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One-pot synthesis of poly(L-lactide) multi-arm star copolymers based on a polyester polyol macroinitiator

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Dedicated to Axel Müller on the occasion of his 65th birthday.

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ABSTRACT

Using a hyperbranched poly(glycolide) (*hb*PGA) macroinitiator the synthesis of poly(L-lactide) (PLLA) multi-arm star polyesters has been achieved via a core-first approach. The star-shaped copolymers were prepared in a one-pot two-step process via $Sn(Oct)_2$-catalyzed ring-opening polymerization (ROP) conducted in the melt. Complete conversion of the end groups of the *hb*polyglycolide polyester polyols is ensured by the reactive primary hydroxyl termini. By adjusting the monomer/initiator ratio a series of star copolymers with varying PLLA arm length has been obtained with molecular weights in the range of 1500 to 10,000 g/mol (SEC). The successful coupling of the PLLA arms to the *hb*PGA core has been confirmed via detailed 1D and 2D NMR spectroscopy. Because of the different hydrodynamic volume of the star polymers in contrast to their linear analogs, the weight-average molecular weight (M_w) was determined both by SEC and static light scattering (SLS). The star-shaped poly(lactide)s reveal different thermal properties in comparison to linear poly(lactide) homopolymers.

1. Introduction

Aliphatic poly(ester)s are well-known materials in the field of medical applications and drug delivery systems [1–3]. Especially, poly(L-lactide) (PLLA) is a widely used material with regard to its biodegradability and biocompatibility [4]. The critical issues of petroleum-based plastics together with the fact that the mechanical properties of PLLA are comparable with those of poly(styrene) (PS) or poly(ethylene terephthalate) (PET) have led to revived interest in polymers based on renewable resources [5]. Although the popularity of PLLA increases, this material bears some disadvantages, i.e., a high degree of crystallization leading to a low degradation rate, which limits the field of application. Several strategies have been developed to optimize the materials properties of PLLA, such as copolymerization, stereocomplexation, variation of polymer architecture or blending. Copolymers of D- and L-lactide [6] as well as PLLA star polymers [7] are well-known to reduce the degree of crystallization of PLLA. In addition, blending with poly(ε-caprolactone) provides commercial PLLA blends with an improved toughness [5].

In the last decades, the interest in complex macromolecular architectures increased, particularly with regard to hyperbranched [8–12], star-shaped [13–16], brush-like [17] or dendrimer-like polyesters [18]. One major advantage of dendritic polymers is their high number of functional end groups, which provide an excellent platform for the introduction of various functionalities via post-polymerization modification. The branched topology leads to improved solubility, low melt viscosity and altered thermal properties [19–22]. In addition, hyperbranched polyols are favorable macroinitiators for the synthesis of multi-arm star copolymers due to their facile one-step preparation [23]. Hyperbranched polyglycerol (*hb*PG), a widely used polyether polyol, has been employed in the synthesis of core–shell architectures based on a grafting-from approach via atom transfer radical polymerization (ATRP) or ring-opening polymerization (ROP). Multi-arm star copolymers of hydrophobic ε-caprolactone (εCL) [24], glycolide (GA) [25], methyl methacrylate (MMA) [26] or L-lactide (LLA) [7,27] with various arm lengths have been prepared with a hydrophilic *hb*PG or a hyperbranched poly(ethylene glycol) (PEG) core to obtain reverse micelles capable of encapsulating and releasing drugs. Besides PG, dendritic core molecules such as hyperbranched polyester polyols or dendrimers like poly(amido amine) (PAMAM) and poly(ethylene imine) (PEI) have been used [28–30]. Derivatization and functionalization of the hydroxyl end groups provide various

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interesting carrier systems [31,32]. The synthesis of star copolymers may be pursued in two different ways: (i) linear polymer chains are chemically coupled to the core molecule – the "grafting through" method. Alternatively, (ii) the polymer chains grow directly from the initiating core with its multiple functionalities in a "grafting-from" approach [16,33]. The unique properties of star-shaped polyesters in comparison to their linear analogs, particularly with regard to their thermal behavior and crystallization tendency, motivate further research in this area [34].

In the current work, we present the rapid, one-pot two-step synthesis of PLLA multi-arm stars based on a hyperbranched poly(glycolide) (*hb*PGA) copolymer core via solvent-free, $Sn(Oct)_2$-catalyzed ROP (Fig. 1). The polyol macroinitiator was prepared by combining ROP and melt AB_2-polycondensation, as described recently by our group [35]. The obtained star block copolymers were investigated with respect to their molecular weight, the average PLLA arm length and their thermal properties.

2. Experimental section

2.1. Reagents

L-Lactide and glycolide were purchased from Purac (Gorinchem, Netherlands) and used as received. Tin(II)-2-ethylhexanoate ($Sn(Oct)_2$, 95% Sigma Aldrich) and 2,2-bis(hydroxymethyl)butyric acid (BHB, 98% Sigma Aldrich) were used as received. All solvents were of analytical grade and used as received.

2.2. Instrumentation

^{1}H NMR spectra were recorded at 400 MHz on a Bruker AMX400 and are referenced internally to residual proton signals of the deuterated solvent. ^{13}C NMR spectra were recorded at 75 MHz and referenced internally to the solvent signals (^{1}H NMR signal: 2.50 ppm (DMSO-d_6), 7.27 ppm ($CDCl_3$); ^{13}C NMR signal: 39.52 ppm (DMSO-d_6), 77.00 ppm ($CDCl_3$)). For SEC measurements in DMF (containing 1 g/L of lithium bromide as an additive), an Agilent 1100 series was used as an integrated instrument including a PSS Gral column ($10^4/10^4/10^2$ Å porosity) and an RI detector. Calibration was achieved with poly(styrene) standards provided by Polymer Standards Service (PSS).

Differential scanning calorimetry (DSC) analysis was performed on a Perkin–Elmer 7 Series thermal analysis system with autosampler in the temperature range of −100 to +180 °C with heating rates of 40 °C/min. The melting points for indium (T_0 = 156.6 °C) and Millipore water (T_0 = 0 °C) were used for calibration.

Dynamic and static light scattering (DLS and SLS) measurements were performed with a helium-neon laser of 623 nm wavelength operating at 22 mW, an ALV/CGS-3 MD goniometer with 8 APD detectors and dual ALV-7004 Multiple-Tau digital correlator. For SLS angle dependent measurements were carried out between 25° and 152° in steps of 1° at a temperature of 23 °C. The DLS measurements were carried out in the range of 26° and 138° in two different angle steps (8 detectors with 16° difference) with 4°

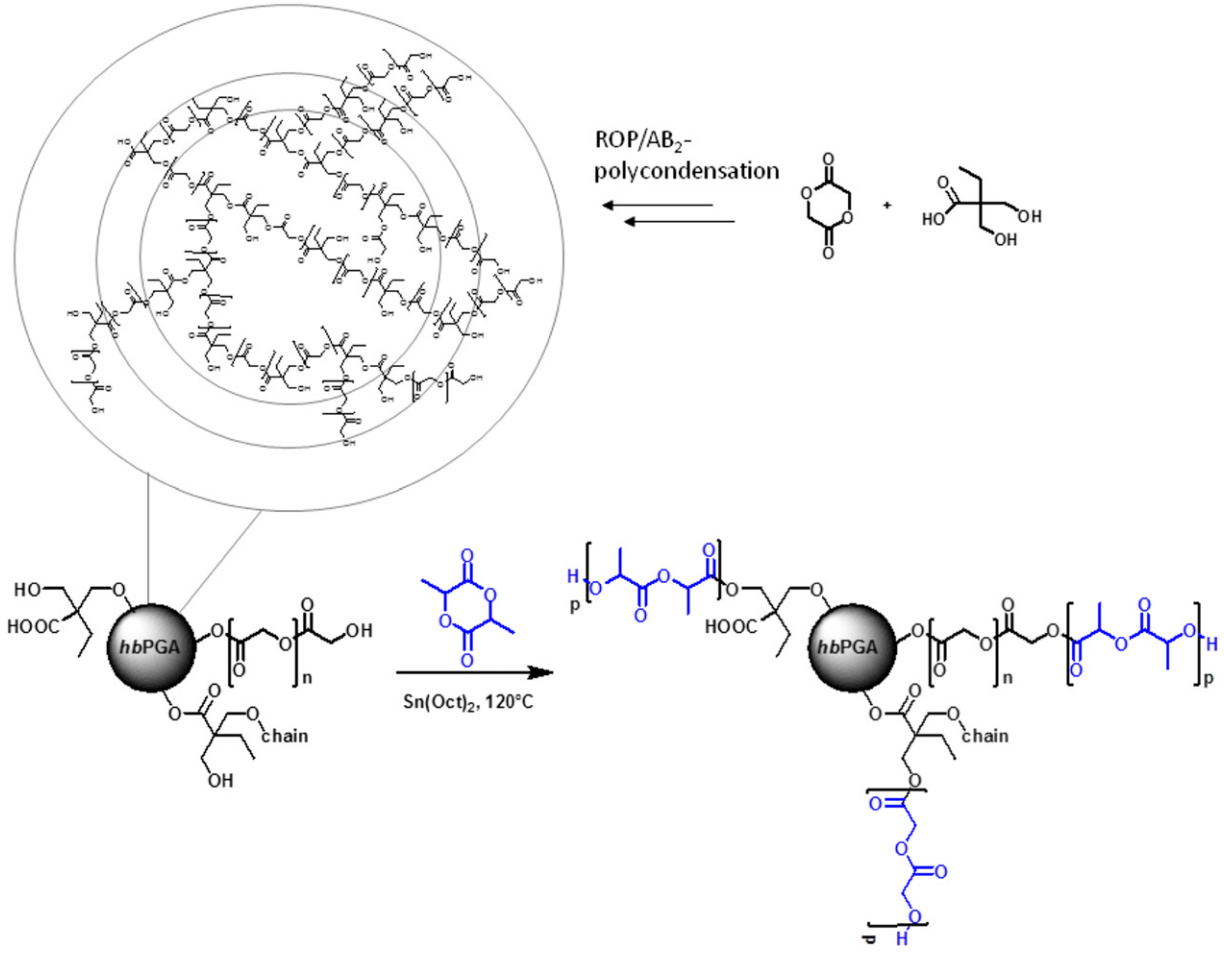

Fig. 1. Synthesis of PLLA multi-arm stars based on a hyperbranched PGA copolymer core via a *grafting-from* approach.

difference (26, 42, 58, 74, 90, 106, 122, 138 und 30, 46, 62, 78, 94, 110, 126, 142).

Angular dependent DLS data analysis was done according to literature using cumulant fitting functions [36].

SLS-data evaluation was achieved with the ALV-STAT Software for Multi-Detector Goniometer Systems (for WINDOWS-2000/2003/XP/Vista/7). Prior to both DLS and SLS measurements, all the solutions were filtered through 0.02 μm Anotop membrane filters. The refractive index increment, dn/dc, has been measured with a PSS dn/dc detector (DnDc2010) with a 620 nm light source. The determined dn/dc value of *hb*PGA-*g*-PLLA$_{10}$ has been used as reference for all measurements (see Table 2).

The Zimm equation has been used for the calculation of M_w from SLS measurements [37,38]:

$$\frac{Kc}{\Delta R_\theta} = \frac{1}{M_w}\left[1 + \frac{q^2 R_g^2}{3}\right] + 2A_2 c \qquad (1)$$

with the optical parameter $K = 4\pi^2 n^2 (dn/dc)^2 / N_A \lambda^4$, the scattering vector for vertically polarized light $q = 4\pi n_0 \sin(\theta/2)/\lambda$, the refractive index of the liquid medium n, the Avogadro's constant N_A, the wavelength of the laser λ and the excess Rayleigh ratio [$\Delta R_\theta = R_\theta$(solution)-R$_\theta$ (solvent)]. M_w is determined by extrapolation of the concentration c and the angle θ to zero.

2.3. General synthesis of the hbPGA-g-PLLA multi-arm stars

The preformed *hb*PGA macroinitiator has been prepared according to literature procedures [35] and has been used in the subsequent ROP of lactide without further prior work-up. To a one-necked Schlenk flask, charged with the precursor and equipped with a magnetic stir bar as well as a rubber septum, L-lactide has been added in the quantities required. The flask was evacuated for 10 min, purged with argon and completely immersed in an oil bath preheated to 120 °C. To the homogenous melt 0.1 mol% Sn(Oct)$_2$ were added as a catalyst for the ROP. The mixture was stirred at 120 °C for 3 h under argon atmosphere. After cooling, the mixture was dissolved in chloroform ($CHCl_3$) and precipitated twice in methanol. The purified polymer was isolated by decantation of the solvent and dried in vacuo at 40 °C. The obtained colorless waxy solid (for a shorter PLLA chain length) or powder was soluble in a broad range of solvents, i.e., chloroform and tetrahydrofurane (THF). The synthesis has also been performed in a one-pot procedure without transferring the macroinitiator to a different flask by successive addition of the amount of lactide and catalyst (at room temperature) in the quantities required in the same flask and subsequent stirring of the reaction mixture at 120 °C.

^{1}H NMR (DMSO-d$_6$): δ (ppm) 5.47–5.49 (OH); 5.11–5.21 (CH_{LA}, linear); 4.78–4.91 (CH_2OR_{GA}; CH_{LA}, terminal); 4.10–4.35 (CH_2OR_{BHB}); 1.35–1.70 ($CH_{3,LA}$, linear; $CH_{2,BHB}$); 0.70–0.90 ($CH_{3,BHB}$).

^{13}C NMR (DMSO-d$_6$): δ (ppm) 174.05 (CO_{LA} terminal); 173.07 ($COOH_{BHB}$); 170.82 ($COOR_{BHB}$); 169.23–169.71 (CO_{LA} linear); 166.70 (CO_{GA} linear); 68.51–67.76 (CH_{LA} linear); 65.52 (CH_{LA} terminal); 63.28 (CH_2OR_{BHB}); 60.70–60.79 (CH_2OR_{GA}); 49.84 (C_q, dendritic); 49.21 (C_q, focal dendritic); 23.10 ($CH_{2,BHB}$); 20.33 ($CH_{3,LA}$ terminal); 16.46–16.57 ($CH_{3,LA}$ linear); 7.73–7.86 ($CH_{3,BHB}$).

3. Results and discussion

The hyperbranched poly(glycolide) copolymers with various poly(lactide) arms have been prepared in a one-pot two-step approach as shown in Fig. 1. First, the hyperbranched poly(-glycolide) (*hb*PGA) core was synthesized by the combined ROP/AB$_2$-polycondensation in melt using 2,2-bis(hydroxymethyl) butyric acid (BHB) as a branching unit, as described previously [35]. The polymerization starts with Sn(Oct)$_2$-catalyzed ring-opening polymerization of glycolide, initiated from BHB, followed by a melt polycondensation of the *in-situ* preformed AB$_2$ macromonomers. In contrast to the linear PGA homopolymer, the hyperbranched copolymers are soluble in a wide range of organic solvents as for example acetone, ethyl acetate and dimethyl sulfoxide (DMSO). In addition, the introduction of branching points in the polymer backbone results in an amorphous material with low glass temperatures (T_g) ranging from 19 to 26 °C [35].

In a subsequent step, the polyester polyol formed was used directly as a macroinitiator for the ring-opening polymerization of L-lactide by Sn(Oct)$_2$-catalysis without further purification steps. All polymerizations were carried out in bulk within 3 h at 120 °C by addition of a 10 vol%-solution of Sn(Oct)$_2$ in toluene (present for transfer of the catalyst). By varying the monomer/initiator ratio a number of PLLA stars with different average PLLA chain length were obtained. With increasing lactide content, the hydrophilicity decreased and as a consequence PLLA stars with molecular weights >2000 g/mol were insoluble in DMSO. As it is shown in Table 1, the polydispersity indices (PDI) of the prepared star polymers are in the range of 1.26–2.17. These values arise with regard to the non-monodisperse macroinitiator (PDI = 2.33) obtained by a polycondensation reaction (Fig. 2). Probability theories have shown a relation between the polydispersity index of star polymers and the polydispersity index of the arms, resulting in a reduced PDI for the star polymer after grafting a number of f polydisperse arms to a multifunctional core molecule [39]. This effect and the increase of molecular weight contribute to the reduced polydispersity of the obtained star copolymers. Comparison of the SEC traces of the PLLA stars with the hyperbranched macroinitiator evidences the absence of pre-polymer after ROP of L-lactide.

The chemical nature of the multiple hydroxyl end groups at the *hb*PGA macroinitiator plays a key role in the further functionalization step. Preceding work in our group ascertained a considerable difference in the reactivity of primary and secondary hydroxyl groups in the ring-opening multibranching polymerization (ROMBP) of lactide and 5-hydroxymethyl-1,4-dioxan-2-one (5HDON) [8]. The ROP of lactide is initiated first by the primary hydroxyl site of the 5HDON lactone, generating secondary hydroxyl termini. The ring-opening of 5HDON, which leads to new initiation sites, occurs mainly until the conversion of lactide is completed. In our case, the primary hydroxyl termini of the poly(glycolide)-based polyester polyol are considerably more reactive than the secondary hydroxyl groups formed upon ring-opening of the lactide monomer. This should lead to a quantitative end group functionalization with PLLA chains and also aid to avoid transesterification reactions upon grafting of lactide.

Table 1
Characterization of the *hb*PGA-*g*-PLLA multi-arm stars and the *hb*PGA copolymer core.

Sample	M_n [a] (g/mol)	M_w/M_n [a]	T_g [b] (°C)	T_m [b] (°C)	ΔH_m (J/g)	LA units[c]
*hb*PGA$_{0.6}$ [d]	1000	2.33	19.1	–	–	–
*hb*PGA-*g*-PLLA$_5$	1500	2.17	29.8	–	–	5
*hb*PGA-*g*-PLLA$_8$	4800	1.57	42.1	119.0	35.6	8
*hb*PGA-*g*-PLLA$_9$	6500	1.36	49.0	126.5	44.7	9
*hb*PGA-*g*-PLLA$_{10}$	10,000	1.40	49.4	145.6	50.9	10

[a] SEC: DMF as eluent with 0.1 g/L LiBr PS standard for calibration.
[b] Determined from the 2nd heating scan.
[c] Average number of L-lactide units per PLLA arm, calculated from inverse gated-decoupling ^{13}C NMR spectra.
[d] Hyperbranched PGA copolymer (60 mol% glycolide, DB = 0.43).

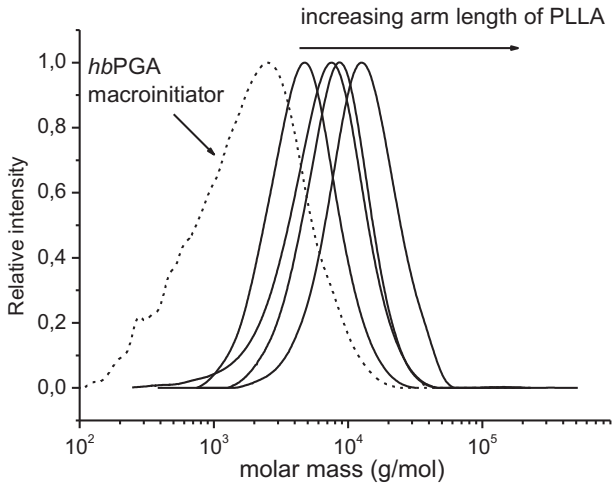

Fig. 2. SEC traces (DMF, RI) of the PLLA multi-arm star copolymers obtained by a grafting-from approach based on *hb*PGA$_{0.6}$ (60 mol% glycolide, DB = 0.43) as a multifunctional initiator.

3.1. Structural investigation by 1D/2D NMR analysis

The ^{1}H NMR spectrum of a multi-arm star copolymer in comparison with the hyperbranched PGA polymers is shown in Fig. 3. Evidence for the successful linkage of the PLLA arms to the hyperbranched PGA core is obtained from the disappearance of the signals corresponding to the terminal glycolic acid units (CH_2OH_{GA}: 4.00 ppm; 4.10 ppm) and the free hydroxymethylene protons of the bishydroxy acid (CH_2OH_{BHB}: 3.49 ppm). The signal assignment was confirmed by detailed 2D NMR spectroscopy and is consistent with our previous work [35].

NMR studies also allowed for the determination of the molecular composition and the average PLLA arm length. Unfortunately, the signal of the terminal lactic acid unit is superimposed by the signals of esterified BHB hydroxymethylene protons in the ^{1}H NMR spectrum, and therefore the average PLLA chain length had to be calculated from the inverse gated-decoupled ^{13}C NMR spectrum. In Fig. 4 ^{1}H NMR spectra of the star copolymer samples with different monomer compositions are shown. As expected, the signal intensity of the *hb*PGA core decreases with increasing content of L-lactide. The NMR spectra measured in $CDCl_3$ show a characteristic splitting of the signal of the BHB methyl group (**A**) associated with the presence of only two different BHB units (focal dendritic (**Fd**) and dendritic (**D**) unit). The main resonances of the linear PGA units are in the range of 5.20–5.50 ppm (**F**). The signals of the lactide backbone (CH_{lin}, **E**) are well separated from the other lactide arm related signals **E'**, **B** and **B'**. In addition, the ^{1}H NMR spectrum measured in DMSO-d_6 (Fig. 3) shows a signal due to the protons of the terminal hydroxyl group of the lactide arms at 5.50 ppm. This signal assignment was confirmed by an ^{1}H COSY NMR experiment (s. Supporting Information S2), relying on the cross correlation of the methyl (**B'**) or methine (**E'**) proton with the hydroxyl proton and by an ^{1}H, ^{13}C COSY NMR experiment (HMBC) (Fig. 7) referring to the cross correlation of the carbonyl carbon (**K'**) with the hydroxyl proton.

Evidence for the successful linkage of the PLLA arms with the *hb*PGA core is as well given by the ^{13}C NMR spectrum in Fig. 5. The presence of only two BHB repeating units (**Fd, D**) underlines the successful conversion of the focal linear (**Fl**) and linear (**L**) BHB units. ^{13}C NMR signals arising due to non-esterified terminal glycolic acid units with regard to the carbonyl carbons resonating at 172.16–173.16 ppm and the methylene carbons at 59.32 and 59.43 ppm have not been identified, which confirms quantitative lactide grafting.

For the sequential synthesis of the PLLA stars it is essential that no transesterfication rearrangements between the preformed PGA core and the lactide monomer occur during the polymerization process. Therefore 2D NMR spectroscopy experiments (HMBC) were performed to exclude such side reactions. Fig. 6 shows a section of the heteronuclear multiple bonds coherence (HMBC) spectrum with zoom into the region of the carbonyl carbons.

In case of undesired transesterification reactions (1) a cross correlation of the glycolide carbonyl carbon and the lactide methine protons should be observed (visualized in Fig. 7). Instead, only the cross correlation (2) between the glycolide methylene protons and the lactide carbonyl carbon (**K/f**) is detectable, which confirms the attachment of PLLA to the hydroxyl-terminated PGA

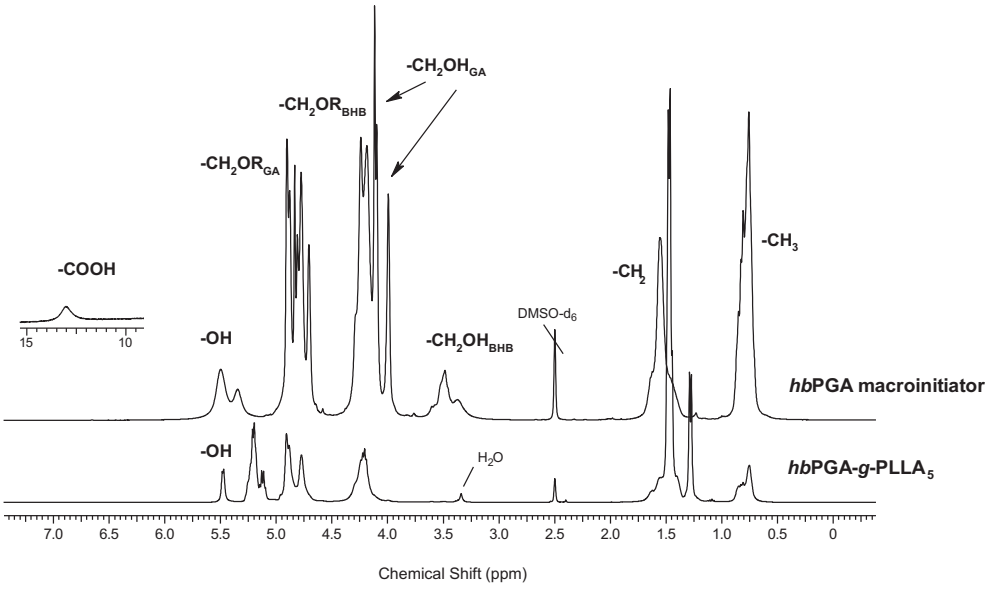

Fig. 3. ^{1}H NMR analysis (400 MHz, DMSO-d_6) of the polyol macroinitiator in comparison with the *hb*PGA-*g*-PLLA$_5$ star copolymer.

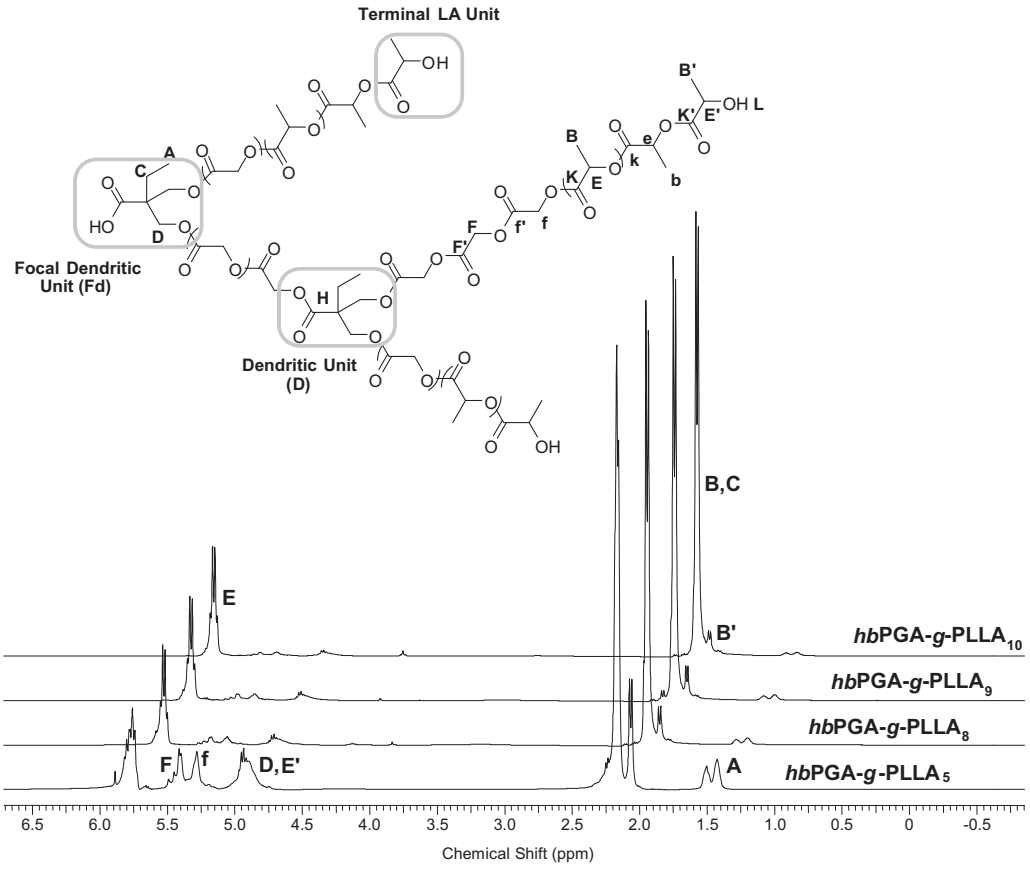

Fig. 4. ^{1}H NMR analysis (400 MHz, $CDCl_3$) of the star block copolymers *hb*PGA-*g*-PLLA$_x$ with increasing lactide to macroinitiator ratio (bottom to top; with x = average number of lactic acid units per PLLA arm; the top spectrum refers to the scale bar).

core (Fig. 6) and the absence of comonomer sequences one would expect from transesterification.

Furthermore, ^{1}H and ^{13}C NMR analysis give distinct information of the sequence distribution of glycolyl and lactyl units as described in literature [40]. Especially the carbonyl carbon signals are very sensitive to sequence effects. After polymerization glycolyl-lactyl sequences (LLG, GLG, LGL, LGG) associated with a random incorporation of the lactone monomers due to

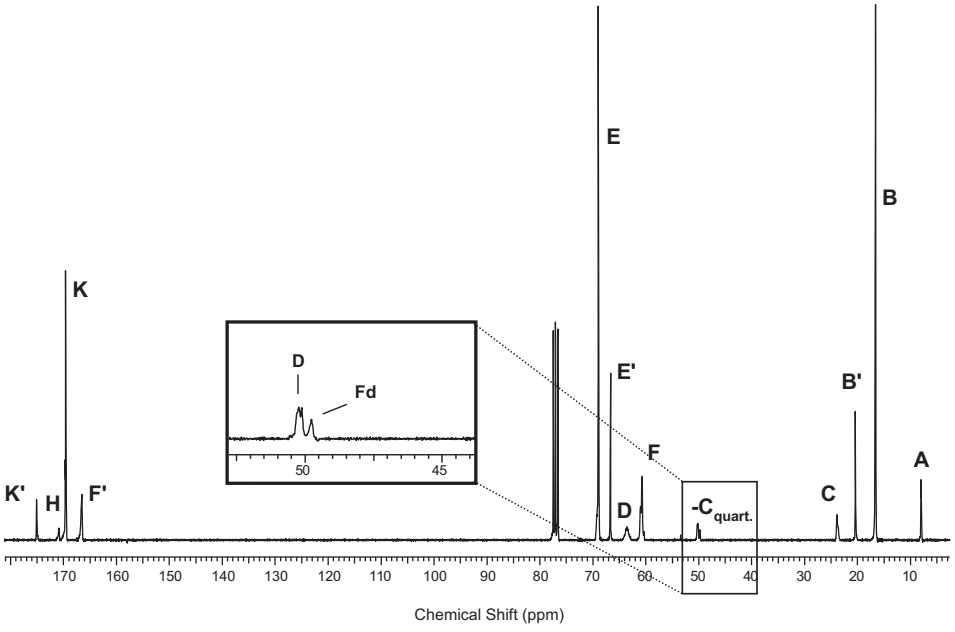

Fig. 5. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of the synthesized *hb*PGA-*g*-PLLA$_5$ multi-arm star copolymer with zoom into the region of the quaternary carbons.

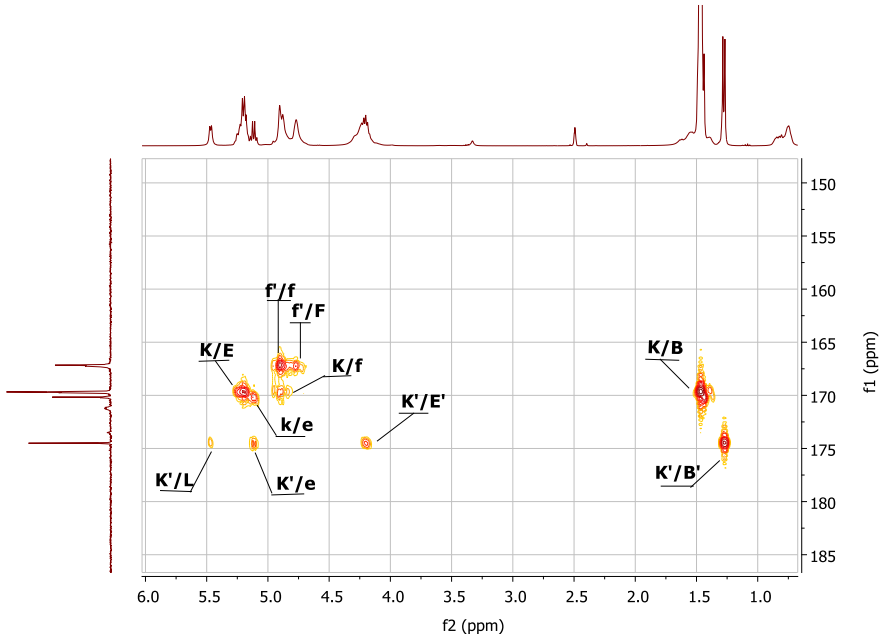

Fig. 6. ^{13}C, ^{1}H-correlation: Zoom into HMBC NMR spectrum (full spectrum, see Supporting Information Fig. S1) of *hb*PGA-*g*-PLLA$_5$ measured in DMSO-d$_6$.

transesterification rearrangement are absent. In addition, the carbonyl carbon signals belonging to the GLL, LLL and GGG sequences can be clearly assigned.

3.2. Thermal properties

The thermal properties of the *hb*PGA-*g*-PLLA star copolymers have been investigated by DSC analysis. In Table 1 the results obtained from SEC and DSC analysis with respect to the average PLLA arm length are summarized. The *hb*PGA macroinitiator is an amorphous material, which exhibits a glass transition temperature (T_g) at 19.1 °C. In contrast, the linear PLLA homopolymer possesses a T_g of 55 °C and a melting temperature (T_m) of 175 °C [41]. PLLA star copolymers with more than 5 lactic acid units per arm show a sharp melting point, which increases with increasing PLLA chain length. As expected, crystallization of the PLLA blocks is possible above a critical chain length. The glass transition temperature of the prepared multi-arm stars is lowered (29–49 °C) in comparison to linear PLLA, and an increase of the T_g with increasing PLLA arm length is observed (see Fig. 8). This dependency is known as well for linear polymers [41]. For all star copolymers an increase of the melting enthalpy (ΔH_m) with increasing PLLA chain length per arm is obtained. In contrast to the copolymers quenched from melt, all of the star copolymers precipitated from solution show a T_m in the first heating scan, indicating a lowered crystallization rate of the PLLA chains (see Fig. 9). This observation emphasizes that the prior thermal treatment of the sample exerts an important influence on the material properties. In addition, the large number of end groups also has a great influence on the thermal behavior of polymers, which was studied on the basis of PLLA stars with different number of hydroxyl termini [14]. In the second heating run, the sample *hb*PGA-*g*-PLLA$_{10}$ shows the characteristic transition curves, including the glass transition, the cold recrystallization and the melting. The phenomenon of two melting peaks results from the two different crystal structures (α/α') formed by PLLA. The α' structure is the thermodynamically less preferred structure [42,43]. This observation might be due to the slow crystallization rate of the PLLA chains, which leads to an inhomogeneous crystallization upon quenching. In fact, the star topology with the hyperbranched PGA core contributes to a depressed melting point compared to the linear PLLA homopolymer. Due to the lowered crystallization rate the morphology of the star copolymers strongly depends on the prior thermal treatment of the sample ranging from amorphous to crystalline materials.

3.3. Solution properties

The hydrodynamic radius (R_h) was determined by Dynamic Light Scattering (DLS) measurements, no angular dependence was observed. Static Light Scattering (SLS) measurements were carried out at different scattering angles (25°–152°) and different

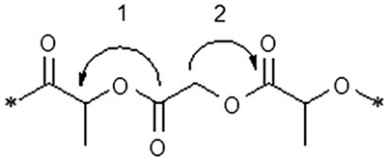

Fig. 7. Visualisation and identification of a sequence pattern in the case of transesterification rearrangements.

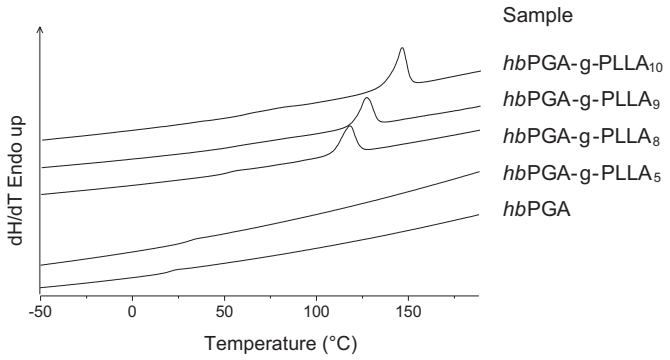

Fig. 8. DSC heating traces of the PLLA multi-arm stars and the polyester polyol (*hb*PGA) obtained from the 1st heating scan with a heating rate of 40 °C/min.

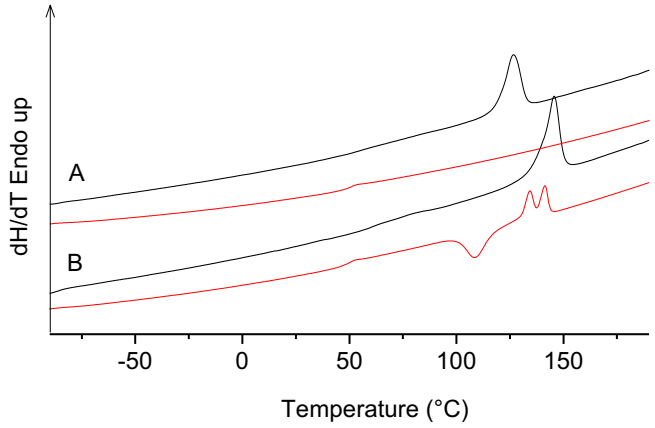

Fig. 9. DSC heating curves of quenched (red line) star copolymers from melt and those precipitated from solution, comparing the first (black line) and second heating run (red line) with each other: (A) *hb*PGA$_{0.6}$-*g*-PLLA$_9$ and (B) *hb*PGA$_{0.6}$-*g*-PLLA$_{10}$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

concentrations (2–10 g/L) to determine the weight-average molecular weight (M_w) of the star copolymers. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) was chosen as a standard solvent for the SLS measurements because of the low value of the refractive index increment (dn/dc) of PLA in tetrahydrofurane (THF) and chloroform ($CHCl_3$) [41]. Due to undesired aggregation, other possible solvents, as for example acetone or pyridine, were not used. Table 2 shows the hydrodynamic radii of the different multi-arm stars obtained by DLS measurements in HFIP. As expected, the size of the particles increases with increasing PLLA arm length.

All obtained results for the star copolymers derived from SLS and DLS are summarized in Table 2. The SEC data for the stars (see Table 1) are based on a poly(styrene) (PS) standard and therefore are not comparable with the SLS-data. In fact, it is known that conventional SEC has limited suitability to determine the molecular weight of star copolymers due to their compact structure and therefore smaller hydrodynamic volume compared with linear copolymers. Hence, it is appropriate to determine the absolute M_w by SLS instead of SEC in order to gain information about the actual dimensions, regardless of the macromolecular architecture. SLS is known to lead to poor resolution for low molecular weight polymers; therefore no SLS and DLS data have been obtained for the macroinitiator and the star copolymer with the lowest molecular weight. Since we were not able to determine the radius of gyration (R_g) due to low resolution capacity; the calculation of the R_g/R_h ratio has not been possible, a valuable parameter in the characterization of star copolymers.

Surprisingly, the weight-average molecular weight, which has been determined by SLS measurements in HFIP ($M_{w,\ SLS}$) is similar to the values obtained from SEC analysis ($M_{w,SEC}$). The hydrodynamic radii (R_h) of the star copolymers, which have been determined by DLS in THF, are in the range of 2.6–3.1 nm, indicating the absence of aggregation and thus the suitability of the utilized solvent. Generally, star polymers obtain smaller radii in comparison to their linear analogs with identical molecular weight. The effect of the topology on the solution behavior increases with increasing number of arms as described by Burchard [44]. In our case, the solution properties might be influenced both by the number of arms and the hyperbranched core.

Table 2
Hydrodynamic radius (R_h) and weight-average molecular weight (M_w) of *hb*PGA-*g*-PLLA star copolymers.

Sample	R_h [a]/nm (DLS)	M_w [b]/g mol^{-1} (SLS)	M_w [c]/g mol^{-1} (SEC)
*hb*PGA-*g*-PLLA$_5$	n.d.	n.d.	3300
*hb*PGA-*g*-PLLA$_8$	2.6	7570	7540
*hb*PGA-*g*-PLLA$_9$	2.9	10,200	8840
*hb*PGA-*g*-PLLA$_{10}$	3.1	12,200	14,000

[a] Determined by DLS measurements at 23 °C in THF.
[b] Determined by SLS measurements at 23 °C in HFIP with dn/dc (mL/g) = 0.162 ± 0.0022.
[c] Determined from SEC analysis in DMF with PS standard calibration.

4. Conclusion

Poly(lactide) multi-arm stars have been synthesized in a grafting-from approach by Sn(Oct)$_2$-catalyzed ring-opening polymerization using a hyperbranched polyester polyol, obtained from poly(glycolide) in a solvent-free procedure in bulk as a macroinitiator. Importantly, a detailed 1D/2D NMR analysis confirmed successful conversion of all hydroxyl termini and permitted the identification of a single glycolyl-lactyl sequence, which excludes possible transesterification rearrangements during the ROP of L-lactide. By varying the monomer/initiator ratio, a systematic series of star polymers with varied molecular weights was obtained in a controlled fashion. The glass transition and the melting point were found to be lower in comparison with linear PLLA due to the influence of the hyperbranched PGA core on the crystallization of the PLLA arms. In fact, the crystallization of the PLLA arms was effectively adjustable by the prior treatment of the samples. As expected, both DLS and SLS measurements revealed an increase of R_h and M_w with increasing PLLA block length. Due to the degradable PGA core and the biocompatible PLLA side chains, these polyester star block copolymers possess promising potential for biomedical applications. Further current studies are focused on the effect of the PLLA chain length on the degradation time of the star polymers. The merely aliphatic polyester structure of the materials might be useful for controlled release systems, since a wide range of degradation rates should be achievable by simply adjusting the *hb*PGA/PLLA molar ratio.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.polymer.2012.12.044.

References

[1] Albertsson A-C, Varma IK. Biomacromolecules 2003;47:1466–86.
[2] Kataoka K, Harada A, Nagasaki Y. Adv Drug Deliv Rev 2001;47:113–31.
[3] Liechty WB, Kryscio DR, Slaughter BV, Peppas NA. Annu Rev Chem Biomol Eng 2010;1:149–73.
[4] Tokiwa Y, Calabia BP. Appl Microbiol Biotechnol 2006;72:244–51.
[5] Anderson KS, Schreck KM, Hillmyer MA. Polym Rev 2008;48:85–108.
[6] Dove AP. Chem Commun 2008;48:6446–70.
[7] Schömer M, Frey H. Macromol Chem Phys 2011;212:2478–86.
[8] Wolf FK, Frey H. Macromolecules 2009;42:9443–56.
[9] Smet M, Gottschalk C, Frey H. Macromol Chem Phys 2005;206:2421–8.
[10] Skaria S, Smet M, Frey H. Macromol Rapid Commun 2002;23:292–6.
[11] Choi J, Kwak S-J. Macromolecules 2003;36:8630–7.
[12] Žagar E, Žigon M. Progr Polym Sci 2010;36:53–88.
[13] Xi W, Jiang N, Gan Z. Macromol Biosci 2008;8:775–84.
[14] Hao Q, Li F, Li Q, Li Y, Jia L, Yang J, et al. Biomacromolecules 2005;6:2236–7.

[15] Klok H-A, Becker S, Schuch F, Pakula T, Müllen K. Macromol Biosci 2003:729–41.
[16] Cameron DJA, Shaver MP. Chem Soc Rev 2011;40:1761–76.
[17] Li Y, Vollhand C, Kissel T. Polymer 1998;39:3087–97.
[18] Trollsås M, Hedrick JL. J Am Chem Soc 1998;120:4644–51.
[19] Voit BI, Lederer A. Chem Rev 2009;109:5924–73.
[20] Jikei M, Kakimoto M-A. Prog Polym Sci 2001;26:1233–85.
[21] Gao C, Yan D. Prog Polym Sci 2004;29:183–275.
[22] Hult A, Johansson M, Malmström E. Adv Polym Sci 1999;143:1–34.
[23] Burgath A, Sunder A, Neuner I, Mülhaupt R, Frey H. Macromol Chem Phys 2000;201:792–7.
[24] Jones M-C, Leroux J-C. Soft Matter 2010;6:5850–9.
[25] Wolf FK, Fischer AM, Frey H, Beilstein J. Org Chem 2010;6(67).
[26] Chen Y, Shen Z, Barriau E, Kautz H, Frey H. Biomacromolecules 2006;7:919–26.
[27] Gottschalk C, Wolf FK, Frey H. Macromol Chem Phys 2007;208:1657–65.
[28] Ternat C, Kreutzer G, Plummer CJG, Nguyen TQ, Herrmann A, Ouali L, et al. Macromol Chem Phys 2007;208(2):131–45.
[29] Zhao Y-L, Cai Q, Jiang J, Shuai X-T, Bei J-Z, Chen C-F, et al. Polymer 2002;43:5819–25.
[30] Adeli M, Haag RJ. Polym Sci Part A: Polym Chem 2006;44:5740–9.
[31] Aryal S, Prabarahan M, Pilla S, Gong S. Int J Biol Macromol 2009;44:346–52.
[32] Gillies ER, Fréchet JMJ. Drug Discov Today 2005;10(1):35–43.
[33] Hirao A, Yoo H-S. Polym J 2011;43:2–17.
[34] Nunez E, Ferrando C, Malmström E, Claesson H, Werner P-E, Gedde UW. Polymer 2004;45:5251–63.
[35] Fischer AM, Frey H. Macromolecules 2010;43:8539–48.
[36] Schärtl W. Light scattering from polymer solutions and nanoparticle dispersions. Springer Laboratory: Springer; 2007.
[37] Yang L, Qi X, Liu P, El Ghzaoui A, Li S. Int J Pharm 2010;294:43–9.
[38] Zimm BH. J Chem Phys 1948;16:1093–9.
[39] Gao H. Macromol Rapid Commun 2012;33:722–34.
[40] Kasperczyk J. Polymer 1996;37:201–3.
[41] Donald GJ. Polym Envir 2001;9:63–84.
[42] Pan P, Zhu B, Kai W, Dong T, Innoe Y. Macromolecules 2008;41:4296–304.
[43] Rathi S, Kalish JP, Coughlin EB, Hsu SL. Macromolecules 2011;44:3410–5.
[44] Burchard W. Adv Polym Sci 1999;143:114–94.