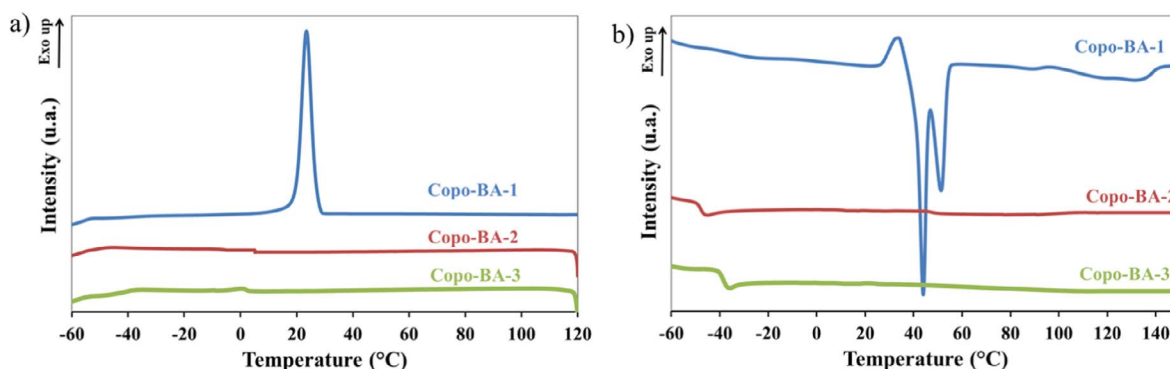**Fig. 4.** WAXS patterns of PHB, Copo-BA-1, Copo-BA-2 and PBA.

Fig. 5. DSC (a) cooling and (b) second heating runs of poly(HB-*co*-BA) copolyesters.

which are formed when T_c < 28 °C [48].

The thermal properties of copolyesters were studied by DSC. Prior to this, it has been verified, from TGA results, that no significant degradation occurred in the DSC analyses temperature range. DSC curves of cooling and second heating runs of copolyesters are presented in Fig. 5, whereas data are summarized in Table 2. During the first heating run, only Copo-BA-1 showed melting phenomena at 51 and 142 °C assigned to the PBA and PHB crystalline phase, respectively. During the cooling run, Copo-BA-1 exhibited a significant exothermic phenomenon at 23 °C assigned to the crystallization, whereas Copo-BA-2 and Copo-BA-3 showed no crystallization. Copo-BA-1 showed easier crystallization, resulting from its block structure, contrary to the two other random copolyesters. During the second heating run, two small endothermal baseline deviations associated to the glass-transition (T_g) phenomenon were observed for Copo-BA-1 at approx. −59 and 1 °C, and were ascribed to BA and HB blocks since they were close to the T_g of their corresponding homopolyesters (*i.e.* approx. −60 and 4 °C for PBA [49] and PHB [1]), respectively. After that, a small cold-crystallization peak followed by a double melting phenomenon at approx. 50 °C were observed for Copo-BA-1 and were ascribed to the PBA crystalline phase. This complex phenomenon was probably due to the fusion-recrystallization process commonly observed for aliphatic polyesters such as PBA and PBS [34,38,48]. A second melting phenomenon assigned to the PHB crystalline phase was observed at 131 °C. The crystallization rate of both segments was, thus, sufficient for the co-crystallization of Copo-BA-1. For their part, Copo-BA-2 and Copo-BA-3 exhibited an amorphous thermal behavior with the presence of a unique T_g between the ones of both homopolyesters. As expected, T_g increased with the HB content. The crystallinity (X_c) of the two copolyester phases in Copo-BA-1 was calculated from the second heating run with the help of Eq. (1) using the melting enthalpy value of 100% crystalline phase ($\Delta H_m°$) of PBA (determined from the groups contribution method as proposed by Van Krevelen) and PHB (experimentally determined). $\Delta H_{m,PBA}°$ and $\Delta H_{m,PHB}°$ are 135 and 146 J/g, respectively [50,51]. X_c of 35 and 8% for PBA and PHB crystals were calculated and reported in Table 1.

Based on the study of the poly(HB-*co*-BA) synthesis, the titanium-catalyzed transesterification in bulk was more interesting than the process in solution. However, due to the low average sequence length of BA units (L_{BA}), synthesized random poly(HB-*co*-BA) copolyesters were amorphous at room temperature. For its part, PBS, which has a higher T_m than PBA and a significant crystallinity [35–37], could be a suitable starting homopolyester for the synthesis of a solid HB-based copolyester at room temperature.

3.2. Study of the titanium-catalyzed bulk transesterification process during the synthesis of poly(HB-co-BS) copolyesters

Several poly(HB-*co*-BS) copolyesters were synthesized in high yields (~85–90 wt.%) in bulk under vacuum at high temperature with TTIP as catalyst. To homogenize the reaction mixture, a small amount of anhydrous 1,2-dichlorobenzene was added at the beginning of the reaction in order to solubilize both copolyesters, then this solvent was removed under vacuum.

The final chemical structure of poly(HB-*co*-BS) copolyesters was verified by ^{1}H-, ^{13}C-NMR and FTIR. ^{1}H-, ^{13}C-NMR and FTIR spectra of poly(HB-*co*-BS) copolyesters are presented in Figs. SI.1b, SI.2b and SI.3b, respectively. All the spectra of poly(HB-*co*-BA) and poly(HB-*co*-BS) copolyesters look alike due to the close structure between PBS and PBA homopolyesters. Nevertheless, the complete ^{1}H- and ^{13}C-NMR peaks assignments of poly(HB-*co*-BS) copolyester are presented in SI.3 and SI.4, respectively. The HB/BS

Table 2
Thermal properties of poly(HB-*co*-BA) copolyesters at 10 °C/min.

Sample	Cooling		Second heating									
	T_c °C	ΔH_c J/g	$T_{g,1}$	$T_{g,2}$ °C	T_{cc} °C	ΔH_{cc} J/g	$T_{m,1}$ °C	$\Delta H_{m,1}$ J/g	$X_{c,1}$ %	$T_{m,2}$ °C	$\Delta H_{m,2}$ J/g	$X_{c,2}$ %
Copo-BA-1	23	52	−59	1	27	5	50	47	35	131	12	8
Copo-BA-2	1	1	−48	–	–	–	–	–	0	–	–	0
Copo-BA-3	0	1	−38	–	–	–	–	–	0	–	–	0

Table 3
Copolyesters obtained from organometallic transesterification of PHB and PBS.

Sample	Experimental conditions						Yield	^{1}H NMR		SEC		^{13}C-NMR		
	Feed HB/BS mol.%	$M_{n,PBS}$ kg/mol	$M_{n,PHB}$ kg/mol	Temp.[a] ℃	TTIP amount mol.%	Distillation before T TIP addition	wt.%	Exp. HB/BS[b] mol.%	Thermal. degrad.[c] %	M_n kg/mol	Đ	L_{BS}	L_{HB}	R
Copo-BS-1	1/1	28.0	15.0	175	0.25	No	89	1/0.86	0	12.1	2.2	∞	∞	0.
Copo-BS-2	1/1	28.0	15.0	175	0.5	No	87	1/1.08	0	28.4	1.7	∞	∞	0
Copo-BS-3	1/1	28.0	15.0	175	1	No	92	1/1.13	0	22.4	1.9	∞	∞	0
Copo-BS-4	1/1	10.8	4.0	150	1	No	88	1/1.12	0	6.7	2.0	21.0	17.7	0.10
Copo-BS-5	1/1	10.8	4.0	175	0	No	81	1/1.10	0	6.6	1.9	∞	∞	0
Copo-BS-6	1/1	10.8	4.0	175	0.5	No	84	1/1.16	0	8.4	2.2	17.2	7.3	0.19
Copo-BS-7	1/1	10.8	15.0	175	0.5	No	88	1/1.07	0	13.8	2.0	29.3	12.9	0.11
Copo-BS-8	1/1	10.8	4.0	175	1	No	87	1/1.16	0	10.2	2.4	8.7	4.4	0.34
Copo-BS-9	1/1	10.8	4.0	200	1	No	85	1/1.17	3	14.9	1.9	4.5	2.1	0.70
Copo-BS-10	1/1	10.8	4.0	175	1	Yes	89	1/1.09	2	12.6	1.8	3.0	1.5	1.01
Copo-BS-11	1/3	10.8	4.0	175	1	Yes	90	1/2.90	2	15.1	1.7	6.8	1.3	0.93
Copo-BS-12	1/5	10.8	4.0	175	1	Yes	90	1/5.16	0	15.5	1.8	17.5	1.2	0.95

[a] Reaction temperature.
[b] Experimental HB/BS molar ratio determined by ^{1}H-NMR.
[c] Percentage of PHB thermal degradation calculated using ^{1}H-NMR.

composition of poly(HB-*co*-BS) copolyesters was calculated using Eq. (2) and relative intensities of protons in 1,4-BDO (δ = 4.12 ppm) and HB (δ = 5.25 ppm) repetitive units. All synthesized copolyesters presented HB/BS molar ratio close to the initial feed ones.

Likewise, ^{13}C-NMR spectra were used to determine the average sequence length of HB and BS units (L_{HB} and L_{BS}, respectively) and R using Eqs. (3)–(5) and intensities of carbonyl carbons of the different triads at δ = 169–172 ppm (Fig. SI.5). Determined HB and BS contents in the chains, L_{HB}, L_{BS} and R values are presented in Table 3 together with the SEC results. The transesterification rate and final molar masses were particularly discussed in function of (i) initial homopolyesters molar masses, (ii) the reaction temperature, (iii) the time of introduction of the catalyst and (iv) the HB/BS molar ratio.

As previously stated, no significant transesterification (R = 0, L = ∞) occurred when starting from high molar mass homopolyesters (Table 3, Copo-BS-1 to 3), leading to a mixture of two homopolyesters. However, decreasing the molar mass of only one of the two homopolyesters led to improved transesterification rate (Table 3, Copo-BS-7) but only a block copolyester is obtained (R = 0.11, L_{BS} = 29, L_{HB} = 13). Likewise, the absence of TTIP as catalyst prevented any transesterification leading to a blend of homopolyesters (Table 3, Copo-BS-5). As expected, the transesterification rate and copolyesters molar mass increased with the TTIP amount (Table 3, Copo-BS-5, 6 and 8) and the reaction temperature (Table 3, Copo-BS-4, 8 and 9). However, increasing the temperature to 200 ℃, for Copo-BS-8, led to PHB thermal degradation as previously observed during the poly(HB-*co*-BA) copolyester synthesis. Reaction temperature higher than 175 ℃ was, thus, avoided. Likewise, due to the high T_m of small chain length PHB and even if T_m decreased with the molar mass (Fig. SI.6), small chain length PHB did not melt very well at 150 ℃ and reactive systems became solid quickly after the solvent distillation preventing an efficient transesterification. As a result, only blocky copolyesters of low molar mass were obtained for such low temperature (Copo-BS-4).

The crucial point of the catalyst efficiency was the presence or not of the "homogenization solvent" during the TTIP addition in the reaction mixture. Indeed, for copolyesters with the "distillation after TTIP addition" process (Scheme 1), the transesterification was null (mixture of two homopolyesters) using both high molar mass homopolyesters and partial (block copolyesters) using lower molar masses. However, random copolyesters were obtained only *via* the "distillation before TTIP addition" process (Table 3, Copo-BS-10 to 12), as it was also the case in the poly(HB-*co*-BA) copolyester study. To explain the difference between the two processes, as observed when comparing Copo-BS-8 and Copo-BS-11, one can suppose a partial deactivation of the catalyst during the homogenization step or some catalyst removal during the distillation of the large amount of solvent. Indeed, titanium alkoxides catalysts can be hydrolyzed by water to form TiO_2 and R'OH molecules, which show no catalytic effect [52]. Even if an anhydrous solvent was used to minimize this risk, when TTIP was added before the removal of the "homogenization solvent", TTIP was then diluted in a much larger amount of solvent and the risk of titanium hydrolysis was, thus, increased. Otherwise, one can suppose that during the "distillation after TTIP addition" process, a non-negligible amount of catalyst was pulled away by the high amount of solvent during the distillation and thus removed from the reaction mixture.

Finally, the HB/BS molar ratio seemed to have no effect on the transesterification rate since Copo-BS-10 to 12 exhibited a random structure. Nevertheless, the molar mass seemed to slightly decrease with the HB content in agreement with the study of Impallomeni et al. [33]. Likewise, the PHB thermal degradation increased with the HB content and the temperature.

The poly(HB-*co*-BS) copolyesters thermal stability was investigated by TGA. TGA curves are presented in Fig. 6, with corresponding data summarized in Table SI.1, and compared to their homopolyesters (Fig. SI.4). All copolyesters were thermally stable until 220 ℃. Poly(HB-*co*-BS) copolyesters degradation profiles were almost similar to the one of poly(HB-co-BA) copolyesters previously presented, with a two-step degradation in which the first degradation was assigned to PHB degradation ($T_{deg,max}$ ~ 280 ℃) with its intensity increasing with the HB content and the second one was ascribed to PBS degradation
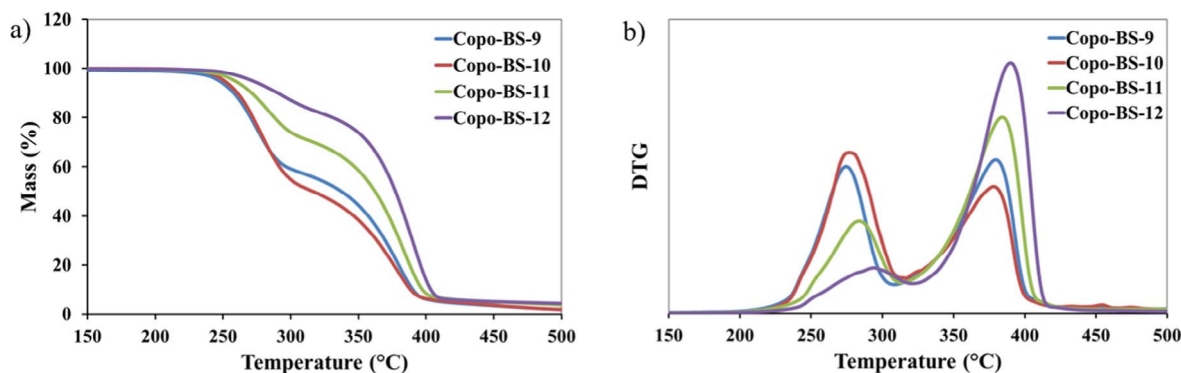
Fig. 6. (a) Mass loss and (b) DTG curves of different poly(HB-co-BS) copolyesters.

$(T_{deg,max} \sim 385\ °C)$.

The crystalline structure and thermal properties of copolyesters according to their structure were studied by WAXS and DSC. The WAXS patterns of different poly(HB-co-BS) copolyesters with the same composition but different randomness degree is presented in Fig. 7. All these copolyesters exhibited signals at $2\theta = 19.5, 21.7$ and $22.4°$ assigned to the PBS crystalline phase, even for random structures, contrary to poly(HB-co-BA) [48]. The intensity of these signals decreased with the randomization and, thus, decreased with L_{BS}. The two peaks at $2\theta = 13.5$ and $17.0°$ were ascribed to the PHB crystalline phase. As for poly(HB-co-BA), only copolyesters with $L_{HB} \geq 7$ and, thus, a marked blocky structure were able to show a PHB crystalline phase.

DSC traces of some poly(HB-co-BS) copolyesters are presented in Fig. 8 and data are summarized in Table 4. Copo-BS-1, which is composed of a mixture of two homopolyesters, was the only sample showing the presence of two melting phenomena at 112 and 140 °C assigned to the PBS and PHB crystalline phases, respectively. All other copolyesters exhibited only one melting phenomenon during the first heating run, even for random structures (Copo-BS-10 to 12), contrary to poly(HB-co-BA) copolyesters. For poly(HB-co-BS) copolyesters of a given composition with nearly equimolar HB and BS contents (Table 3, Copo-BS-1 and Copo-BS-8 to 10), as L_{BS} and L_{HB} decreased due to the randomization, T_m, T_c, ΔH_c and ΔH_m of the PBS crystal phase decreased too, due to the disruption of the symmetry in the chain. Likewise, after the first heating run, Copo-BS-9 and Copo-BS-10 were not able to crystallize during the cooling or the second heating run leading to amorphous materials. The randomization decreased drastically the crystallization ability and, thus, the crystallinity. X_c for poly(HB-co-BS) copolyesters was calculated from the second heating run using Eq. (1) and the experimentally determined $\Delta H_m°$ value of PBS (210 J/g) [40]. Moreover, as for poly(HB-co-BA) copolyesters, T_g of poly(HB-co-BS) copolyesters determined during the second heating run was comprised between the T_g of both homopolyesters and tended to decrease with the randomization. One can suppose that, due to the decrease of the BS crystallization ability with the randomization, the crystallinity after the cooling run decreased and, thus, the amorphous phase of copolyesters was more concentrate in BS repetitive units, hence the decrease of T_g. Finally, for a given R value, L_{BS} increased as the molar content of HB decreased leading to an increase of T_m and ΔH_m (see Table 4, Copo-BS-10 to 12).

3.3. Comparison between enzymatic and organometallic transesterification on the synthesis of poly(HB-co-BS) copolyesters

The synthesis of poly(HB-co-BS) copolyesters by lipase-catalyzed transesterification from PBS and PHB-diol oligomers ("two-step
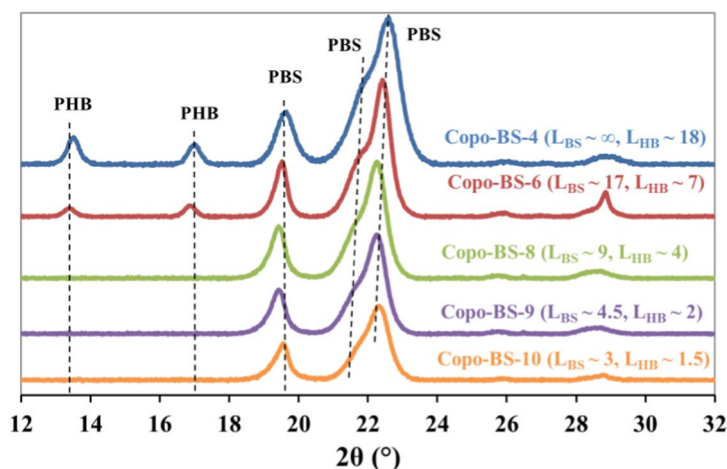

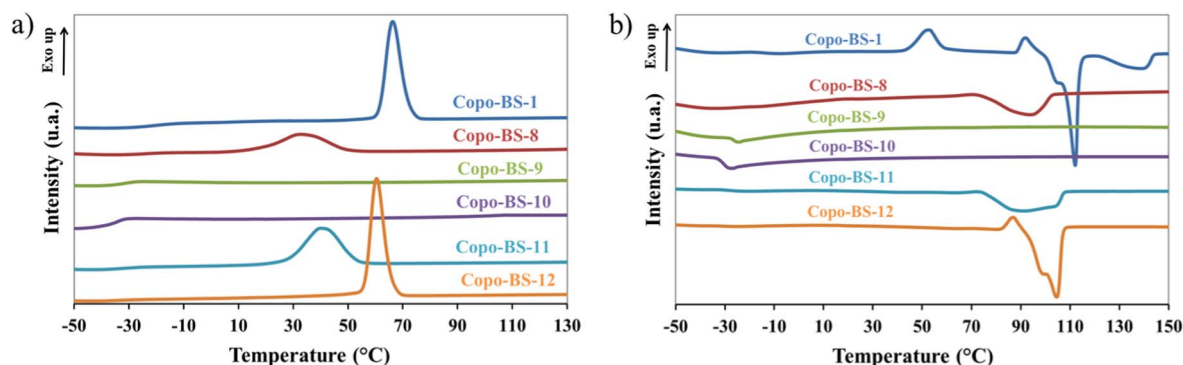**Fig. 7.** WAXS patterns of different poly(HB-co-BS) copolyesters.

Fig. 8. DSC (a) cooling and (b) second heating scans of poly(HB-*co*-BS) copolyesters.

reaction") in solution under vacuum using the immobilized form of *Candida antartica* lipase B (CALB) on acrylic beads (Novozyme 435) as catalyst has been previously reported [34]. This two-step enzymatic transesterification procedure is summarized in Scheme 2. Then, similarities and differences between the results of titanium- and CALB-catalyzed transesterification on the synthesis of poly(HB-*co*-BS) copolyesters are discussed.

As for the titanium-catalyzed transesterification in bulk, the PHB thermal degradation could be avoided in the enzymatic process by controlling the reaction process. Both processes performed under vacuum permitted to obtain copolyesters with (i) similar feed and final compositions, (ii) micro-block or random structures according to the reaction conditions and (iii) molar mass of ~15–20 kg/mol for copolyesters with low HB content. By increasing the HB content, the titanium process was more suitable since no significant molar mass decrease was reported contrary to the enzymatic process.

The main advantage of the organometallic process was the much lower reaction time to obtain random copolyesters (2 h maximum), even if titanium-catalyzed transesterification required much higher reaction temperatures (175 °C) and vacuum (1–3 mbar) compared to the enzymatic process (72 h, 90 °C and 20 mbar, respectively). Likewise, contrary to the enzymatic process, the titanium one permitted to start with homopolyesters of higher molar mass, particularly for PHB. Indeed, PHB oligomers higher than 2 kg/mol had to be avoided for the enzymatic process due to the insolubility of long PHB-diols in reaction solvents and the low reactivity of long PHB oligomers with CALB. The previous reaction (*i.e.*, PHB alcoholysis to obtain small chain length PHB) was thus faster since PHB homopolyesters > 5000 g/mol can be used for the organometallic transesterification. Moreover, the titanium-catalyzed transesterification in bulk permit to synthesize copolyesters using directly diacids and not diacid derivatives such as diesters dicarboxylic acid used for the enzymatic transesterification. Furthermore, the titanium-catalyzed process in bulk permitted to use three times less solvent than the enzymatic one, which is one of the key point of the green chemistry [53].

On the other side, the enzymatic catalysis permitted to perform the reaction with a non-toxic catalyst which can be removed and reused after the reaction contrary to the titanium catalyst. This allowed the synthesized material to may be biocompatible permitting it use in additional applications which are not possible for the same material synthesized *via* the titanium-catalyzed process. Moreover, provided that PHB-diol oligomers were small enough, high molar mass random copolyesters were synthesized under mild conditions with a great control of the macromolecular architecture and without PHB thermal degradation.

4. Conclusion

A family of biobased copolyesters was obtained by titanium-catalyzed transesterification of PHB and PBS or PBA homopolyesters performed in bulk or in solution. Both processes permitted the synthesis of final copolyesters with the same molar composition than

Table 4
Thermal properties of poly(HB-*co*-BS) copolyesters.

Samples	First heating		Cooling		Second heating					
	T_m °C	ΔH_m J/g	T_c °C	ΔH_c J/g	T_g °C	T_{cc} °C	ΔH_{cc} J/g	T_m °C	ΔH_m J/g	X_c %
PBS	115	83	84	67	−35	104	4	115	67	32
PHB	176	90	115	84	2	–	–	173	93	64
Copo-BS-1	112/141[a]	43/13[a]	66	40	−14	53	14	112/139[a]	46/14[a]	22/10[a]
Copo-BS-8	94	43	32	35	−25	–	–	94	41	20
Copo-BS-9	65	21	–	–	−26	–	–	–	–	0
Copo-BS-10	41	17	–	–	−30	–	–	–	–	0
Copo-BS-11	93	46	40	45	−28	–	–	91	42	20
Copo-BS-12	106	62	61	58	−30	87	4	105	60	29

[a] Presence of two crystalline phases: PBS phase/PHB phase.
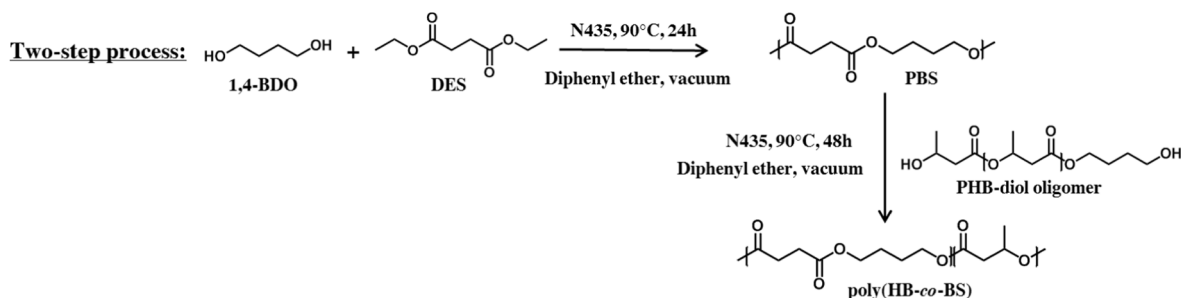
Scheme 2. Enzymatic synthesis of poly(HB-*co*-BS) copolyesters catalyzed by CALB according to a two-step process [34].

the initial feed ratio. The titanium-catalyzed transesterification in bulk was the most appropriate way for the synthesis of copolyesters. Its main advantages are (i) higher molar masses for the copolyesters, (ii) a fast transesterification rate with a negligible PHB thermal degradation and (iii) a low amount of catalyst.

On one side, random poly(HB-*co*-BA) copolyesters were amorphous at room temperature with a T_g increasing with the HB content. They possessed a good thermal stability until 220 °C. On the other side, poly(HB-*co*-BS) copolyesters were solid at room temperature and exhibited a crystalline phase due to the PBS part. The melting temperatures and the crystallinity of these copolyesters decreased with (i) the randomization of the structure due to the decrease of the average sequence length of the BS segment and (ii) the HB content. These copolyesters also exhibited a good thermal stability with an absence of mass loss until 230 °C.

Contrary to the enzymatic process, the titanium-catalyzed transesterification process in bulk permitted to quickly obtain random structures with a similar range of molar mass (∼ 15 kg/mol) to the enzymatic process and using small chain length PHB with higher molar mass. The titanium-catalyzed transesterification process was particularly interesting to synthesize copolyesters with high HB contents due to the low influence of the HB contents on the final copolyester molar mass contrary to the enzyme-catalyzed process. Nevertheless, since the titanium catalyst is complicate to remove from the copolyester matrix, only biomedical and tissue engineering applications that tolerate the presence of residual metal catalyst can be envisaged for such titanium-catalyzed HB-based copolyesters.

Finally, these copolyesters could be also used as compatibilizers in blends based on two non-miscible matrixes, such as PHB with PBS (or PBA) to improve the miscibility, the final properties and the range of applications of these blends [6–8]. More specifically, the use of oligomers or small chain length of PHB may contribute to a greater industrial development of PHAs in terms of applications. Besides, poly(HB-*co*-BS) and poly(HB-*co*-BA) copolyesters could be interesting for thermoplastic applications where a high biobased content and biodegradable or biocompatible properties are targeted, such as short term packaging, agriculture, or in biomedical area. Nevertheless, to complete the investigation of these materials, some additional tests must be fulfilled such as the study of the reaction time during the bulk transesterification, biodegradability or biocompatibility, mechanical, processing and ageing behaviors.

Acknowledgements

Appendix A. Supplementary material

The reaction protocol for the synthesis of small chain length PHB by alcoholysis, the reaction protocol for the titanium-catalyzed synthesis of PBS and PBA, ^{1}H- and ^{13}C-NMR details of different polyesters studied, the FTIR spectra of copolyesters, the TGA data of poly(HB-*co*-BA) and poly(HB-*co*-BS) copolyesters, the main mechanisms of polyester thermal degradation, the method to determine the sequence distribution of poly(HB-*co*-BS) copolyesters by ^{13}C-NMR and the variation of T_m of small chain length PHB with their molar mass are supplied in supporting information. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eurpolymj.2017.03.006.

References

[1] E. Pollet, L. Avérous, Production, chemistry and properties of polyhydroxyalkanoates, in: D. Plackett (Ed.), Biopolym. – New Mater. Sustain. Films Coat, John Wiley & Sons, Ltd., 2011, pp. 65–86accessed February 16, 2016 <http://onlinelibrary.wiley.com/doi/10.1002/9781119994312.ch4/summary>.

[2] Perrine Bordes, Eric Pollet, Luc Avérous, Potential use of polyhydroxyalkanoate (PHA) for biocomposite development, Nano-Biocomposites, CRC Press, 2009, pp. 193–226accessed January 6, 2016 <http://www.crcnetbase.com/doi/abs/10.1201/9781420080292-c8>.

[3] E. Hablot, P. Bordes, E. Pollet, L. Avérous, Thermal and thermo-mechanical degradation of poly(3-hydroxybutyrate)-based multiphase systems, Polym. Degrad. Stab. 93 (2008) 413–421, http://dx.doi.org/10.1016/j.polymdegradstab.2007.11.018.

[4] H. Abe, Thermal degradation of environmentally degradable poly(hydroxyalkanoic acid)s, Macromol. Biosci. 6 (2006) 469–486, http://dx.doi.org/10.1002/mabi.200600070.

[5] N. Grassie, E.J. Murray, P.A. Holmes, The thermal degradation of poly(-(d)-β-hydroxybutyric acid): Part 1—Identification and quantitative analysis of products, Polym. Degrad. Stab. 6 (1984) 47–61, http://dx.doi.org/10.1016/0141-3910(84)90016-8.

[6] Z. Qiu, T. Ikehara, T. Nishi, Poly(hydroxybutyrate)/poly(butylene succinate) blends: miscibility and nonisothermal crystallization, Polymer 44 (2003)

2503–2508, http://dx.doi.org/10.1016/S0032-3861(03)00150-2.

[7] Z. Qiu, T. Ikehara, T. Nishi, Miscibility and crystallization behaviour of biodegradable blends of two aliphatic polyesters. Poly(3-hydroxybutyrate-co-hydroxyvalerate) and poly(butylene succinate) blends, Polymer 44 (2003) 7519–7527, http://dx.doi.org/10.1016/j.polymer.2003.09.029.

[8] P. Ma, D.G. Hristova-Bogaerds, Y. Zhang, P.J. Lemstra, Enhancement in crystallization kinetics of the bacterially synthesized poly(β-hydroxybutyrate) by poly (butylene succinate), Polym. Bull. 71 (2014) 907–923, http://dx.doi.org/10.1007/s00289-014-1101-x.

[9] A. Meszynska, E. Pollet, K. Odelius, M. Hakkarainen, L. Avérous, Effect of oligo-hydroxyalkanoates on poly(3-hydroxybutyrate-co-4-hydroxybutyrate)-based systems, Macromol. Mater. Eng. 300 (2015) 661–666, http://dx.doi.org/10.1002/mame.201500026.

[10] X. Gao, J.-C. Chen, Q. Wu, G.-Q. Chen, Polyhydroxyalkanoates as a source of chemicals, polymers, and biofuels, Curr. Opin. Biotechnol. 22 (2011) 768–774, http://dx.doi.org/10.1016/j.copbio.2011.06.005.

[11] S.J. Park, T.W. Kim, M.K. Kim, S.Y. Lee, S.-C. Lim, Advanced bacterial polyhydroxyalkanoates: towards a versatile and sustainable platform for unnatural tailor-made polyesters, Biotechnol. Adv. 30 (2012) 1196–1206, http://dx.doi.org/10.1016/j.biotechadv.2011.11.007.

[12] J.M.B.T. Cavalheiro, E. Pollet, H.P. Diogo, M.T. Cesário, L. Avérous, M.C.M.D. de Almeida, M.M.R. da Fonseca, On the heterogeneous composition of bacterial polyhydroxyalkanoate terpolymers, Bioresour. Technol. 147 (2013) 434–441, http://dx.doi.org/10.1016/j.biortech.2013.08.009.

[13] H. Arslan, G. Adamus, B. Hazer, M. Kowalczuk, Electrospray ionisation tandem mass spectrometry of poly [(R, S)-3-hydroxybutanoic acid] telechelics containing primary hydroxy end groups, Rapid Commun. Mass Spectrom. 13 (1999) 2433–2438, http://dx.doi.org/10.1002/(SICI)1097-0231(19991230)13:24 < 2433::AID-RCM808 > 3.0.CO;2-X.

[14] R.W. Lenz, Z. Jedlinski, Anionic and coordination polymerization of 3-butyrolactone, Macromol. Symp. 107 (1996) 149–161, http://dx.doi.org/10.1002/masy.19961070115.

[15] S.M. Guillaume, L. Annunziata, I. del Rosal, C. Iftner, L. Maron, P.W. Roesky, M. Schmid, Ring-opening polymerization of racemic β-butyrolactone promoted by rare earth trisborohydride complexes towards a PHB-diol: an experimental and DFT study, Polym. Chem. 4 (2013) 3077–3087, http://dx.doi.org/10.1039/C3PY00056G.

[16] C.G. Jaffredo, J.-F. Carpentier, S.M. Guillaume, Poly(hydroxyalkanoate) block or random copolymers of β-butyrolactone and benzyl β-malolactone: a matter of catalytic tuning, Macromolecules 46 (2013) 6765–6776, http://dx.doi.org/10.1021/ma401332k.

[17] G.A.R. Nobes, R.J. Kazlauskas, R.H. Marchessault, Lipase-catalyzed ring-opening polymerization of lactones: a novel route to poly(hydroxyalkanoate)s, Macromolecules 29 (1996) 4829–4833, http://dx.doi.org/10.1021/ma951774g.

[18] W. Xie, J. Li, D. Chen, P.G. Wang, Ring-opening polymerization of β-butyrolactone by thermophilic lipases, Macromolecules 30 (1997) 6997–6998, http://dx.doi.org/10.1021/ma970722j.

[19] X. Shuai, Z. Jedlinski, M. Kowalczuk, J. Rydz, H. Tan, Enzymatic synthesis of polyesters from hydroxyl acids, Eur. Polym. J. 35 (1999) 721–725, http://dx.doi.org/10.1016/S0014-3057(98)00164-5.

[20] U.D. Lengweiler, M.G. Fritz, D. Seebach, Synthese monodisperser linearer und cyclischer Oligomere der (R)-3-Hydroxybuttersäure mit bis zu 128 Einheiten, Helv. Chim. Acta 79 (1996) 670–701, http://dx.doi.org/10.1002/hlca.19960790311.

[21] G.R. Saad, Y.J. Lee, H. Seliger, Synthesis and thermal properties of biodegradable poly(ester-urethane)s based on chemo-synthetic poly[(R, S)-3-hydroxybutyrate], Macromol. Biosci. 1 (2001) 91–99, http://dx.doi.org/10.1002/1616-5195(20010301)1:3 < 91::AID-MABI91 > 3.0.CO;2-8.

[22] T.D. Hirt, P. Neuenschwander, U.W. Suter, Telechelic diols from poly[(R)-3-hydroxybutyric acid] and poly{[(R)-3-hydroxybutyric acid]-co-[(R)-3-hydro-xyvaleric acid]}, Macromol. Chem. Phys. 197 (1996) 1609–1614, http://dx.doi.org/10.1002/macp.1996.021970503.

[23] X.M. Deng, J.Y. Hao, Synthesis and characterization of poly(3-hydroxybutyrate) macromer of bacterial origin, Eur. Polym. J. 37 (2001) 211–214, http://dx.doi.org/10.1016/S0014-3057(00)00090-2.

[24] E.T. Baran, N. Özer, V. Hasirci, Poly(hydroxybutyrate-co-hydroxyvalerate) nanocapsules as enzyme carriers for cancer therapy: an in vitro study, J. Microencapsul. 19 (2002) 363–376, http://dx.doi.org/10.1080/02652040110105355.

[25] J.M. Bergamaschi, E.J. Pilau, F.C. Gozzo, M.I. Felisberti, Synthesis of polyurethane from poly(3-hydroxybutyrate) and poly(p-dioxanone): molar mass reduction via sodium borohydrate, Macromol. Symp. 299–300 (2011) 10–19, http://dx.doi.org/10.1002/masy.200900103.

[26] F. Ravenelle, R.H. Marchessault, One-step synthesis of amphiphilic diblock copolymers from bacterial poly([R]-3-hydroxybutyric acid), Biomacromolecules 3 (2002) 1057–1064, http://dx.doi.org/10.1021/bm025553b.

[27] Y. Ke, Synthetic routes to degradable copolymers deriving from the biosynthesized polyhydroxyalkanoates: a mini review, Express Polym. Lett. 10 (2015) 36–53, http://dx.doi.org/10.3144/expresspolymlett.2016.5.

[28] M.S. Reeve, S.P. McCarthy, R.A. Gross, Preparation and characterization of (R)-poly(.beta.-hydroxybutyrate)-poly(.epsilon.-caprolactone) and (R)-poly(.beta.-hydroxybutyrate)-poly(lactide) degradable diblock copolymers, Macromolecules 26 (1993) 888–894, http://dx.doi.org/10.1021/ma00057a002.

[29] L. Wu, L. Wang, X. Wang, K. Xu, Synthesis, characterizations and biocompatibility of novel biodegradable star block copolymers based on poly[(R)-3-hydroxybutyrate] and poly(ε-caprolactone), Acta Biomater. 6 (2010) 1079–1089, http://dx.doi.org/10.1016/j.actbio.2009.08.014.

[30] S. Dai, Z. Li, Enzymatic preparation of novel thermoplastic di-block copolyesters containing poly[(R)-3-hydroxybutyrate] and poly(ε-Caprolactone) blocks via ring-opening polymerization, Biomacromolecules 9 (2008) 1883–1893, http://dx.doi.org/10.1021/bm8001396.

[31] J. Li, X. Li, X. Ni, K.W. Leong, Synthesis and characterization of new biodegradable amphiphilic poly(ethylene oxide)-b-poly[(R)-3-hydroxy butyrate]-b-poly (ethylene oxide) triblock copolymers, Macromolecules 36 (2003) 2661–2667, http://dx.doi.org/10.1021/ma025725x.

[32] G. Impallomeni, M. Giuffrida, T. Barbuzzi, G. Musumarra, A. Ballistreri, Acid catalyzed transesterification as a route to poly(3-hydroxybutyrate-co-ε-caprolactone) copolymers from their homopolymers, Biomacromolecules 3 (2002) 835–840, http://dx.doi.org/10.1021/bm025525t.

[33] G. Impallomeni, G.M. Carnemolla, G. Puzzo, A. Ballistreri, L. Martino, M. Scandola, Characterization of biodegradable poly(3-hydroxybutyrate-co-butyleneadipate) copolymers obtained from their homopolymers by microwave-assisted transesterification, Polymer 54 (2013) 65–74, http://dx.doi.org/10.1016/j.polymer.2012.11.030.

[34] T. Debuissy, E. Pollet, L. Averous, Enzymatic synthesis of a biobased copolyester from poly(butylene succinate) and poly((R)-3-hydroxybutyrate) – study of reaction parameters on the transesterification rate, Biomacromolecules (2016), http://dx.doi.org/10.1021/acs.biomac.6b01494.

[35] M. Gigli, M. Fabbri, N. Lotti, R. Gamberini, B. Rimini, A. Munari, Poly(butylene succinate)-based polyesters for biomedical applications: a review, Eur. Polym. J. 75 (2016) 431–460, http://dx.doi.org/10.1016/j.eurpolymj.2016.01.016.

[36] J.-W. Rhim, H.-M. Park, C.-S. Ha, Bio-nanocomposites for food packaging applications, Prog. Polym. Sci. 38 (2013) 1629–1652, http://dx.doi.org/10.1016/j.progpolymsci.2013.05.008.

[37] S.Y. Hwang, E.S. Yoo, S.S. Im, The synthesis of copolymers, blends and composites based on poly(butylene succinate), Polym. J. 44 (2012) 1179–1190, http://dx.doi.org/10.1038/pj.2012.157.

[38] T. Debuissy, E. Pollet, L. Avérous, Synthesis of potentially biobased copolyesters based on adipic acid and butanediols: kinetic study between 1,4- and 2,3-butanediol and their influence on crystallization and thermal properties, Polymer 99 (2016) 204–213, http://dx.doi.org/10.1016/j.polymer.2016.07.022.

[39] K. Chrissafis, K.M. Paraskevopoulos, D.N. Bikiaris, Effect of molecular weight on thermal degradation mechanism of the biodegradable polyester poly(ethylene succinate), Thermochim. Acta 440 (2006) 166–175, http://dx.doi.org/10.1016/j.tca.2005.11.002.

[40] G.Z. Papageorgiou, D.N. Bikiaris, Crystallization and melting behavior of three biodegradable poly(alkylene succinates). A comparative study, Polymer 46 (2005) 12081–12092, http://dx.doi.org/10.1016/j.polymer.2005.10.073.

[41] J. Yang, H. Zhu, C. Zhang, Q. Jiang, Y. Zhao, P. Chen, D. Wang, Transesterification induced mechanical properties enhancement of PLLA/PHBV bio-alloy, Polymer 83 (2016) 230–238, http://dx.doi.org/10.1016/j.polymer.2015.12.025.

[42] N. Jacquel, F. Freyermouth, F. Fenouillot, A. Rousseau, J.P. Pascault, P. Fuertes, R. Saint-Loup, Synthesis and properties of poly(butylene succinate): efficiency of different transesterification catalysts, J. Polym. Sci. Part Polym. Chem. 49 (2011) 5301–5312, http://dx.doi.org/10.1002/pola.25009.

[43] C.-H. Chen, J.-S. Peng, M. Chen, H.-Y. Lu, C.-J. Tsai, C.-S. Yang, Synthesis and characterization of poly(butylene succinate) and its copolyesters containing minor amounts of propylene succinate, Colloid Polym. Sci. 288 (2010) 731–738, http://dx.doi.org/10.1007/s00396-010-2187-9.

[44] Y. Cai, J. Lv, J. Feng, Spectral characterization of four kinds of biodegradable plastics: poly (lactic acid), poly (butylenes adipate-co-terephthalate), poly (hydroxybutyrate-co-hydroxyvalerate) and poly (butylenes succinate) with FTIR and Raman spectroscopy, J. Polym. Environ. 21 (2012) 108–114, http://dx.doi.

org/10.1007/s10924-012-0534-2.

[45] O. Persenaire, M. Alexandre, P. Degée, P. Dubois, Mechanisms and kinetics of thermal degradation of Poly(ε-caprolactone), Biomacromolecules 2 (2001) 288–294, http://dx.doi.org/10.1021/bm0056310.

[46] N. Grassie, E.J. Murray, P.A. Holmes, The thermal degradation of poly(-(d)-β-hydroxybutyric acid): Part 3—The reaction mechanism, Polym. Degrad. Stab. 6 (1984) 127–134, http://dx.doi.org/10.1016/0141-3910(84)90032-6.

[47] Khasanah, K.R. Reddy, H. Sato, I. Takahashi, Y. Ozaki, Intermolecular hydrogen bondings in the poly(3-hydroxybutyrate) and chitin blends: their effects on the crystallization behavior and crystal structure of poly(3-hydroxybutyrate), Polymer 75 (2015) 141–150, http://dx.doi.org/10.1016/j.polymer.2015.08.011.

[48] P. Pan, Y. Inoue, Polymorphism and isomorphism in biodegradable polyesters, Prog. Polym. Sci. 34 (2009) 605–640, http://dx.doi.org/10.1016/j.progpolymsci.2009.01.003.

[49] B.D. Ahn, S.H. Kim, Y.H. Kim, J.S. Yang, Synthesis and characterization of the biodegradable copolymers from succinic acid and adipic acid with 1,4-butanediol, J. Appl. Polym. Sci. 82 (2001) 2808–2826, http://dx.doi.org/10.1002/app.2135.

[50] D.W. Van Krevelen, Chapter 5 – calorimetric properties, Prop. Polym. Third Complet. Revis. Elsevier, Amsterdam, 1997, pp. 109–127 accessed March 8, 2016 <http://www.sciencedirect.com/science/article/pii/B9780444828774500123>.

[51] P.J. Barham, A. Keller, E.L. Otun, P.A. Holmes, Crystallization and morphology of a bacterial thermoplastic: poly-3-hydroxybutyrate, J. Mater. Sci. 19 (1984) 2781–2794, http://dx.doi.org/10.1007/BF01026954.

[52] J. Otera, Transesterification, Chem. Rev. 93 (1993) 1449–1470, http://dx.doi.org/10.1021/cr00020a004.

[53] P.T. Anastas, J.C. Warner, Green Chemistry: Theory and Practice, Oxford Univ. Press, Oxford, 2000.