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Thermoplastic polyester amides derived from oleic acid

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ABSTRACT

Three lipid-based Polyester Amides (PEAs) with varying ratios of ester and amide linkages were synthesized. Oleic acid was used as the starting material to produce the intermediates, characterized by MS and NMR, used for polymerization. PEAs were characterized by FTIR and GPC. The PEAs were constrained to have similar number average molecular weights, in the 2×10^4 range, thereby enabling comparison of their physical properties from a structural perspective. The thermal behavior of the polymers was assessed by DSC, DMA and TGA. Thermal degradation was not affected by ester/amide ratios, but T_g increased non-linearly with decreasing ester/amide ratios and correlated with hydrogen-bond density and repeating unit chain length. Crystallinity was studied by XRD and DSC. Degree of crystallization and multiple melting behavior as a function of cooling kinetics were explained well by hydrogen-bond density, repeating unit chain length and density of ester moieties. Mechanical properties were investigated by DMA and Tensile Analysis, with a non-linear increase of storage and tensile moduli recorded as a function of decreasing ester/amide ratios. The findings suggest how approaches to the synthesis of lipid-based PEAs can be targeted to the delivery of specific physical properties.

1. Introduction

Polyester amides (PEAs) have been extensively studied for several years; because they generally demonstrate desired properties of both polyesters and polyamides [1]. PEAs are mainly developed from three building blocks: amino acids, diols and diacyl chlorides [2–5]. Polyamides generally demonstrate preferred mechanical and processing properties, such as thermal stability, tensile strength and biocompatibility, but are generally not biodegradable [6]. Polyesters demonstrate varying degrees of biodegradability; however, lack of the preferred physical properties demonstrated for example by polyamides limits their applications. Therefore when these two different types of linkages are combined in the main chain of one single polymer, the biodegradability caused by the ester linkage and the enhanced thermal and mechanical properties caused by amide-induced intermolecular hydrogen bonds can be combined in one polymer [7], giving rise to a superior material which could be applied in a wide variety of areas.

Biomedical applications is one of the most important areas to which PEAs have generally been applied; this includes absorbable surgical materials, tissue engineering materials as well as carriers in drug delivery systems [4,6]. Most of today's plastics and polymeric materials are made from petroleum-based products. However, in the last few years, environmental issues and concerns have drawn significant attention to petroleum-based products, especially in polymeric materials. Petroleum-based polymers are generally non-degradable, and are implicated in the pollution of the natural environment. Petroleum is also regarded as a finite and dwindling resource. The desire to obtain various products from non-toxic natural resources, and use bio-based renewable products as alternatives for the petroleum-based products is increasing in our society [8–17].

Several investigations have been conducted on producing PEAs from bio-based sustainable resources, such as linseed oil, nahar seed oil and pongamia glabra oil [18–20]. However, the building blocks chosen to connect the lipid-based monomers were not from natural resources, and were mostly toxic. The toxicity of these PEAs limits their applications and motivates the development of alternative building blocks. Several other fatty acid-based PEAs were studied and synthesized from sustainable resources; however, the fatty acid chosen, e.g., gallic acid [21], was much less abundant than oleic acid.

This present study is targeted at the development of lipid-based polymers that would be tough, thermally stable and biodegradable, yet be safe to use in a wide variety of areas. In particular, introducing amide units to enhance the material's cohesion thorough

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hydrogen bonding is proposed. In order to understand the structure–property relationship and assess any underlying trend, three PEAs with different ratios of ester to amide groups, i.e., 1:1 (PEA (I)), 1:2 (PEA (II)) and 1:3 (PEA (III)) were prepared. The lipid-based, non-toxic components, oleic acid-derived diol, amino acid and azelaoyl chloride (also derived from oleic acid) were chosen as the building blocks of the new polymeric materials. Furthermore, the synthesis procedures were simple and performed under mild conditions. The PEA samples were synthesized with similar number average molecular weights, in the 2.08×10^4 to 2.26×10^4 range, to enable comparison of their physical properties. Wide angle X-ray diffraction (WAXD), DSC, TGA, DMA and tensile techniques were used to investigate the crystal structure, and thermal and mechanical properties of the polymers.

2. Experimental

2.1. Materials

All reagents, Oleic Acid (90% purity), Potassium hydroxide (KOH), Potassium permanganate ($KMnO_4$), Lithium aluminum hydride ($LiAlH_4$), 1,3-propane diol, 4-(Dimethylamino) pyridine (DMAP), N, N′-Dicyclohexylcarbodiimide (DCC), sodium borohydride ($NaBH_4$), Boc-Ala-OH (N-tert-butoxycarbonyl protected alanine), Trifluoroacetic acid (TFA), Azelaoyl chloride, N-methyl-2-pyrrolidone (NMP), and propylene oxide, were purchased from Sigma–Aldrich.

2.2. Synthesis of diols from oleic acid

2.2.1. 1,9-Nonanediol

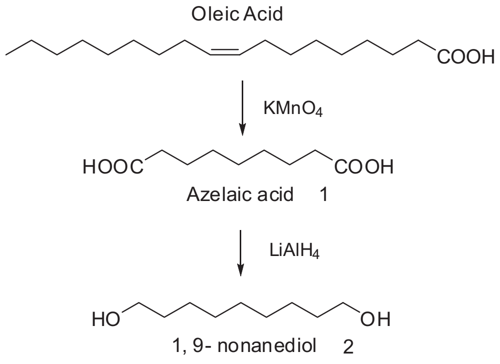
1,9-Nonanediol was synthesized by a two-step procedure, starting from oleic acid (Scheme 1). First $KMnO_4$ was used to oxidize the double bonds of the oleic acid, forming azelaic acid, following procedures in the literature [22] (Yield: 80%). 1,9-Nonanediol was then prepared according to the literature by reducing the azelaic acid with $LiAlH_4$ [23] (Yield: 88%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.67–3.62 (t, 4H, $C\underline{H}_2OH$), 1.59–1.55 (m, 4H, $C\underline{H}_2CH_2OH$), 1.32 (m, 10H, $C\underline{H}_2$). MS (ESI): calcd for $C_9H_{20}O_2$ 160.15, found m/z 183.0 ($[M + Na]^+$).

2.2.2. Di-ester diol

Di-ester diol was synthesized by a two-step procedure as shown in Scheme 2.

Step 1. 1, 3-propane diol (7.6 g, 0.1 mol) and oleic acid (69 g, 90% purity, 0.22 mol) were dissolved in 200 mL of dichloromethane (DCM) in a round bottom flask. The reaction mixture was kept at 0 °C using an ice bath. DMAP (3.6 g, 0.03 mol) was added, followed by adding DCC (49.4 g, 0.24 mol) slowly to the reaction mixture. The ice bath was removed and the reaction was stirred at room temperature for 24 h. The resulting mixture was filtered to remove the solid. The crude products were collected by evaporating DCM under vacuum. Column chromatography was used to purify the product (hexane/ethyl acetate 30:1) (Yield: 88%).



Scheme 1. 1, 9-Nonanediol from oleic acid.

Step 2. Di-ester 3 (30.2 g, 0.05 mol) was dissolved in 300 mL of anhydrous ethanol in a three-necked round bottom flask and cooled to −20 °C using an ice salt bath. Ozone was bubbled into the solution with a flow rate of 5 L/min. The reaction was monitored by thin layer chromatography (TLC) until the starting material was gone. After the reaction, nitrogen was purged through the mixture for 20 min to remove the extra ozone in the flask. Next, 3.8 g $NaBH_4$ (0.1 mol) was slowly added into the ozonolysis mixture. The reaction was stopped after 4 h, and then water and dilute hydrochloride acid were added into the reaction mixture to eliminate the extra $NaBH_4$. The resulting mixture was extracted by 2 × 200 mL of ethyl acetate. The ethyl acetate phase was washed by brine, and dried over Na_2SO_4. The crude products were collected by removing the solvent under vacuum. The desired product was purified by recrystallization using ethyl acetate and hexanes with a ratio around 1:3 (Yield: 72%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 4.16–4.12 (t, 4H, $C\underline{H}_2OCOR$), 3.64–3.61 (t, 4H, $C\underline{H}_2OH$), 2.31–2.27 (t, 4H, $C\underline{H}_2COOR$), 1.99–1.93 (m, 2H, $C\underline{H}_2CH_2OCOR$), 1.63–1.52 (m, 8H, $C\underline{H}_2CH_2COOR$ and $C\underline{H}_2CH_2OH$), 1.36–1.27 (m, 16H, $C\underline{H}_2$). MS (ESI): calcd for $C_{21}H_{40}O_6$ 388.28, found m/z 411.3 ($[M + Na]^+$).

2.2.3. Tetra-ester diol

Tetra-ester diol was synthesized by a two-step procedure as shown in Scheme 3. First, tetra-ester 5 was synthesized by reacting the di-ester diol and oleic acid (Yield: 86%); the esterification reaction between diol and oleic acid has been described in the synthesis procedure of di-ester 3. Then tetra-ester diol was synthesized by breaking the double bonds and changing them to hydroxide groups, using ozonolysis and $NaBH_4$. This reaction has been described in the synthesis of di-ester diol 4 (Yield: 50%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 4.17–4.03 (m, 8H, $C\underline{H}_2OCOR$), 3.66–3.61 (t, 4H, $C\underline{H}_2OH$), 2.32–2.26 (t, 8H, $C\underline{H}_2COOR$), 1.99–1.94 (m, 2H, $ROCOCH_2C\underline{H}_2CH_2OCOR$), 1.61–1.53 (m, 24H, $C\underline{H}_2CH_2COOR$ and $C\underline{H}_2CH_2OH$), 1.32–1.28 (m, 24H, $C\underline{H}_2$). MS (ESI): calcd for $C_{39}H_{72}O_{10}$ 700.51, found m/z 723.8 ($[M + Na]^+$).

2.3. Polymerization

2.3.1. Syntheis of diamines

Because three polymers were synthesized in this study, a general synthesis procedure to prepare polymers is shown in Scheme 4 and described as follows. First, a selected diol (10 mmol) and Boc-Ala-OH (22 mmol) were dissolved in DCM in a round bottom flask. The flask was kept at 0 °C in an ice bath. DMAP (3 mmol) was then added to the mixture. DCC (24 mmol) was slowly added over 30 min. The ice bath was removed and the reaction was stirred at room temperature for 24 h, and the resulting mixture was then filtered. The crude products were collected by removing DCM under vacuum. Column chromatography was used to purify the product.

TFA was added drop wise to this product in DCM in a round bottom flask. The reaction was stirred at room temperature until the starting materials had all reacted; the reaction was monitored by TLC. After the reaction, DCM was evaporated by rotary