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Synthesis of diblock copolymer poly(10-hydroxydecanoic acid) /polystyrene by combining enzymatic condensation polymerization and ATRP

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Summary

The diblock copolymers poly(10-hydroxydecanoic acid)-block-polystyrene (PHDA-*b*-PSt) were synthesized by combining enzymatic condensation polymerization of 10-hydroxydecanoic acid (HDA) and atom transfer radical polymerization (ATRP) of styrene (St). PHDA was firstly obtained via enzymatic condensation polymerization catalyzed by Novozyme-435. Subsequently one end of poly(10-hydroxydecanoic acid) (PHDA) chains was modified by reaction with α-bromopropionyl bromide and the other was protected by chlorotrimethylsilane (TMSCL), respectively, the resulting monofunctional macroinitiator was used in the ATRP of St using CuCl/2,2′-bipyridine (bpy) as the catalyst system to afford the diblock copolymers including biodegradable PHDA blocks and well-defined PSt blocks.

Introduction

In recent years, enzymatic polymerization has been evaluated as a new methodology for polymer synthesis. Enzymatic polymerization using environmentally benign process is a promising alternative technique to the chemical catalyzed polymerization employing organometallic catalysts [1-2]. In addition, from the technological point of view enzymatic polymerization is significant due to the advantages such as nontoxicity, recyclability, high enantio-, regio- and chemoselectivities and so on. [3]. For example, Lipase B from Candida Antarctica (CALB) immobilized on an acrylic macroporous resin (Novozyme-435) has been proven as an effective biocatalyst in polymer synthesis via both ring-opening polymerization (ROP) of lactones [4-5] (i.e. ε-CL) [6-8] and polycondensation of either dicarboxylic acids/diols [9-10] or hydroxyacids [11]. Whereas lipase-catalyzed procedure is not strictly a controlled/living polymerization, as a living/controlled radical polymerization [12] ATRP [13-14] is the most versatile and popular due to the mild reaction conditions and being suitable for most of the common monomers, therefore it enables the preparation of novel well-defined polymeric materials.

Much attention has been likewise focused on the development of block copolymer using as surfactants, adhesives, thermoplastic elastomers and dispersants [15], because of the fact that their special structures can bring on the unique polymer properties to yield novel materials. Different techniques for the preparation of

copolymer have been developed, in which the difunctional initiator carrying two different radical forming sites has been used. For example, Andreas Heise et al firstly incorporates enzymatic ROP with ATRP initiated by a difunctional initiator to obtain the diblock copolymer poly(ε-caprolactone)-*block*-poly (styrene) (PCL-*b*-PSt) [16], which shows very good control during polymerization [17]. At the same time, block polymerization initiated with macroinitiator formed by transformation of homopolymer end groups is thought of as another elegant method, which can combine various polymerization mechanisms to obtain block copolymers with novel properties. Our group has successfully used this technique to synthesize di/triblock copolymers PCL-*b*-PSt / PSt-*b*-PCL-*b*-PSt by combining enzymatic ROP of ε-CL and ATRP of St [18]. However, this strategy has not yet been used to carry out the chemoenzymatic synthesis of the diblock copolymer by the integration of enzymatic condensation polymerization and ATRP.

In this paper we firstly report the synthesis of diblock copolymer PHDA-*b*-PSt by combining the enzymatic condensation polymerization of HDA with the ATRP of St. The composition, molecular weight and polydispersity of the diblock copolymer are confirmed by 1H-NMR and GPC analysis.

Experimental

Materials

Novozyme-435, (7000PLU/g) was a gift from Novo Nordisk A/S and was employed without further purification. 10-hydroxydecanoic acid (HDA) (Beijing chemical Co.), chlorotrimethylsilane (TMSCL) (Shanghai chemical Co.), α-bromopropionyl bromide (Fluka) and 2, 2´-bipyridine (Beijing chemical Co.) were employed without further purification. CuCl (Beijing chemical Co.) was purified by precipitation from acetic acid to remove Cu^{2+}, filtrated and washed with ethanol and then dried. Triethylamine (Beijing chemical Co.) was refluxed for 12h in the presence of CaH_2 and distilled under vacuum. Toluene (Beijing chemical Co.) was dried with CaH_2 and distilled. Styrene (Beijing chemical Co.) was also dried with CaH_2 and distilled under vacuum before use.

Instruments

^{1}H-NMR spectra was recorded on a Bruker ARX-500 spectrometer with $CDCl_3$ as solvent at 500 MHz. Chemical shifts (in parts per million, ppm) were reported downfield from 0.00 ppm using trimethylsilane (TMS) as internal standard. Gel permeation chromatography (GPC) was carried out at room temperature using a Waters 410 GPC. THF was used as the eluent at a flow rate of 1 ml/min. Molecular weights were calculated using polystyrene standards.

Synthesis of PHDA

Novozyme-435 (0.96g, 5% w/w of the monomer weight), dried over P_2O_5 in a vacuum desiccator (0.1mmHg, 25 ^oC, 24h), was transferred into oven-dried 50 ml vial under an argon atmosphere, which was coppered with rubber septa and sealed with Teflon tape. The monomer 10-hydroxydecanoic acid (1.92 g) in toluene (5ml) solvent was transferred into the 50ml vial, stirring at 70 ^oC. After the reaction was terminated, enzyme was removed by filtration. The filtrate was concentrated by rotary evaporation and was poured into a large amount of methanol. The resulting precipitate was separated by filtration, following by drying in vacuum to give the polymer.

Synthesis of α- bromester terminated macroinitiator

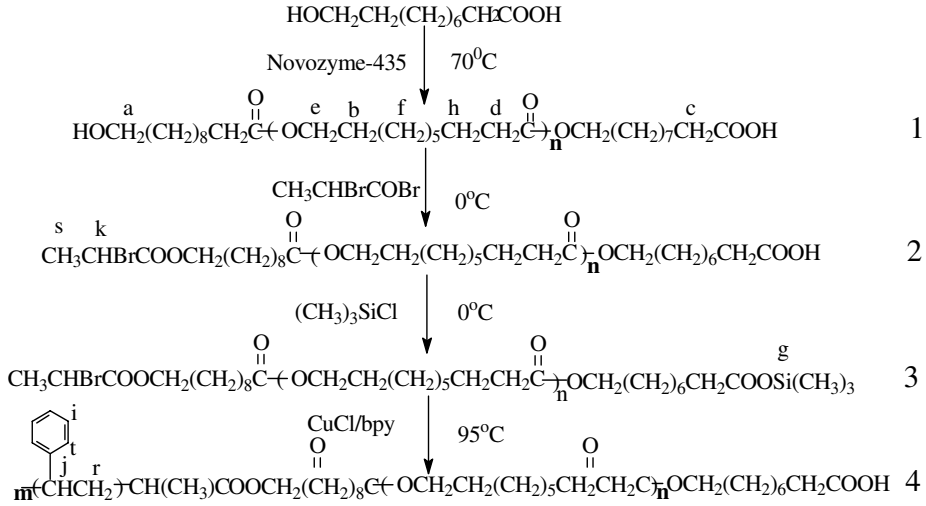
The PHDA (0.5g) was added into a vial with dry dichloromethane (5 ml). Subsequently triethylamine (1 ml) was added and cooled in an ice bath (0 °C) at the same time. After stirring for 5 min, dichloromethane (5 ml) solution containing α-bromopropionyl bromide (0.6 ml) was added dropwise to the system over a period of 0.5h. The reaction was carried out at 0 °C for 2 h and then at room temperature for 22 h. The color of the solution changed to yellow. The white precipitate was filtrated, and then large part of the filtrate was removed by rotary evaporation and precipitated in methanol.

Synthesis of chlorotrimethylsilane protected macroinitiator

The resulting macroinitiator was dissolved in dry dichloromethane (5 ml). Then triethylamine (1 ml) was added into the vial, cooled in an ice bath (0 °C) at the same time. After stirring for 5 min, dichloromethane (5 ml) solution containing chlorotrimethylsilane (0.6 ml) was dropwise added to the system over 0.5h. The reaction was carried out at 0 °C for 2 h and then at room temperature for 8 h. The white precipitate was filtrated and then large part of the filtrate was removed by rotary evaporation and precipitated in methyl ether.

ATRP of St from macroinitiator

All the different solids (0.019g CuCl, 0.091g bpy, 0.2g macroinitiator protected by chlorotrimethylsilane) were introduced into a toasted flask. A cycle of vacuum-argon was repeated three times to remove the oxygen; then the liquids (1 ml toluene, 1 ml St) were added by syringe under argon. The flask was immersed into 95 °C oil bath with sufficient stirring. After 4 hours the reaction was terminated with ice bath. The reaction mixture was dissolved in dichloromethane and filtered over alumina column to remove the catalyst, and the filtrate was poured into methanol to obtain the product.. The resulting diblock polymer was dried in a vacuum oven.



Scheme 1. The synthesis of AB-type diblock copolymer.

Results and discussion

Early reports on lipase-catalyzed synthesis by direct condensation between diacids and diols indicate the formation of low molar mass polyesters [19]. However, with the occurrence of immobilized enzyme (e.g. Novozyme-435) important progress has been made in lipase-catalyzed copolymerization of acid and alcohol building blocks to obtain higher molar mass polymer. The rational for the choice of Novozyme-435 (lipase CALB immobilized on an acrylic resin) as the catalyst has been described elsewhere [9, 11]. Based on the above reason, we used biocatalyst Novozyme-435 to carry out lipase-catalyzed condensation polymerization of HDA at 70^{o}C in toluene. In this system, Novozyme-435 catalyzed condensation of HDA gave the polyester ***1*** in 82% isolated yield, one chain end was occupied by hydroxyl and the other by carboxyl acid group.

Novozyme-435 catalyzed condensation polymerization of HDA give PHDA ***1*** as shown in ***Scheme 1***. The structure of the polymer was identified using ^{1}H-NMR experiments. In the ^{1}H-NMR spectrum （***Figure1.1***） , the appearance of the signal ***e*** at 4.10 ppm indicated the formation of the ester linkages in the polymer. The triplet signal ***a*** and ***c*** at 3.65 ppm and 2.34 ppm corresponded to the methylene protons of the terminal hydroxyl and carboxyl acid groups respectively. This clarified the formation of PHDA ***1***. Moreover, the unimodal and symmetrical shape of the trace for polymer ***1*** obtained at GPC (***Figure 2***) also proved this result. Combining GPC analysis, it was clear that the molecular weight of ***1*** (3900g/Mol) calculated form the ^{1}H-NMR spectrum (***Figure1.1***) approach to the GPC measurement (4100g/Mol), during which polystyrene was used for calibration.

The terminal hydroxyl group of the PHDA ***1*** was functionallized by α-bromopropionyl bromide to give the macroinitiator ***2*** with the terminal carboxyl acid group, which is difficult to be directly polymerized by ATRP because of interaction of the carboxylic acid functionalities with catalyst. Presumably, carboxylic acids react with Cu^{2+}species by displacing the halogen atom, resulting in the metal carboxylates, which inhibit deactivation. Additionally, since many of the ligand systems utilized in ATRP are nitrogen based, protonation of the nitrogen may occur, disrupting its coordination to the Cu center [14]. Therefore, the carboxylic acid group was functionallized by TMSCL to give the protected macroinitiator ***3*** for ATRP. In the two process triethylamine was used as the catalyst and absorbed HX (X=Br, Cl, respectively) from the solution to generate a precipitate of quaternary ammonium halide $(CH_3CH_2)_3NH^+X^-$, which benefited the esterification. The disappearance of the signal ***a*** at 3.65 ppm and appearance of the signal ***k*** and ***s*** at 4.34 and 1.8 ppm, respectively, indicated that formed macroinitiator ***2*** from ***Figure 1.2***. Because of chain end hydroxyl group was functionallized by α-bromopropionyl bromide incorporate an alkyl bromide functionality. Furthermore, in the ***Figure 1.3***, the disappearance of signal ***c*** at 2.34 ppm indicated that the terminal carboxylic acid group was protected successfully with TMSCL. The signal ***g*** at 0.02 ppm was often concealed within the signal of trimethylsilane (TMS) (internal standard of NMR). As shown in ***Figure 2***, it was interesting to note that polydispersity was usually lower than that of the starting PHDA ***1*** after the esterification reaction. On the contrary, number average molecular weight (Mn=4500g/Mol) was slightly higher. This could be due to inevitable fractionation of macroinitiator during the course of precipitation after the reaction.

The ATRP of styrene from protected macroinitiator ***3*** was carried out at 95^{o}C, using CuCl/bpy as the catalyst and toluene as the solvent. After 6h, 9% monomer conversion was reached and the final copolymer ***4*** (***Scheme 1***)with Mn of 13400 g/Mol

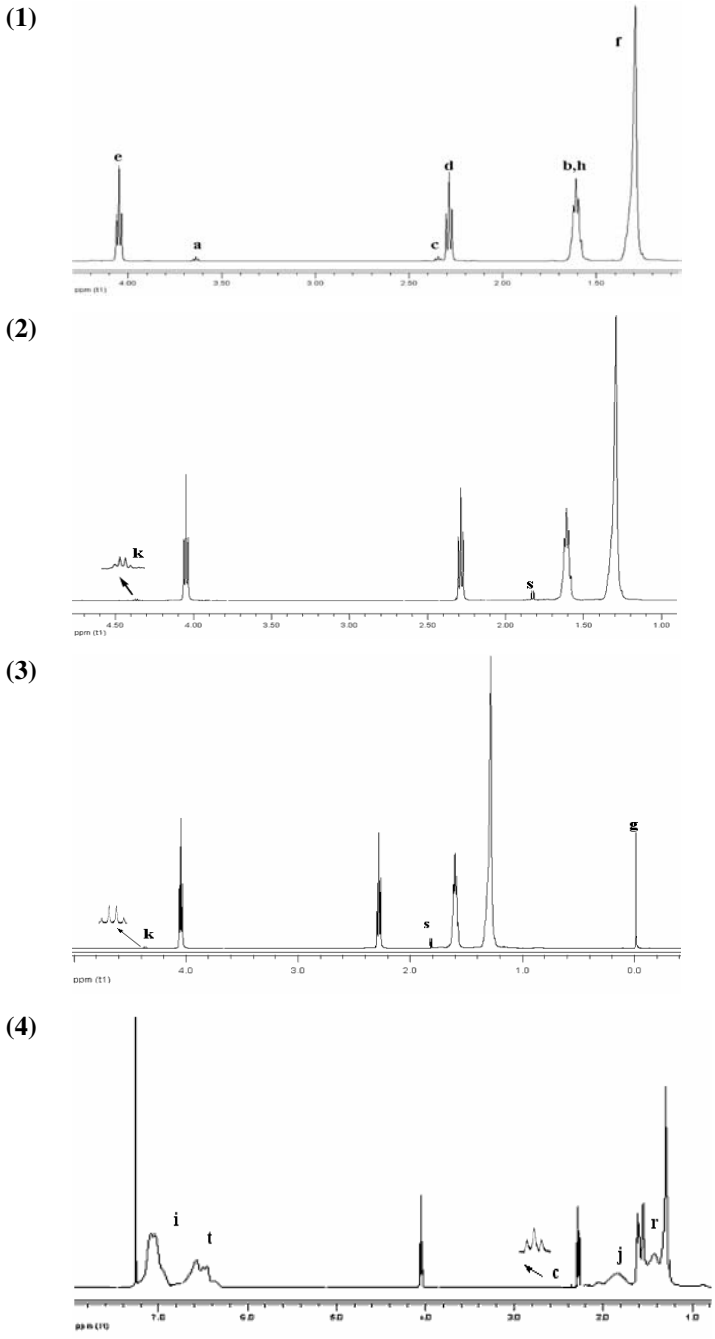


Figure 1. ^{1}**H-NMR** ($CDCl_3$) Specatra of PHDA **(1)** (3900g/Mol, Mn.nmr=($I_{4.05}/I_{3.64}$)*M_{HDA}), macroinititaor **(2)**, protected macroinitiator **(3)** and AB-type diblock copolymer PHDA-*b*-PSt **(4)** (13000g/Mol, Mn.nmr=($2I_{6.8\text{-}7.2}/I_{2.35}$)*Mst+Mn.**3**)**,** the molecular weight (Mn.nmr) were calculated form the ^{1}H-NMR integrated peak areas **I** of peak **n** (**In**), **Mz** represented the molecular weight of **Z.** The signal assignment is shown in ***Scheme 1***.

and polydispersities of 1.21 was obtained (***Figure 2***). Furthermore, the TMS groups were hydrolyzed in the process of diblock copolymer precipitates in methanol without a purposely deprotected course[20]. The conversion was determined gravimeterically, the GPC traces of the starting PHDA ***1***, macroinitiator ***3*** and the final block copolymer ***4*** were shown in ***Figure 2***. It was clear that the ATRP of styrene using macroinitiator ***3*** resulted in an increase in molecular weight and a decrease in polydispersity. From the ^{1}H-NMR spectra of the diblock copolymer ***4*** (***Figure 1.4***), the signal at 6.5-7.0 ppm corresponding to aromatic protons ***i*** and ***t*** of the PSt block suggest the formation of the block copolymer (PHDA-*b*-PSt). Moreover, Mn (13400g/Mol) determined by GPC was in good agreement with the theoretical one (13000g/Mol) calaulated from NMR (***Table 1***).

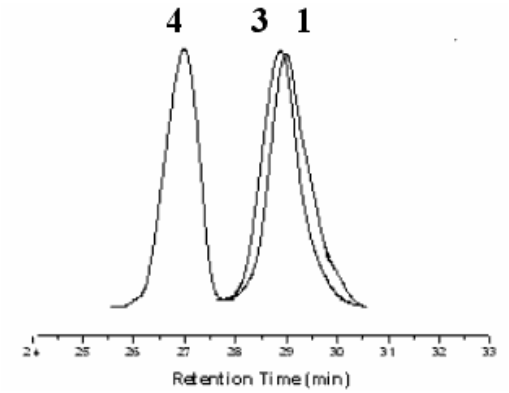


Figure 2. GPC traces of enzymatically polymerized PHDA ***1*** (4100g/Mol, PDI=1.45), macroinitiator ***3*** (4500g/Mol, PDI=1.28) and AB-type diblock copolymer ***4*** (13400g/Mol, PDI=1.21). The molecular weight and polydispersities (PDI) were by GPC calibrated with polystyrene.

Table 1. The results of PHDA ,Macrointiator and dibock copolymer

PHDA	t(h)	Mn.nmr[a]	Mn.GPC[b]	Mw/Mn[b]	Yield(%)
1	36	3900g/mol	4100g/mol	1.45	82
Macroinitiator		mol% Degree of end functionalization[a]	Mn.GPC[b]	Mw/Mn[b]	Yield(%)
3		98%	4500g/mol	1.28	90
Copolymer	t(h)	Mn.nmr[a]	Mn.GPC[b]	Mw/Mn[b]	HDA/St[c]
4	6	13000g/mol	13400g/mol	1.21	23/91

a. determined by 1H-NMR analysis; b. determined by GPC measurement; c. the degree of polymerization of PHDA/PSt caculated from the by 1H- NMR spectrum.

Conclusions

By combining enzymatic condensation polymerization of HDA and ATRP of St, the synthesis of block copolymers had been demonstrated. PHDA was prepared by

lipase-catalyzed condensation polymerization of HDA in the presence of Novozyme 435. Both terminals of the PHDA chain were functionalized by the esterification of the resulting polymer with α-bromopropionyl bromide and chlorotrimethylsilane, respectively, to obtain macroinitiator for subsequent ATRP. The unimodal and symmetrical shape of the trace at GPC and the structure determined by ^{1}H-NMR confirmed the successful synthesis of the diblock copolymer PHDA-*b*-PSt.

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