Branched copolylactides: the effect of the synthesis method on their properties

V V Istratov¹, A V Polezhaev²

¹,²A.N. Nesmeyanov Institute of Organoelement Compounds RAS, Moscow, Russian Federation

E-mail: ¹slav@ineos.ac.ru

Abstract. In this work, L-lactide, acting as a cyclic AB monomer, was copolymerized with various AB2 comonomers. Depending on the nature of the AB2 comonomer, it was either a combination of L-lactide ring-opening polymerization with glycidol polymerization or a combination of L-lactide ring-opening polymerization with 2,2-bis(hydroxymethyl) propionic acid (BHP) polycondensation. Both synthetic methods resulted in branched copolyesters. A number of polymers with varying degrees of branching were obtained by systematically changing the proportion of comonomer AB2. The polymers were characterized using ¹H NMR spectroscopy and SEC, and their thermal properties were studied using differential scanning calorimetry and thermogravimetric analysis. Also were investigated the viscosity of the solution and the wettability of the branched copolymers. Although structurally similar macromolecules were formed in both synthesis methods, polymers with BHP as AB2 comonomers have higher melting- and glass transition temperatures, higher thermal stability, solution viscosity and lower wettability than polymers with glycidol as AB2 comonomers.

Keywords: polylactide, copolymers, viscosity, copolyesters

1. Introduction

Poly-L-lactide (PLLA), one of the widely produced and extensively studied bio-based thermoplastic polyesters, is the “preferred polymer” for many biomedical applications due to its complex of valuable properties, the most important of which are biodegradability and biocompatibility. [1] Unlike other bioplastics such as poly-(ε-caprolactone) (PCL), polyhydroxyalkanoates (PHA), polyethylene glycol (PEG), etc., PLLA has good mechanical properties (bending and tensile strength), and a wide range of processing methods such as injection molding, film extrusion, blow molding, thermoforming or fiber spinning. PLLA has mechanical properties comparable to commercial polymers such as polyethylene (PE), polypropylene (PP), polystyrene (PS), and poly (ethylene terephthalate) (PET). [2] and has become a promising substitute for petroleum-derived plastics in specific applications [3]. Since the 1970s, PLA-based (co) polymers have been widely used for the production of sutures, bone fixation and repair implants, extended-release pharmaceuticals, tissue engineering scaffolds, and coatings. [4, 5] However, the inherent disadvantages of PLLA limit its use; These disadvantages include low elongation (less than 5%), high brittleness, low impact strength and high melt viscosity, high crystallinity, and hydrophobicity.

Much research effort is currently underway to tune the properties of PLLA without significantly degrading other valuable characteristics such as biodegradability. This is achieved, for example, by copolymerization with diglycolide, β-caprolactone, mesolactide or other comonomers, mixing PLLA with other polymers, and adding plasticizers or cross-linking agents [6-10]. One such strategy for creating PLLAs with unusual rheological and mechanical properties in combination with an altered biodegradation profile is macromolecule branching. Many branched polylactide architectures are known, for example, long-chain branched, grafted, star-shaped, dendritic and/or cross-linked PLLAs. [11-22] Although a number of studies have produced polymers of similar architecture, the dependence
of polymer properties on the synthesis method has not yet been investigated. This work is devoted to the solution to this problem.

2. Experimental Section

2.1. Materials.
L-Lactide (98%, ABCR) was recrystallized from ethyl acetate before use; Glycidol (97%, Merck) was distilled under reduced pressure; 2,2-Bis(hydroxymethyl)-propionic acid (BHP, 98%, Aldrich Chemical Co.) was dried in a vacuum over dry silica gel for 24 h prior to use. Stannous(II) 2-ethylhexanoate (Sn(Oct)2, 95%, Aldrich Chemical Co.) was used as received. Chloroform, THF and DMSO ("Himmed", Russia) were purified by standard methods [23].

2.2. Polymerization.
Branched polylactide copolyesters were prepared by copolymerizing L-lactide and the corresponding AB2 comonomer (glycidol or BHP). All syntheses were carried out at 140 °C for 24 h in bulk using Sn(Oct)2 as a catalyst (molar ratio L-lactide : catalyst = 2000 : 1) according to figure 1 and 2. The degree of branching of the obtained polylactides was set by the ratio L-lactide to AB2comonomer in the monomer feed.

Thus, to obtain branched copolyactides with 30% AB2 comonomer, the Sn(Oct)2 catalyst (0.008g, 0.02 mmol) was placed in a two-necked glass flask in the form of a 10% solution in THF, after which the solvent was distilled off under reduced pressure. Then, 2.883g, 20.0 mmol of L-lactide and 20.0 mmol of AB2 comonomer (1.482g of glycidol or 2.683g of BHP) were added to the flask. The flask was equipped with a mechanical overhead stirrer and heated to 140 °C using a heating mantle for 24 hours. In the synthesis of polymers with BHP as an AB2 comonomer, the synthesis was carried out for the last 20 hours at a reduced (5 mm Hg) pressure.
The resulting crude product was dialyzed in CHCl₃ (Roth "ZelluTrans" membrane, MWCO = 1000 Da) for 48 hours. Then the solvent was evaporated and the polymer was dried under vacuum for 48 hours. Polymers 1a – 3a (AB₂ comonomer = Glycidol) ¹H NMR (500 MHz, CDCl₃), δ: 1.51 (Lactide -CH₃), 3.46 - 4.19 (Glycidol -O-CH₂-, >CH-), 5.10 (Lactide >CH-).

Polymers 1b – 3b (AB₂ comonomer = BHP) ¹H NMR (500 MHz, CDCl₃), δ: 1.23 (BHP -CH₃), 1.51 (Lactide -CH₃), 3.60–4.27 (BHP -CH₂-O-), 5.10 (Lactide >CH-).

2.3. Characterization.

The ¹H NMR spectra were recorded on a Bruker spectrometer with operating frequency ¹H - 600.22 MHz at 25 °C using CDCl₃ as solvent and TMS as an internal standard.

Size exclusion chromatography (SEC) of the copolymers was carried out on a "Waters 150" chromatograph (eluent - THF (1 ml/min), column - PL-GEL 5u MIXC (300x7.5 mm)).

The differential scanning calorimetry (DSC) and Thermogravimetric analysis (TGA) were performed using a Perkin-Elmer DSC 6000 PerkinElmer TGA 4000 Thermal analyzers, respectively. The Tg was determined as the midpoint of the heat capacity increase of the second heating process and Tm as the endothermal peak in the DSC curve of the second heating process; Weight loss temperatures of 5% in the TGA curves were chosen as a criterion for the thermal stability of the polymers.

Viscosimetry was performed for DMSO solutions using a glass Ubbelohde viscometer at a temperature of 25 °C; the intrinsic viscosity ([η]) of the polymers was determined from a plot of specific viscosity vs. concentration.

The contact angle between the polymer films and water drops was measured by the sessile drop method on a "Tracker" automatic drop shape analyzer (Teclis-Scientific, France) for drops of 100 seconds age at a temperature of 25° C and about 100% relative humidity.

3. Results and Discussion

In this work, L-lactide has been employed as cyclic AB monomer, which was copolymerized with an AB₂ comonomer. Depending on the nature of AB₂ comonomer, it was either a combination of lactide ring-opening polymerization with glycidol polymerization (Scheme 1), or a combination of lactide ring-opening polymerization with 2,2-bis (hydroxymethyl) propionic acid (BHP) polycondensation (Scheme 2). Both synthetic methods resulted in branched copolyesters. By systematic variation of the AB₂ comonomer fraction, a series of branched copolyesters with different degree of branching (DB) have been prepared and studied with respect to their properties.

All copolymerization reactions of L-lactide (L-LA) and 2,2-bis(hydroxymethyl)butyric acid (BHB) were carried out in bulk, using Sn(Oct)₂ as catalyst, which catalyzes both ROP and polymerization of the AB₂ comonomers. Reaction conditions (temperature, catalyzed content, reaction time) were chosen according [24] to produce a polymer with the highest molecular weight. By systematic variation of the fraction of the AB₂ comonomer, a series of long-chain branched polylactide copolymers with varied degree of branching (DB) have been prepared. The polymers were obtained in the form of yellowish very viscous substances, soluble in dimethylsulfoxide (DMSO), chloroform and tetrahydrofuran. An increase of the AB₂ comonomer content in the polymers resulted in an increased rate of solubility of the latter in ethanol, thus changing from insoluble to completely soluble. All the polymers were characterized by NMR spectroscopy and SEC. The spectra obtained are summarized in figure 3.
The incorporation of the AB2 comonomer was confirmed by the $^1$H NMR spectroscopy for the both series of PLLA-based copolyesters; thus, the fraction of AB2 comonomer incorporated was determined from the respective $^1$H NMR signal intensity. Incorporated Glycidol and BHP monomer units show characteristic signals at 3.46 - 4.19 and 3.60–4.27 ppm, respectively, that can be used to quantify their fraction by comparison with the signals of the (CH-) group of the lactide monomer units located at 5.1 ppm. With an increasing amount of the AB2 comonomer in the copolyester the signals of the lactide units (5.10 and 1.51 ppm) show an increasingly complex splitting pattern, which is caused by the polymer microstructure; i.e., an increasing amount of combinations between lactide and the AB2 comonomer units is observed. From the data presented in Table 1, it can be seen that both the yields and
the amount of comonomer AB2 included in the polymer tend to decrease with increasing amount of comonomer AB2 in the feed.

**Table 1.** Characterization data of the branched copolylactides

| Copolymer | AB2 comonomer | Yield | Quantity of AB2 comonomer* | DB* | Mn** | Mw/Mn** |
|-----------|---------------|-------|-----------------------------|-----|------|---------|
| 1a        | Glycidol      | 86    | 5                           | 4.7 | 0.09 | 38000   |
| 2a        | Glycidol      | 71    | 10                          | 11.7| 0.19 | 28500   |
| 3a        | Glycidol      | 57    | 30                          | 28.7| 0.35 | 17400   |
| 1b        | BHP           | 82    | 5                           | 4.8 | 0.09 | 35000   |
| 2b        | BHP           | 68    | 10                          | 9.8 | 0.16 | 27000   |
| 3b        | BHP           | 50    | 30                          | 25.4| 0.32 | 18500   |

* - Quantity of AB2 comonomer in branched polylactides (Scheme 1; Scheme 2), determined from monomer load (calculated) and from NMR spectra of the polymers (measured);

** - Obtained by GPC.

At the same time, the ratio of the AB2 comonomer in the polymer significantly and systematically changes depending on its amount in the feed. Obviously, this is due to the different reactivity of the comonomers - lactide and AB2 comonomers - under the given reaction conditions. Sn(Oct)2, being a very good catalyst for the polymerization of lactide, shows not very good performance in the polymerization of glycidol and the polycondensation of BHP. It is important that determined amounts of comonomer AB2 were similar for the polymers of different series (1a-1c and 2a-1c), but with the same calculated amount of this comonomer. Since the calculated and experimentally determined amounts of the AB2 comonomer are comparable, we assumed that the obtained structures are close to the calculated ones.

The degrees of branching (DB) for the copolymers were in the range of 0.09-0.35, according to the definition for AB/AB2 copolymers presented by Frey and Hölter [25]:

\[
DB_{AB/AB2} = 2 (r + 1) / (r = 2)^2
\]

where \( r \) is the monomer ratio = [AB]/[AB2] in polymer.

The DB of the hyperbranched copolymers increased with the AB2 comonomer ratio in the feed. The synthesized polymers had molecular weights defined by SEC in the range of 38000 - 17400 g/mol, decreasing with increasing AB2 comonomer content in the polymer. All branched copolyesters showed a monomodal molecular weight distribution with a polydispersity (SEC) in the range 1.9-3.6. Since the hydrodynamic volume of branched polymers is a function of the degree of branching, SEC calibration with commonly used linear polystyrenes results in lower molecular weights, and their actual molecular weights should be higher.

Thus, we have synthesized two series of polymers differing in the structure of branched monomer units, and the ratio of monomer units in the series of these polymers changes in a similar way. From a material science point of view, the effect of polymer branching on decomposition temperature, melting point, glass transition, crystallinity and solution viscosity is extremely important for further processing and use. The thermal properties of the hyperbranched polylactide copolymers have been characterized by means of TGA and DSC analysis. As expected, the incorporation of small fractions of AB2 comonomer resulted in a decrease of the melting point and the Tg (Tabl. 2).

The use of comonomer AB2 in the synthesis of polymers in an amount of more than 5% led to the formation of completely amorphous materials. In both series of polymers (1a-1c, 2a-2c), the glass transition temperature decreased with an increase in the AB2 comonomer content; The peak on the DSC curve corresponding to polymer melting is observed only for polymers with a low AB2 comonomer content — samples 1a and 2a.
Table 2. Thermal and solution properties of branched copolylactides

| Copolymer | Tg (°C) | Tm (°C) | T5%*(°C) | [η], dL/g |
|-----------|---------|---------|----------|----------|
| 1a        | 48.5    | 140.0   | 305      | 16.3     |
| 2a        | 38.6    | -       | 292      | 10.1     |
| 3a        | 16.8    | -       | 275      | 5.7      |
| 1b        | 49.1    | 142.6   | 307      | 18.6     |
| 2b        | 40.3    | -       | 300      | 14.8     |
| 3b        | 19.1    | -       | 286      | 9.5      |

*-Weight loss temperatures of 5% in the TGA curves

Obviously, this indicates a high degree of amorphousness of the branched copolymers. The thermal stability of polymers also decreased with an increase in the comonomer content in branched AB2 macromolecules, and the decrease in thermal stability was 7–9%. Characteristically, all thermal parameters (characteristics) of polymers containing branched BHP units were slightly higher than those of polymers containing branched glycidol units. At the same time, the decrease in these characteristics with an increase in the AB2 comonomer content in polymers containing BHP monomer units was less than in polymers containing glycidol units.

Intrinsic viscosity [$\eta$] has also been determined for all polymers. In all cases, the intrinsic viscosity was significantly lower than that of linear PLLA and decreased with increasing AB2 comonomer content. It is interesting to note that the intrinsic viscosity of polymers with the same number of AB2 units was lower for macromolecules containing glycidol than for macromolecules containing BHP units.

This may represent an important finding with respect to processing of branched polylactides. It should be mentioned that the viscosity decrease observed is due to both the decrease in molecular weight and the increasingly branched structure, as is obvious from a comparison with linear samples of similarly low molecular weight.

Since branched macromolecules contain a large number of terminal hydroxyl groups, wettability is one of the important characteristics of these polymers. The contact angle is the main parameter that characterizes the wettability of a solid surface, as well as one of the properties of the interface that can be measured directly.

Table 3. The values of water contact angle on various polymer substrates (θ, grad).

| Polymer | θ, grad | Polymer | θ, grad |
|---------|---------|---------|---------|
| 1a      | 70      | 1b      | 72      |
| 2a      | 62      | 2b      | 66      |
| 3a      | 33      | 3b      | 42      |

For all studied copolylactides, partial surface wettability was observed (contact angle $\theta < 90^\circ$). With an increase in the AB2 comonomer content, the surface wettability of the copolyllactide increased, and the contact angle decreased. The surfaces of polyesters containing glycidol showed higher wettability than those of polyesters containing BHP.

4. Conclusion

We have demonstrated that both synthesis methods - a combination of lactide ring opening polymerization with glycidol polymerization or a combination of lactide ring opening polymerization with polycondensation of 2,2-bis (hydroxymethyl) propionic acid lead to the formation of branched high molecular weight polymers.

These synthetic pathways effectively control the degree of branching of macromolecules. Changing the ratio of comonomers AB/AB2 allows us to control the thermal and rheological properties of materials, as well as the wettability of copolymers.

Although structurally similar macromolecules were formed in both synthesis methods, polymers with BHP as AB2 comonomers have higher melting- and glass transition temperatures, higher thermal stability, solution viscosity and lower wettability than polymers with glycidol comonomers.
Acknowledgments

Polymer testing was performed with the support of the Ministry of Science and Higher Education of the Russian Federation using scientific equipment from the Center for Molecule Composition Studies of the INEOS RAS. This work was supported by the Competence Center of the National Technological Initiative (NTI) "Digital Materials Science: New Materials and Substances" of the Bauman Moscow State Technical University.

References

[1] Goddard E D, Gruber J V 1999 Principles of Polymer Science and Technology in Cosmetics and Personal Care ed. Goddard E. D., Gruber J. V. Marcel Dekker, Inc. New York 667 p.

[2] Nampoothiri K M, Nair N R, Jonh R P 2017 Synthesis, Characterization and Biodegradation of Gum Arabic-based Bioplastic Membranes Bioreavour Technol 4(2) pp 32-42

[3] Lim L, Auras R, Rubinio M 2008 Processing Technology for Poly(lactic acid). Prog Polym Sci 33 pp 820-852.

[4] Lizundia E, Meaurio E, Laza J M, Vilas J L, León Isidro L M 2015 Study of the chain microstructure effects on the resulting thermal properties of poly (L-lactide)/poly (N-isopropylacrylamide) biomedical materials Materials Science and Engineering: C 50 pp 97-106.

[5] Bhavesh P, Subhashis C 2013 Biodegradable polymer: An emerging excipient in pharmaceutical and medical device industry J. Excipients and Food Chemicals 4(4) pp 126-157.

[6] Wang J Z, You M L, Ding Z Q and Ye W B 2019 Deformation and fracture mechanisms of gradient nanograin pure Ti produced by a surface rolling treatment Materials Science and Engineering C 754 pp 121-128.

[7] Saiful Islam Md, Moynul Islam Md 2021 Advances in Sustainable Polymer Composites 1st Edition ed. Rahman M. R. Woodhead Publishing 306 p.

[8] Okada M 2002 A Comparative Study on the Mechanical and Biodegradation Characteristics of Starch-Based Composites Reinforced with Different Lignocellulosic Fibers Prog. Polym. Sci. 27 pp 2434–2447.

[9] Calori I R., Braga G, de Jesus P D C C., Bi H, Tedesco A C 2020 Polymer scaffolds as drug delivery systems European Polymer Journal, 129 109621

[10] Thakur V K, Thakur M K 2015 Handbook of Polymers for Pharmaceutical Technologies: Biodegradable Polymers Scrivener Publishing LLC, Beverly, MA 3 529p.

[11] Corneillie S, Smet M 2015 PLA architectures: the role of branching Polym. Chem. 6 pp 850-867.

[12] Bandyopadhyay A, Sengupta S, Das T 2018 Hyperbranched Polymers for Biomedical Applications Springer Nature Singapore Pte Ltd 178 p.

[13] Wurm F., Frey H. 2011 Linear–dendritic block copolymers: The state of the art and exciting perspectives Prog Polym. Sci. 36(1) pp 1-52.

[14] Michalski A., Brzezinski M., Lapienis G., Biela T. 2019 Star-shaped and branched polylactides: synthesis, characterization, and propertiesProg Polym Sci 89 pp 159-212.

[15] Su Z., Zhang R., Yan X.-Y., Guo Q.-Y., Huang J., Shan W., Liu Y., Liu T., Huang M., Cheng S.Z.D. 2020 High-defect hydrophilic carbon cuboids anchored with Co/CoO nanoparticles as highly efficient and ultra-stable lithium-ion battery anodes Prog Polym Sci 4 pp 10166-10173.

[16] Yildirim I., Weber C., Schubert U.S. 2018 Self-Healing Functional Polymeric Materials Prog Polym Sci, 76 pp 111-125.

[17] Sun H., Kabb C.P., Sims M.B., Sumerlin B.S. 2019 Architecture-transformable polymers: Reshaping the future of stimuli-responsive polymers Prog Polym Sci, 89 pp 61-75.

[18] Basu A., Kunduru K R, Doppalapudi S, Domb A J, Khan W 2016 Injectable formulations of poly (lactic acid) and its copolymers in clinical use Adv. Drug Deliv. Rev. 107 pp 213-227.

[19] Maharana T, Pattanaik S, Routaray A, Nath N, Sutar A K 2015 Synthesis and characterization of poly(lactic acid) based graft copolymers React Funct Polym 93 pp 47-67.

[20] Tambe P, Kumar P, Paknikar K M, Gajbhiye V 2019 Smart triblock dendritic unimolecular
micelles as pioneering nanomaterials: Advancement pertaining to architecture and biomedical applications. *J. Contr. Rel.* **299** pp 64-89.

[21] Jahandideh A, Muthukumarappan K 2017 Star-shaped lactic acid based systems and their thermosetting resins; synthesis, characterization, potential opportunities and drawbacks *Eur Polym J.* **87** pp 360-379.

[22] Rasal R M, Janorkar A V, Hirt D E 2010 Poly (lactic acid) modifications *Prog Polym Sci* **35(3)** pp 338-356.

[23] Armarego W L F 2003 Purification of Laboratory Chemicals *ed. Armarego, W.L.F.; Li, C.; Chai, L. Butterworth Heinemann, Amsterdam* 632p.

[24] Zhou Z H, Liu X P, Liu L H 2008 Synthesis of ultra-high weight average molecular mass of poly-l-lactide *Int. J. Polym. Mater.* **57(5)** pp 532-560.

[25] Frey H, Höltcr D 1999 Degree of branching in hyperbranched polymers. 3 Copolymerization of AB/H-monomers with AB and AB7,-monomers *Acta Polym., 50(2)* pp 67-76.