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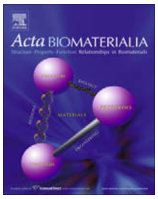

Synthesis, characterizations and biocompatibility of novel biodegradable star block copolymers based on poly[(*R*)-3-hydroxybutyrate] and poly(ε-caprolactone)

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ABSTRACT

Star block copolymers based on poly[(*R*)-3-hydroxybutyrate] (PHB) and poly(ε-caprolactone) (PCL), termed SPHBCL, were successfully synthesized with structural variation on arm numbers and lengths via coupling reactions and ring opening polymerizations. Arm numbers 3, 4 and 6 of SPHBCL were synthesized by using different multifunctional cores, such as trimethyol propane, pentaerythiritol and dipentaerthritol, respectively. Gel permeation chromatography (GPC) and ^{1}H and ^{13}C nuclear magnetic resonance were used to characterize the structure of SPHBCL. GPC failed to produce accurate molecular weights of the SPHBCL due to the discrepancy of star copolymer structures. The melting temperature of SPHBCL decreased with increasing degree of branching. Thermal decomposition temperature was revealed to be lower than that of linear block copolymer LPHBCL counterparts based on PHB and PCL. Films made from various SPHBCL copolymers had different porous or networking surface morphology, and all possessed improved biocompatibility in terms of less blood clotting and more osteoblast cell growth compared with their corresponding homopolymers PHB and PCL. Among them, it was found, however, that the 4-arm star block copolymer 4SPHBCL-25 showed unique surface properties, i.e. a regular nanoravine structure was observed by scanning electron microscopy and atomic force microscopy. This 4-arm star copolymer also showed the best biocompatibility.

1. Introduction

Biodegradable and biocompatible polyesters are being increasingly investigated worldwide in both fundamental and applied research for pharmacological, biomedical and environmental purposes [1–6]. One such polyester, poly[(*R*)-3-hydroxybutyrate] (PHB), is a typical natural biopolyester that is produced by many microorganisms and acts as an intracellular carbon and energy storage compound [7]. PHB has attracted the attention of industry as it is an environmentally degradable material that can be used for a wide range of agricultural, marine, and medical applications based on renewable biomass and environmentally friendliness [7].

The majority of studies on developing biodegradable polyesters have focused on linear polymers, including PHB, poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate), poly(3-hydroxybutyrate-*co*-4-hydroxybutyrate), poly(3-hydroxybutyrate-*co*-3-hydroxyhexanoate), poly(butylene succinate), poly(lactide), poly(ε-caprolactone) (PCL), and their diblock and triblock copolymers [8–13], whereas much less attention has been paid to the star polymers.

Polymers with complex molecular architectures have drawn much interest for their possible use in applications requiring nanostructured materials, as new or improved properties can be achieved by altering their specific molecular architectures [14,15]. One group of polymers with complex molecular architectures is the multi-arm star polymers, which can be distinguished by their structure, which contains several linear arms of similar molecular weight that emanate from a central core, representing a special case of branched polymers. Generally, star polymers can be prepared by two different routes – the arm-first strategy [16] and the core-first approach [17,18] – with a multifunctional core being used as the initiator. Due to their highly functionalized globular architectures, star polymers exhibit different properties from those of their linear counterparts, such as less entanglement in the solid state [14], high solubility in various solvents, low melt viscosity [19–22] and fast molecular motion [23]. Trollasas and Hedrick [24] reported the synthesis of a dendrimer-like star polylactone using a hexahydroxyl-functional compound initiator and stannous 2-ethylhexanoate (Sn(Oct)$_2$) as the catalyst. Kim et al. [25,26] reported the synthesis of a star-shaped polylactide with pentaerythritol (PTOL) as the initiator and Sn(Oct)$_2$ as the catalyst. Park et al. [27] prepared star-shaped PLLA-PEO block copolymers with 1,3-*N*,*N*′-dicyclohexylcarbodiimide (DCC) and with 4-(dimethylamino)pyridine (DMAP) as the catalyst. However, no study has been reported on star copolymers based on PHB and PCL yet.

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In this paper, for the first time, a series of star copolymers with block star-arm structure, i.e. star block copolymers (SPHBCL) based on PHB and PCL were synthesized via ring opening polymerization of ε-caprolactone (ε-CL) in the presence of multi-arm hydroxyl-terminated oligo-PHB. SPHBCL possess architectural variations on arm numbers and PCL block lengths that were confirmed by both ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy as well as gel permeation chromatography (GPC). The SPHBCL copolymers exhibit a patterned surface morphology and good biocompatibility.

2. Experimental

2.1. Materials

PHB was purchased from Jiangsu Nantian Co. Ltd. (China) and had an average molecular weight of $M_n = 330{,}000 \pm 10\%\ \mathrm{g\ mol^{-1}}$. Trimethylol propane (TMP, 99%), PTOL (99%) and dipentaerythritol (DPTOL, 99%) were obtained from Perstorp Polyols Inc. (USA). Monomer ε-CL (99%) and PCL ($M_n = 50{,}000 \pm 10\%\ \mathrm{g\ mol^{-1}}$) were also purchased from Dow Chemical Company. Chloroform and ε-CL were dried with calcium hydride at room temperature for 48 h, followed by distillation under reduced pressure just before their use. DCC (99%) and DMAP (99%) were purchased from Aldrich. $Sn(Oct)_2$ (Alfa Aesar) was used without further purification. Other organic solvents were of analytical grade and used as received. All glass instruments were dried at 140 °C for 48 h before use.

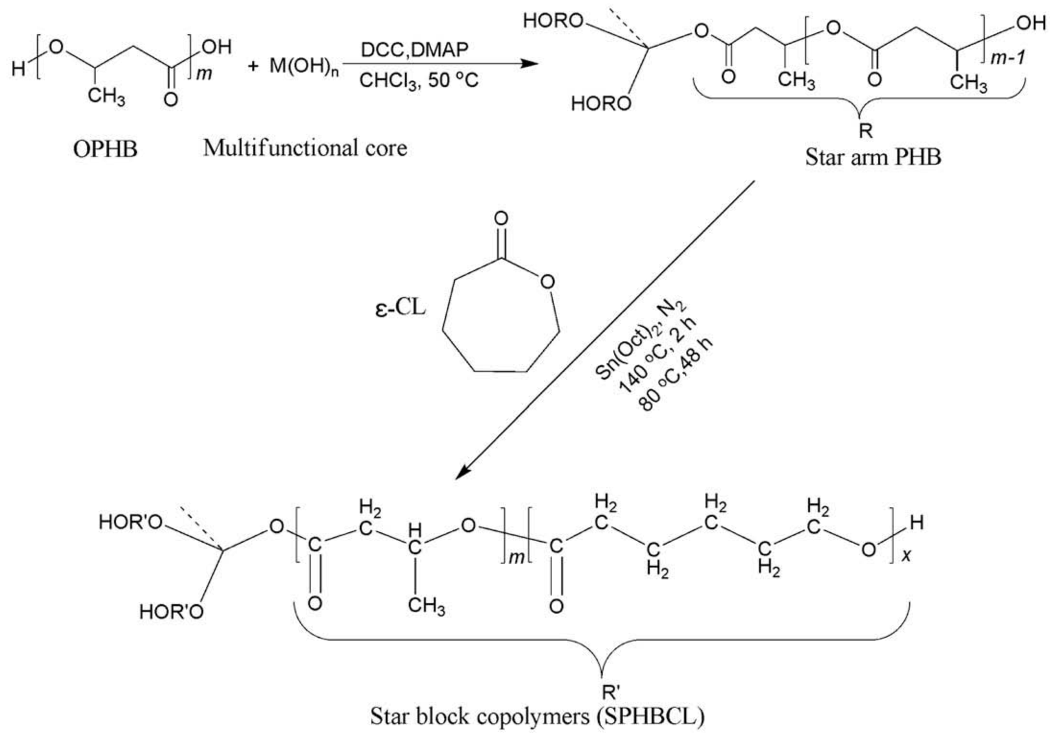
PHB oligomer (OPHB) was prepared through acid degradation using sulfuric acid as the catalyst in chloroform solvent, and the methyl ester-terminated PHB (mPHB) prepolymer was prepared by reaction of PHB with methanol exposed to acid-catalyzed methanolysis [28].

2.2. Synthesis of the macroinitiator multi-star PHB

OPHB (3 g, 1.67×10^{-4} mol, $M_n = 1800\ \mathrm{g\ mol^{-1}}$) and stoichiometric amounts of multifunctional core (TMP, PTOL, DPTOL) and DMAP (30 mg, 2.45×10^{-4} mol) were dried in a 50 ml three-neck flask under vacuum at 60 °C overnight. Anhydrous chloroform 30 ml was added to the flask. The chloroform was removed by distillation in an oil bath at 75 °C to completely remove any water from the system. When the flask was cooled down to room temperature, DCC (24.5 mg, 1.18×10^{-3} mol) dissolved in 5 ml of anhydrous chloroform was added, and the mixture was stirred for 24 h at 50 °C under nitrogen. The reaction mixture was cooled down again to room temperature and poured slowly into an excess of cool methanol. The precipitates were washed with methanol three times and dried at room temperature in vacuum. Yields of 60–86% were obtained on different arm number PHB prepolymers.

2.3. Synthesis of SPHBCL

All the SPHBCL were prepared by ring opening polymerization of monomer ε-CL, which was initiated with star-arm PHB of PHB arm $M_n = 1800\ \mathrm{g\ mol^{-1}}$ in the presence of a catalytic amount of $Sn(Oct)_2$. Variation in the number of arms was accomplished by using different macroinitiator multi-star PHB prepolymers with 3, 4 or 6 arms (Scheme 1). On the other hand, the PCL lengths in each arm were varied by controlling the amount of monomer ε-CL added to the reaction mixtures (weight ratios of [multi-arm PHB]/[CL] (by wt.) were 4:6 to 2:8 in this study). Typically, a 100 ml three-neck round-bottom flask was flame-dried and then degassed and purged with nitrogen. This process was repeated three times. Thereafter, 2.50 g of 3-arm PHB and ε-caprolactone (ε-CL) (3.75 g, 3.3×10^{-2} mol) were placed into the flask under a nitrogen atmosphere. The mixture was heated in an oil bath at 140 °C with magnetic stirring. When the mixture had completely



When the multifunctional core was TMP,or PTOL, or DPTOL, n = 3, or 4, or 6, repectively.

Scheme 1. Synthesis of the novel star block SPHBCL copolymers (TMP, PTOL and DPTOL).