

NOTE

Synthesis, Characterization, and Degradation of α -Amino acid Containing Polyamides

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INTRODUCTION

α -Amino acid-containing polyamides have been investigated interestingly, since the incorporation of α -amino acid into polyamides is expected to lead to biodegradable and biocompatible materials. The physical properties of polyamides could also be modified greatly according to the α -amino acid side group. An alternative nylon 6 copolymer with glycine was reported to be degraded by both fungi and bacteria.^{1,2} Nylons 6 and 66 copolymers with various α -amino acids were prepared by melt polycondensation and it was shown that biodegradability was enhanced with increasing α -amino acid content.³⁻⁷ Recently, an alternative copolyamide of nylon 11 and L-alanine was reported to be degraded by papain as a proteolytic enzyme.⁸

In the present study, various polyamides consisting of terephthalic acid, 1,6-diaminohexane, and α -amino acids such as glycine, alanine, leucine, and phenylalanine were prepared via diaz lactones shown in Scheme 1. The effect of the kind of these α -amino acids on the physicochemical and thermal properties as well as preliminary degradation behavior of polymers was examined.

EXPERIMENTAL

Materials

The α -Amino acids (glycine, L-alanine, L-leucine, and L-phenylalanine) used in this study are shown in

Scheme 1 and were commercially available and used without further purification. Chloroform was purified by distillation. Terephthaloyl chloride was recrystallized from chloroform. 1,6-Diaminohexane was purified by vacuum distillation. Other chemicals were used as received.

Preparation of Terephthaloyl Bis(α -amino acid) (I)⁹

A solution of 50-mmol terephthaloyl chloride in 50-mL dioxane was added to a magnetically stirred ice-cooled vessel containing 110 mmol of α -amino acid and 5 g of magnesium oxide in 75 mL of water over 2 h. After the addition of terephthaloyl chloride was complete, stirring was continued for 30 min at room temperature. The concentrated hydrochloric acid was added to the reaction vessel until a pH of 1–2 was obtained. The precipitated product was filtered and washed with boiling water.

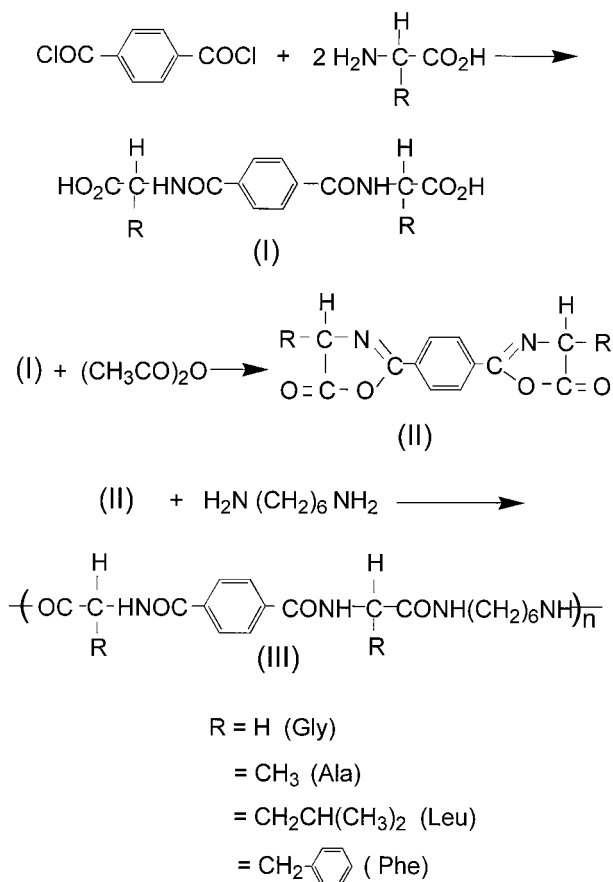
Gly, 72% yield, mp 254–258°C; Ala 71%, 290–295°C; Leu 61%, 260–263; Phe, 84%, 225–226°C.

Preparation of Diazlactone (II)⁹

Twenty milliliters of acetic anhydride (200 mmol) was heated on a hot plate to near boiling. Terephthaloyl bis(α -amino acid) (I), 5 mmol, was then added rapidly, and the reaction mixture was agitated magnetically and maintained near the boiling point for 10 min. The reaction mixture was rapidly cooled in an ice bath. The precipitated crystals were filtered and recrystallized from either benzene (Ala, 43% yield, mp 190–191°C;

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Scheme 1 Reaction scheme of α -amino acid-containing polyamides.

Leu, 60%, 167–168°C; Phe, 57%, 179–180°C) or dioxane (Gly, 62% yield, mp 240–242°C).

ANAL: Calcd for Gly: C, 59.01%; H, 3.31%; N, 11.47%. Found: C, 58.86%; H, 3.45%; N, 11.63%. Calcd for Ala: C, 61.75%; H, 4.45%; N, 10.29%. Found: C, 61.95%; H, 4.58%; N, 10.33%. Calcd for Leu: C, 67.34%; H, 6.87%; N, 7.86%. Found: C, 67.65%; H, 6.98%; N, 8.03%. Calcd for Phe: C, 73.56%; H, 4.76%; N, 6.60%. Found: C, 73.72%; H, 4.83%; N, 6.70%.

Preparation of (III)¹⁰

Diazlactone of (α -amino acid) (II), 2 mmol, was dissolved in 15 mL of chloroform. 1,6-Diaminohexane solution, 2 mmol, dissolved in 5 mL of chloroform was rapidly added to the diazlactone solution under vigorous swirling. After 1 h at the room temperature, the polymer was warmed for 15 min in a water bath. Then, the polymer was filtered from the vessel and dried *in vacuo* at 80°C for 24 h. Hereafter, polyamides III are called

Gly, Ala, Leu, and Phe, respectively, according to polymer code, as shown in Scheme 1.

Characterization

The inherent viscosity was determined with a 0.5% polymer concentration in *m*-cresol at 30°C. Infrared spectra (IR) were recorded on a Shimadzu Model IR-408 spectrophotometer. Wide-angle X-ray scattering (WAXS) was performed with a Rigaku Denki Model RAD-IA X-ray diffractometer with nickel-filtered CuK α radiation. Differential thermal analysis (DTA) was carried out on a Shimadzu DT-30 differential thermal analyzer at a heating rate of 10°C/min in a stream of nitrogen and thermogravimetry (TG) was performed with Shimadzu DT-30 thermogravimetric analyzer at a heating rate of 10°C/min in a stream of nitrogen. Density was determined using a small pycnometer in absolute ethanol at 30°C. The sample size was ca. 100 mg.

In Vitro Degradation

The hydrolysis of polyamides was carried out by using α -chymotrypsin as a proteolytic enzyme in a 1/15-mol phosphate buffer solution (pH 7.2). α -Chymotrypsin (48 unit/mg) was obtained from Sigma (USA) and used as received. A 100-mg powder sample whose particle size is less than 0.3 mm was placed in small bottle containing a 10 mL buffer solution with 10 mg of α -chymotrypsin. The bottle was then incubated at 37°C for various times with shaking. After the reaction, the substrate was recovered by filtration, washed thoroughly with water, and dried at 80°C *in vacuo* to a constant weight. The degradation was determined by the weight loss of the mass and/or by decrease of the inherent viscosity.

RESULTS AND DISCUSSION

It was difficult to prepare α -amino acid-containing polyamides in this work by melt polycondensation, since they degraded during polycondensation and yielded a deeply colored solid. So, the polyamides were synthesized from α -amino acid via diazlactone according to the procedure described in the literature^{9,10} and outlined in Scheme 1. Table I summarizes the results of polycon-

Table I Yields and Inherent Viscosities (η_{inh}) of Polyamides

Polymer Code	Yield (%)	$\eta_{\text{inh}}^{\text{a}}$ (dL/g)
Gly	83	0.39 ^b
Ala	95	0.75
Leu	94	0.68
Phe	96	0.83

^a 0.5% *m*-cresol solution at 30°C.

^b 0.5% dichloroacetic acid at 30°C.

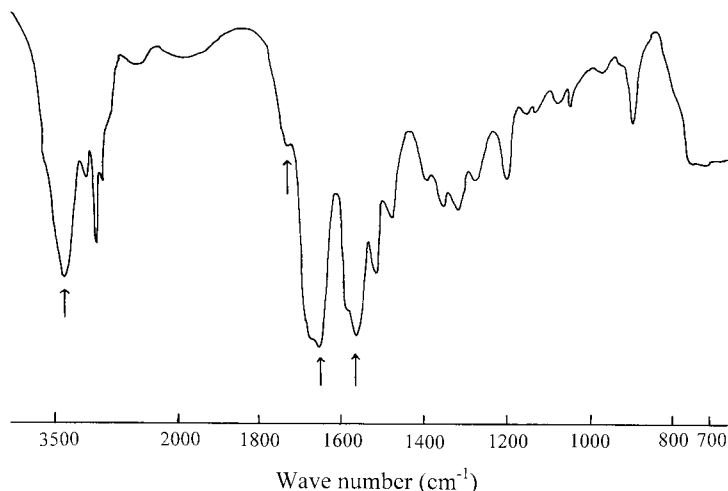


Figure 1 Infrared spectrum of alanine-containing polyamide.

denation. The polyamides having an inherent viscosity of 0.39–0.83 were obtained in excellent yield. The structures of the resulting polymers were confirmed by elemental analysis and infrared spectra (IR). Elemental analysis agreed well with the expected values. Figure 1 shows the IR spectra of Ala. The absorptions due to N—H stretching, C=O stretching (amide I), and N—H bending (amide II) stretched at 3300, 1650, and 1540 cm^{-1} , respectively. The absorption due to the α -amino acid moiety also appeared at 1725 cm^{-1} .⁵ These characteristic absorptions appeared for all the polyamides prepared. Ala, Leu, and Phe were soluble in conventional nylon solvents such as formic acid, *m*-cresol, and DMF and formed transparent, tough, and flexible films by casting from the DMF solution, while Gly was insoluble in these solvents and only soluble in dichloroacetic acid and could not form film by casting from this solution, probably due to the lower solution viscosity.

Figure 2 shows X-ray diffraction intensity curves for polyamides as polymerized. Gly shows a sharp crystalline pattern, while Ala, Leu, and Phe show amorphous patterns, implying that side groups of α -amino acids hinder the crystallization of the polymer chains. It is interesting that two broad but strong diffraction peaks appeared for Leu and Phe, suggesting the formation of a some ordered structure owing to the regular arrangement of both "head-to-tail" and "tail-to-tail" amide groups. The degree of this ordering seems to become lower for Ala, probably due to the smaller side group.

The densities of polyamides were 1.39, 1.31, 1.28, and 1.22 g/cm^3 for Gly, Ala, Leu, and Phe, respectively. The higher density of Gly may be ascribed to the higher crystallinity shown in Figure 2. The density of polyamides decreases with increasing the size of the side group in α -amino acids, implying that packing of the molecular chain is more disturbed by the more bulky side groups.

Figure 3 shows DTA curves of polyamides as polymerized. All the polyamides show a glass transition

temperature (T_g) and a melting temperature (T_m). The cold crystallization temperature appeared for Gly. The T_g 's of these polymers are in the range of 151–182°C. Leu and Phe showed higher T_g values than those of Ala, which could be ascribed to the chain stiffening due to the increase in the rotational energy barrier caused by the more bulky side groups. Gly shows a much higher T_g , reflecting the higher crystallinity shown in

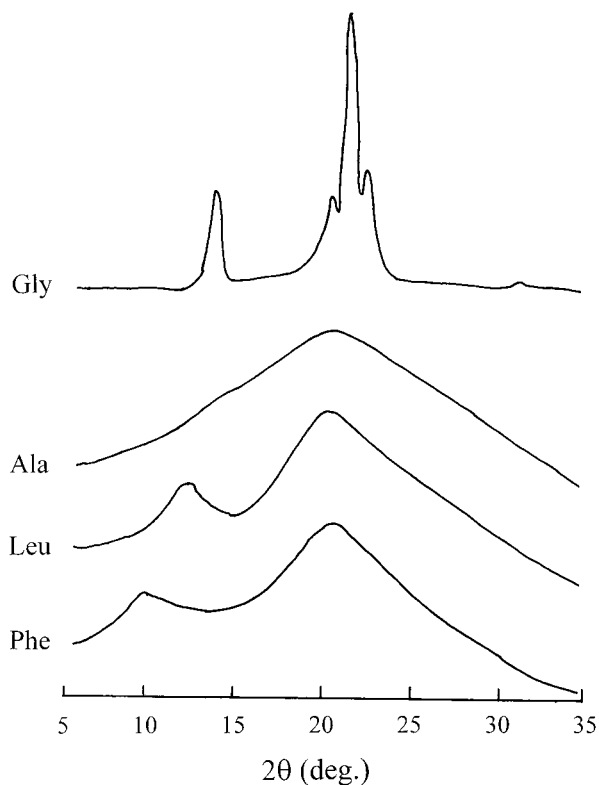


Figure 2 X-ray diffraction intensity curves of α -amino acid-containing polyamides.

Figure 2. Ala, Leu, and Phe melt at a lower temperature than does Gly, suggesting that the crystal growth is disturbed by bulky side groups that interfere with the hydrogen bonding between the polymer chains. The TG curves showed that decomposition starting temperatures (10% weight loss temperature) of polyamides were in the range of 320–330°C.

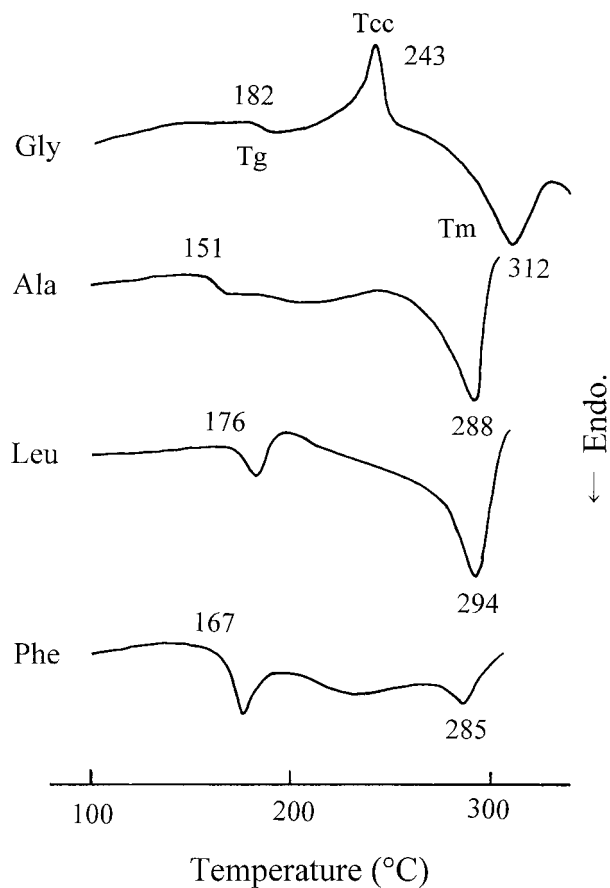


Figure 3 DTA curves of α -amino acid-containing polyamides.

The preliminary degradation test of polyamides was carried out in a phosphate buffer solution with α -chymotrypsin at 37°C. Practically no weight loss was observed for all polyamides after a 4-day incubation with α -chymotrypsin, although there were some weight losses due to a dissolution of the oligomers. The inherent viscosity was also hardly decreased for Gly, Leu, and Phe. These results reveal that Gly, Leu, and Phe are stable against enzymatic degradation. On the other hand, the inherent viscosity of Ala decreased from 0.72 to 0.43 after a 4-day incubation with α -chymotrypsin, suggesting that amide linkages in Ala could be hydrolyzed by α -chymotrypsin. However, these degradation tests are only preliminary. Further work concerning the biodegradability of these polyamides is currently in progress.

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