

Polymer Communication

Melt/solid polycondensation of glycolic acid to obtain high-molecular-weight poly(glycolic acid)

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Abstract

Bulk polycondensation of glycolic acid (GA) was studied to obtain high-molecular-weight poly(glycolic acid) (PGA). At first, a solid oligocondensate was prepared by melt-polycondensation of GA at 190°C, and then it was subjected to solid-state polycondensation at the same temperature to increase the molecular weight. After the catalyst screening, zinc acetate dihydrate was discovered to be the best catalyst. The weight-average molecular weight of PGA reached 91,000, which was at the same level with that of PGA prepared by the conventional ring-opening polymerization of glycolide. This process can afford a facile route to large-scale synthesis of PGA. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Polymer synthesis; Poly(glycolic acid); Polycondensation

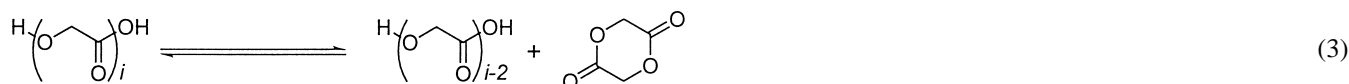
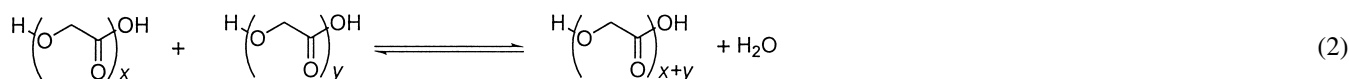
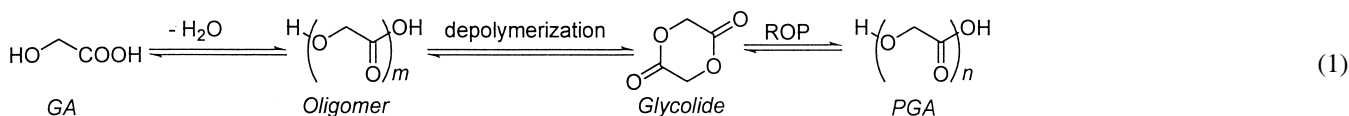
1. Introduction

Poly(α -hydroxy acid)s are a group of aliphatic polyesters that are now attracting great attention as biodegradable polymers having wide applications [1]. These polymers can be assimilated into water and carbon dioxide in the natural environment and microorganisms. In particular, poly(glycolic acid) (PGA) and its copolymers have been most widely used as biomedical materials such as absorbable suture [2].

PGA is usually synthesized by ring-opening polymerization of glycolide that is a cyclic diester monomer prepared from glycolic acid (GA) via an oligomer Eq. (1) [3].

In this process, exhaustive purification of glycolide is needed to obtain high polymers to make the PGA products more expensive. For easier synthesis of PGA, simple polycondensation of GA should be established, although it has been believed to be an inadequate method to obtain high polymers [4]. In the polycondensation system of PGA, two principal equilibrium reactions exist. One is dehydration equilibrium for esterification Eq. (2), and the other is ring-chain equilibrium involving depolymerization to glycolide Eq. (3).

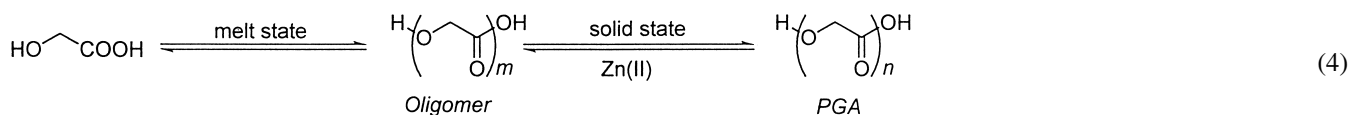
Ordinary melt polycondensation of GA gives a low-molecular-weight oligomer, which likely decomposes into glycolide to prevent the chain-growth of PGA. This is because the



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reaction conditions of high temperature and high vacuum can induce not only dehydration, but also the formation of glycolide in equilibrium with PGA. One possible way to

obtain high polymer of PGA is to use catalysts that can enhance the dehydration rate of oligomer without stimulating its depolymerization to glycolide. In this study, we disclose a new method of polycondensation of GA which can be promoted by the catalysis of Zn(II) and by the polymer crystallization in solid state Eq. (4).



2. Experimental

2.1. Materials

GA was purchased from Nacalai Tesque (Kyoto, Japan). 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) was supplied by Central Glass Co. Ltd (Tokyo, Japan). Nafion[®] NR-50 was a product of Du Pont Co. SnO was prepared by alkaline hydrolysis of SnSO₄ [5]. Other reagents were commercially obtained. A commercial PGA sample, which was prepared by the ring-opening polymerization of glycolide, was supplied by Mitsui Chemical Corp. (Tokyo). Its number-average (M_n) and weight-average molecular weights (M_w) were 45,000 and 93,000 Da, respectively.

2.2. Measurements

The molecular weights were determined by gel permeation chromatography (GPC). The analyzer was made up of a Shimadzu LC-10ADvp pump, a Shimadzu RID-10A RI detector, and a Shimadzu C-R7A Chromatopac data processor. A combination of two styrene–divinylbenzene copolymer gel columns of Shodex HFIP 804 and 806 (8.0 mm × 300 mm, each) was used with HFIP containing 1 mM sodium trifluoroacetate as the eluent at 40°C. The molecular weight was calibrated according to poly(methyl methacrylate) (PMMA) standards. Differential scanning calorimetry (DSC) of the polymeric products was performed on a Mac Science DSC-3100 thermal analyzer at a heating rate of 10°C/min, and α -alumina was used as the reference sample. The first heating of PGA samples showed a sharp melting endotherm at 220°C (T_m) and an inflection point at 40°C (T_g). The crystallinity of PGA was determined by the heat of fusion measured by the former endotherm in reference to its molar heat capacity of 11 kJ/mol [6]. In the cooling scan, a sharp exothermic peak due to the crystallization of the PGA melt was detected at 188°C.

2.3. Polycondensation of GA

In a typical run, a 50.0 g amount of GA was weighed into a 200 mL reaction flask equipped with a magnetic stirrer. Then, a catalyst of an amount of 0.2 or 0.5 wt% relative to GA was added to it. The mixture was heated at 190°C with stirring, first at a reduced pressure of 150 mmHg for 1 h and

then at 30 mmHg for another 4 h. During this reaction the polymerization system turned from liquid to solid. In the next step, the reaction was continued by two procedures. In Procedure A, the condensation product formed (oligomer state) was crushed into powder in a nitrogen atmosphere, and the powder was heated in solid state with stirring at

190°C for 20 h. In Procedure B the condensation product was melted at 230°C for mixing and cooled down to 190°C. The product solidified again was heated at 190°C for 20 h. PGA samples obtained by these procedures were analyzed by DSC and GPC.

3. Results and discussion

When the polycondensation of GA was conducted above 200°C, the condensation product quickly became dark in color probably because of its thermal decomposition. When the same reaction was done below 180°C, the molecular weight (M_w) of the condensation product did not increase above 20,000 Da in spite of being free from discoloration. These data limited us to conduct the polycondensation around 190°C that was around the crystallization temperature (T_c) of PGA. In the early stage of the polycondensation of GA, the condensation product solidified in the flask. This solid product was a PGA oligomer with a M_w less than 10,000 Da. When this was heated to 220–230°C, serious discoloration accompanied. Therefore, the polycondensation of the intermediate oligomer was continued at 190°C in solid state by two ways. In Procedure A, the first-formed oligomer was crushed into powder, and then the reaction was continued at 190°C. In Procedure B, the oligomer was melted at 230°C for a short time and cooled to 190°C, and the reaction was continued in solid state again. The fusion was for the homogenization of the reaction system.

Table 1 summarizes the typical results of the melt/solid polycondensation of GA with various catalysts. The amount of catalysts relative to GA was 0.2 wt% for the soluble ones and 0.5 wt% for the insoluble ones. The molecular weight of the polycondensates was comparable when the soluble tin chloride and the insoluble tin oxide were used as the catalyst (Run No. 1 and 3). With the same catalyst, Procedure B surpassed A in terms of increase in molecular weight of the product (Run No. 3 and 6 or 5 and 11). Nafion[®] NR-50, a solid organic acid containing sulfonic acid, was less effective in polycondensation. Binary catalysts consisting of tin chloride and proton acids were also examined, because they were recently found to be effective for the melt polycondensation of L-lactic acid [7]. In the presence of

Table 1

Results of the melt/solid polycondensation of GA with various catalysts (cf. A commercial PGA (light brown) had $M_n = 49,000$, $M_w = 93,000$, and $M_w/M_n = 1.9$)

Run no.	Procedure ^a	Catalyst (Type) ^b	M_n (Da) ^c	M_w (Da) ^c	M_w/M_n ^c	Appearance	Crystallinity (%) ^d
1	A	SnO (I)	26,000	45,000	1.7	Light brown	39
2	A	SnO + (HPO ₃) _n ^e (I)	24,000	41,000	1.7	Light brown	38
3	A	SnCl ₂ (S)	24,000	48,000	2.0	Light brown	40
4	A	Zn(CH ₃ CO ₂) ₂ (I)	20,000	39,000	2.0	White	34
5	A	Zn(CH ₃ CO ₂) ₂ ·2H ₂ O(I)	24,000	44,000	1.8	White	40
6	B	SnCl ₂ (S)	29,000	57,000	2.0	Light brown	39
7	B	SnCl ₂ + MsOH ^f (S)	24,000	48,000	2.0	Brown	31
8	B	SnCl ₂ + (HPO ₃) _n ^e (S)	20,000	46,000	2.3	Light brown	27
9	B	Nafion [®] NR-50 (I)	23,000	43,000	1.9	Milky white	23
10	B	Zn(CH ₃ CO ₂) ₂ (I)	22,000	47,000	2.1	Brown	33
11	B	Zn(CH ₃ CO ₂) ₂ ·2H ₂ O (I)	45,000	91,000	2.0	Brown	33

^a In Procedure A, first formed oligomer was crushed into powder in a nitrogen atmosphere, which was heated at 190°C for 20 h. In Procedure B, the oligomer was melted by heating at 230°C for some time for mixing and then heated at 190°C for 20 h.

^b I; insoluble catalyst (0.5 wt% of GA), S; soluble catalyst (0.2 wt% of GA).

^c Determined by GPC (eluent: HFIP containing 1 mM sodium trifluoroacetate) relative to PMMA standards.

^d Determined by DSC.

^e Metaphosphoric acid; 33 mol% relative to SnO or SnCl₂.

^f Methanesulfonic acid; 100 mol% relative to SnCl₂.

methanesulfonic acid (Run No. 7) and metaphosphoric acid (Run No. 8), however, the molecular weight of the products became lower than that obtained with the simple tin chloride and oxide catalysts. The highest molecular weight of $M_w = 91,000$ was obtained with zinc acetate dihydrate that was insoluble in the reaction system (Run No. 11). This molecular weight is almost identical with that of the commercially available PGA that is prepared by the conventional ring-opening polymerization of glycolide. Anhydrous zinc acetate was not so effective as its hydrate with regard to the increase in molecular weight by both Procedures A and B.

Fig. 1 shows typical GPC curves of the PGA samples that were prepared with tin oxide, tin chloride, and zinc acetate dihydrate as the catalysts (by Procedure B) as compared with the curve of the commercially available PGA. Each sample showed a small shoulder peak at relatively long elution time because of the involvement of a small amount of oligomer. The amount of oligomer was smaller in the polymer prepared with zinc acetate dihydrate than in the commercially available PGA.

As we previously reported on the solid-state post-polymerization of L-lactide [8], crystallization of the polymer segments can induce concentration of the monomers, polymer tails, and catalyst in the amorphous regions to drive the ring-chain equilibrium in the direction of polymer formation. In this case, the polymerization temperature should be set near the crystallization temperature for the polymer to crystallize as much as possible. This idea was successfully applied to the present solid-state polycondensation of the PGA oligomer, because the crystallization of the polymer segments can induce similar concentration of the polymer tails and their dehydrative condensation. In fact, by Procedure A, the molecular weight was known to increase with increasing crystallinity of the PGA products. By Procedure B also, an identical tendency was observed except the runs with zinc acetate dihydrate as the catalyst for which the crystallinity of the PGA product was slightly lower in spite of the large molecular weight increase. Probably, the polymer/catalyst interaction may have inhibited crystallization of PGA in the heterogeneous catalyst system. The higher catalytic activity of zinc acetate dihydrate over anhydrous zinc acetate may be attributed to the least aggregation of the metal ion sites around which both the carboxyl and hydroxyl tails can coordinate and react. In addition to it, the

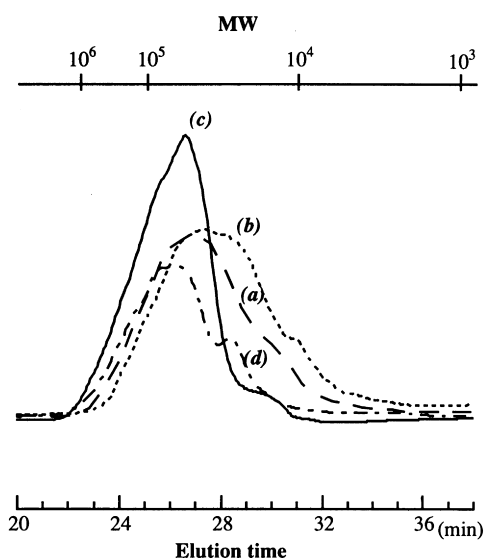


Fig. 1. Typical GPC curves of the PGA samples of Run No.: (a) 6; (b) 9; and (c) 11; and the commercial PGA sample (d).

aqua ligands existing in the surface of the clustering zinc acetate dihydrate can readily be substituted by the polymer tails to afford reactive catalytic sites for dehydration. The polymer tails can also react with the catalyst in higher degree in the melt-mixing stage of Procedure B than in the pulverizing stage of Procedure A, and the chain extension at the segment crystallization of PGA is more highly induced in the former procedure. Further study is necessary for a deeper knowledge of this condensation mechanism.

4. Conclusion

PGA was prepared by the melt/solid polycondensation of GA. This dehydrative polycondensation was discovered to be effectively catalyzed by zinc acetate dihydrate. The weight-average molecular weight of PGA reached 91,000 that was similar to that of PGA prepared by the ring-opening polymerization of glycolide. This synthetic method will give a simple manufacturing process for making PGA and its copolymers.

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