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SYNTHESIS OF POLYAMIDES CONTAINING TYROSINE-LEUCINE LINKAGES

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Key Words: Polyamides; Tyrosine-leucine; DPPA; Biodegradation; TOC

ABSTRACT

Polyamides derived from the tyrosine-leucine (Tyr-Leu) peptide bond were prepared using monomers synthesized via the diphenyl phosphoryl azide (DPPA) coupling method. Spacers of varying chain lengths and functionalities were incorporated between the Tyr-Leu dipeptide. The spacers reported here include poly(oxypropylenediamine) (Jeffamine), and dodecanediamine. The Jeffamine-containing polymers, synthesized by polycondensation with sebacoyl chloride in DMF and chloroform, were found to have an M_w/M_n of 47,600/26,700 and 32,000/23,700, respectively. The polymers derived from the dodecanediamine spacer and sebacoyl chloride gave a polymer with M_w/M_n of 47,000/26,000 as determined by GPC analysis. In another experiment, poly(β-alanyltyrosylleucyl-β-alanine), a previously synthesized polyamide with M_w/M_n of 16,500/5,700, was subjected to enzymatic degradation targeting the Tyr-Leu dipeptide of naturally occurring L-amino acids. The proteases *thermolysin, subtilisin, chymotrypsin*, and *aspergillopeptidase A* were used. The total organic carbon (TOC) analysis method was used to determine the extent of degradation. The polymer was found to degrade with the *thermolysin* protease under appropriate buffer and temperature conditions.

INTRODUCTION

As research in biodegradable polymers, especially those intended for biomedical applications, continues, there is still tremendous interest in polyamides containing the naturally occurring α-L-amino acid linkage because of their inherent biodegradability [1]. Potential applications of these modified polyamides are numerous and include: controlled drug delivery systems, degradable sutures, and artificial skin substitutes, among others [1–4].

Previously, we reported on the use of diphenyl phosphoryl azide (DPPA) for the incorporation of the tyrosine-leucine (Tyr-Leu) dipeptide unit into polyamides [5]. Here, we report some of the results obtained from the enzymatic degradation of one of the polymers, poly(β-alanyltyrosylleucyl-β-alanine), **PATLA, 3.** This polymer was subjected to enzymatic degradation using proteases: *chymotrypsin, thermolysin, subtilisin*, and *aspergillopeptidase A*.

In our effort to improve on the molecular weights and material properties of these polymers containing the enzyme cleavage sites [6], we have been exploring the effect of spacers with different functionalities as well as those having varying chain lengths. Here we also present the technique of incorporating an oligodiamine, poly(oxypropylenediamine), and dodecanediamine as spacers. The results of these modifications in relation to the properties of the polymers are also included.

EXPERIMENTAL

Materials

The amino acid derivatives were obtained from Advanced ChemTech Inc., Louisville, KY, and used without further purification. DPPA, obtained from Aldrich Chemical Company, was purified by distillation under reduced pressure. Poly(oxypropylenediamine) (Jeffamine), molecular weight 400, was obtained from Texaco. Sebacoyl chloride was distilled under reduced pressure while triethylamine was dried over CaH_2 and distilled at atmospheric pressure. Anhydrous DMF was obtained by drying over BaO and distilling under reduced pressure. The proteases used in the enzymatic degradation experiment were obtained from Sigma Chemical Company, St. Louis MO. They included *thermolysin, subtilisin, aspergillopeptidase A*, and *chymotrypsin*.

Measurements

The infrared spectra of the compounds (KBr pellet) were recorded on a Nicolet 60SX FT-IR spectrometer, while the ^{1}H-NMR spectra were obtained on an IBM AF-270 NMR spectrometer (270 MHz), with CF_3COOD as solvent. The molecular weight of Jeffamine was determined using fast atom bombardment mass spectroscopy (FABMS) on a Kratos MS50RF high resolution magnetic sector mass spectrometer. Thermal analysis was performed using a Perkin-Elmer DSC-7 in N_2 at a heating rate of 10°C/min. GPC analysis was conducted in *m*-cresol with a Waters 150-C ALC/GPC equipped with μ-styragel HT columns of 10^5, 10^5 10^3, and 10^3 Å pore sizes at 130°C and a flow rate of 1 mL/min. Polystyrene narrow molecular weight standards were used for calibration. Solubilities were tested with 10-mg polymer samples in 1 mL of solvent.

Enzymatic Degradation

The polymer was ground into fine powder, and 10 mg of the polymer was introduced into a glass tube followed by 1 mg of an enzyme and 3 mL of an appropriate buffer. The following buffers were used: phosphate buffer pH 7.8 (*thermolysin, subtilisin*, and *chymotrypsin*) and biphthalate buffer, pH 2.8 (*aspergillopeptidase A*). A tube deprived of an enzyme (a control) and another excluding a polymer (a blank) were also prepared. The samples were then incubated at 37°C [6] with shaking for 24 hours. The reaction mixture was then filtered through a 0.45-μm membrane. The total amount of soluble organic carbon (TOC) in the filtrate was determined [7].

Synthesis

Monomers

O-Benzyltyrosylleucylpoly(oxypropylenediamine)leucyl-O-benzyltyrosine (Jeffamine-containing monomer, **I**). To a solution of *tert*-butyloxycarbonyl-*O*-benzyl-L-tyrosine [BOC-Tyr(Bz)-OH, 11.13 g, 30 mmol] and L-leucine methyl ester·HCl (H-Leu-OMe·HCl, 6.00 g, 33 mmol) in DMF was added DPPA (7.11 mL) and triethylamine (8.80 mL) in DMF (120 mL) at 0°C or below. The mixture was allowed to stir at the low temperature for 4 hours and then left to react for about 20 hours at room temperature. The protected dipeptide BOC-Tyr(Bz)-Leu-OMe was obtained upon work-up as reported previously [8, 9]. The methyl ester protecting group was deblocked using aqueous NaOH. The incorporation of spacer unit was achieved by reacting 1 equivalent of the amino protected dipeptide, BPC-Tyr(Bz)-Leu-OH, with 0.5 equivalent of the Jeffamine oligomer using DPPA under similar conditions as explained above. The resulting peptide, BOC-Tyr(Bz)-Leu-NHCH-$(CH_3)CH_2[OCH_2CH(CH_3)]_{5.6}$NH-Leu-Tyr(Bz)-BOC, was reacted with anhydrous trifluoroacetic acid (TFA) at room temperature to give the monomer **I** as a TFA salt [mp 225°C (DSC), yield 10.1 g, 60%].

^{1}H NMR (CF_3COOD) δ (ppm): 0.84 (m, 12H, $(CH_3)_2$, Leu), 1.17–1.55 (m, 14H, $CHCH_2$, Leu, CH_3, Jeffamine), 3.06–3.83 (m, 25H, CHNH, OCH_2, Jeffamine, CH_2, Tyr), 4.49–4.59 (m, 4H, CH—N, Tyr, Leu), 5.05 (s 4H CH_2—O, Bz), 6.96–7.27 (m, 18H, aromatic H, Tyr, Bz).

IR (KBr pellet): 3298 cm^{-1} (N—H stretching), 3066 cm^{-1} (C—H stretching, aromatic), 2930 and 2858 cm^{-1} (C—H stretching, aliphatic), 1652 cm^{-1} (amide I), and 1541 cm^{-1} (amide II).

O-Benzyltyrosylleucyliminododecaneiminoleucyl-O-benzyltyrosine (Tyr(Bz)-Leu-dodecanediamine-Leu-Tyr(Bz), dodecanediamine-containing monomer, **II**). BOC-Tyr(Bz)-Leu-OH was prepared as described in the preceding section. In a 300-mL 3-neck flask was then placed 13.3 g (27.4 mmol) of the dipeptide followed by 2.75 g (13.7 mmol) of dodecanediamine (1,12-diaminedodecane). To this mixture was added 150 mL DMF. The mixture was warmed slightly to allow complete dissolution of the dodecanediamine which was not readily soluble in DMF at room temperature. The solution thus formed was cooled in an ice/salt bath, and the coupling reaction was executed using DPPA (6.5 mL, 30.2 mmol) and triethylamine (8.0 mL, 57.6 mmol) as before. During the work-up process, some solubility prob-

lems were encountered with the solid precipitating out even after addition of ethyl acetate diluting solvent. The solid that precipitated was collected and washed thoroughly with HCl, saturated $NaHCO_3$, saturated NaCl, and water. It was dissolved in acetone and reprecipitated by adding water. Analysis of the precipitate fraction showed identical results as the fraction in solution, hence the two samples were recombined to give 11.56 g (76.9%) of the blocked monomer. The sample was then dried in a vacuum oven. A total of 7.05 g sample of BOC-Tyr(Bz)-Leu-NH-$(CH_2)_{12}$NH-Leu-Tyr(Bz)-BOC was deprotected in 40 mL of TFA, which acted both as solvent and reagent. After removal of excess TFA under reduced pressure, the residue sample was triturated in ether several times and then left to stir overnight in ether. A slightly off-white powder sample (6.10 g, 84.5% yield) was obtained.

^{1}H NMR (CF_3COOD) δ (ppm): 0.84 [m, 12H, $(CH_3)_2$, Leu], 1.17–1.55 (m, 26H, $CHCH_2$, Leu, CH_2, dodecanediamine), 3.06–3.83 (m, 8H, CH_2NH, dodecanediamine CH_2, Tyr), 4.49–4.59 (m, 4H, CH—N, Tyr, Leu), 5.05 (s, 4H, CH_2—O, Bz), and 6.96–7.27 (m, 18H, aryl H, Tyr, Bz).

IR (KBr pellet): 3298 cm^{-1} (N—H stretching), 3066 cm^{-1} (C—H stretching, aromatic), 2930 and 2858 cm^{-1} (C—H stretching, aliphatic), 1652 cm^{-1} (amide I), and 1541 cm^{-1} (amide II).

Polymers

Poly(O-benzyl-tyrosylleucypoly(oxypropylenediamine)leucyl-O-benzyltyrosine sebacoyl) (Jeffamine-containing polymers, **1***).* A: Polymer 1a (solution method using DMF). In a 100-mL round-bottomed flask, 1.27 g ($\sim$1.0 mmol) of Jeffamine monomer, **I**, was placed. To the sample was introduced 10 mL DMF followed by triethylamine (1.0 mL). The mixture was cooled in ice while passing argon. A solution of sebacoyl chloride (0.213 mL, 1 mmol) in chloroform was then added, and the reaction mixture was stirred vigorously for about 5 minutes. The reaction mixture took about 2 hours before becoming viscous. It was left to react overnight at room temperature. The polymer was obtained by precipitating the reaction mixture from distilled water, followed by thorough washing with water, methanol, and ether. The sample was dried in a vacuum oven at 60°C. A slightly colored sample was obtained (**1a**, 0.67 g, yield 48.6%, $[\alpha]^{24} = -3.71°$, acetic acid). It had an M_w/M_n of 47,600/26,700 as determined by using GPC.

B: Polymer 1b (solution method using chloroform). A similar approach as in Section A was applied with the same quantities of reagent, but instead of using DMF, anhydrous chloroform was used as the solvent. The polymer (0.60 g, yield 44%, $[\alpha]^{24} = -1.95°$, acetic acid) had an M_w/M_n of 32,000/23,700.

^{1}H NMR (CF_3COOD), δ (ppm): 0.79 [12H, $(CH_3)_2$, Leu], 1.13–1.49 (m, 31H, $CHCH_2$, Leu, CH_3, Jeffamine, CH_2 sebacoyl), 2.33 (m, 4H, CH_2CO, sebacoyl), 2.92–3.30 (m, 25H, CH_2, Tyr, CHN and OCH_2 of Jeffamine unit), 4.50–4.82 (m, 4H, CH—N, Tyr, Leu), 5.02 (s, 4H, O—CH2, Bz) and 6.85–7.23 (m, 18H, aromatic, Tyr, Bz).

IR (KBr pellet): 3286 cm^{-1} (N—H, stretching), 3072 cm^{-1} (C—H stretching, aromatic), 2925 and 2862 cm^{-1} (C—H stretching, aliphatic), 1643 cm^{-1} (amide I), and 1549 cm^{-1} (amide II).

Poly(O-benzyltyrosylleucyiminododecaneiminoleucyl-O-benzyltyrosine sebacoyl), (dodecanediamine-containing polymer, **2***).* In a 100-mL round-bottomed

flask was placed 1.16 g (1.0 mmol of dodecanediamine monomer, **II**). To this solid was added DMF (10 mL) and TEA base (1 mL). The mixture was stirred for some time to ensure complete dissolution of the monomer. A solution of sebacoyl chloride (0.21 mL) in chloroform (1 mL) was then added while passing argon. The reaction mixture became viscous after stirring at room temperature for a few minutes. The reaction mixture was left stirring at room temperature overnight. A similar worked-up as that of polymer **1** above was followed. An off-white polymer sample was obtained in powder form (0.97 g, yield 88.3%, $[\alpha]^{24} = -8.56°$, acetic acid). The polymer was found to have an M_w/M_n of 47,000/26,000.

^{1}H NMR (CF_3COOD) δ (ppm): 0.84 [m, 12H, $(CH_3)_2$, Leu], 1.17–1.55 (m, 38 H, $CHCH_2$, Leu, CH_2, sebacoyl and dodecanediamine), 2.33 (m, 4H, CH_2CO, sebacoyl), 3.06–3.83 (m, 8H, CH_2NH, dodecanediamine CH_2, Tyr), 4.49–4.59 (m, 4H, CH—N, Tyr, Leu), 5.05 (s, 4H, CH_2—O, Bz), and 6.96–7.27 (m, 18H, aryl H, Tyr, Bz).

IR (KBr pellet): 3298 cm^{-1} (N—H stretching), 3072 cm^{-1} (C—H stretching, aromatic), 2927 and 2858 cm^{-1} (C—H stretching, aliphatic), 1645 cm^{-1} (amide I), and 1516 cm^{-1} (amide II).

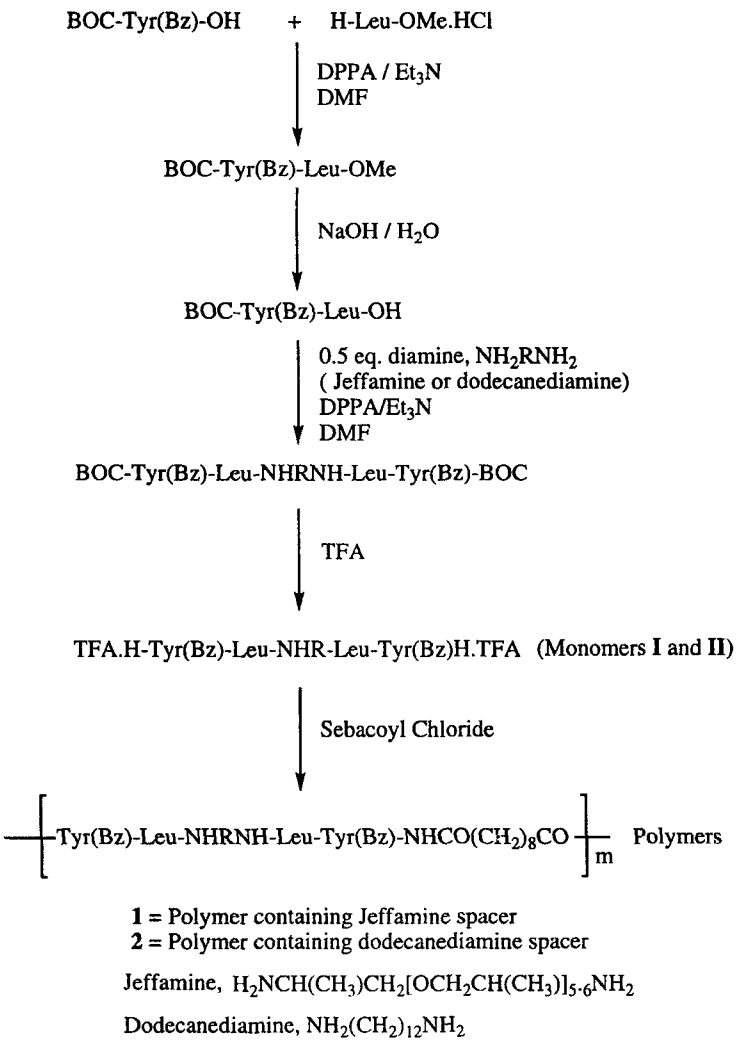
RESULTS AND DISCUSSION

Jeffamine-Containing Monomer, I

The DPPA technique was applied to synthesize the monomer **I** [6, 8–10]. The liquid Jeffamine with an average molecular weight of 400 was reacted with BOC-Tyr(Bz)-Leu-OH to give the BOC protected monomer as shown in Scheme 1. The BOC group was deblocked using TFA in the usual way to give a TFA salt of the Jeffamine monomer **I** in 60% yield. The DSC analysis showed a broad melting peak for the monomer which is expected since the monomer is oligomeric. The NMR of the compound in CF_3COOD shown in Fig. 1 agrees quite well with the structure of this oligomeric monomer. Notable peaks besides the common ones expected for the Tyr-Leu linkage [4, 11] are the multiplet at 3.06 and 3.83 ppm due to CHNH and OCH_2 in the Jeffamine unit, which also coincide with the β-CH_2 in Tyr. The methyl group is within the multiplet at 1.17–1.55 ppm, also comprising the $CHCH_2$ group of Leu. The methylene protons in the benzyl protecting group occur as a singlet at 5.05 ppm, while the aromatic region (6.96–7.27 ppm) is broad due to the benzyl and Tyr protons.

Dodecanediamine-Containing Monomer, II

The monomer containing the dodecanediamine spacer was synthesized in a similar manner as that containing the Jeffamine spacer. It is also worth noting that the coupling reaction involving the dodecanediamine did not proceed as smoothly as that involving the Jeffamine spacer due to decreased solubility of the former in DMF. The decrease in the solubility is due to the high hydrophobicity of the dodecanediamine because of the long chain containing 12 methylene units. The structure of the monomer **II** did not show major differences from that of **I** as is evident from the NMR spectrum shown in Fig. 2 except for the absence of the OCH_2 peak at 3.06–3.83 ppm and in the peak integration between 1.2 and 1.5 ppm.



SCHEME 1. Synthesis of Tyr-Leu monomers and polymers containing diamine spacers.

Poly(β-Alanyltyrosylleucyl-β-alanine), PATLA, 3

The synthesis of poly(β-alanyltyrosylleucyl-β-alanine), **3**, was previously reported, and the structure is given in Fig. 3 [5]. It was synthesized using DPPA and obtained in 55.4% yield as a white powder with an M_w/M_n of 16,500/5,700 as determined using GPC.

Jeffamine-Containing Polymers, 1a and 1b

The polycondensation of monomer **I** with sebacoyl chloride was carried out in the usual manner [12] and is presented in Scheme 1. The reaction was carried out in chloroform and DMF so as to determine the effects of solvents on the polymeriza-

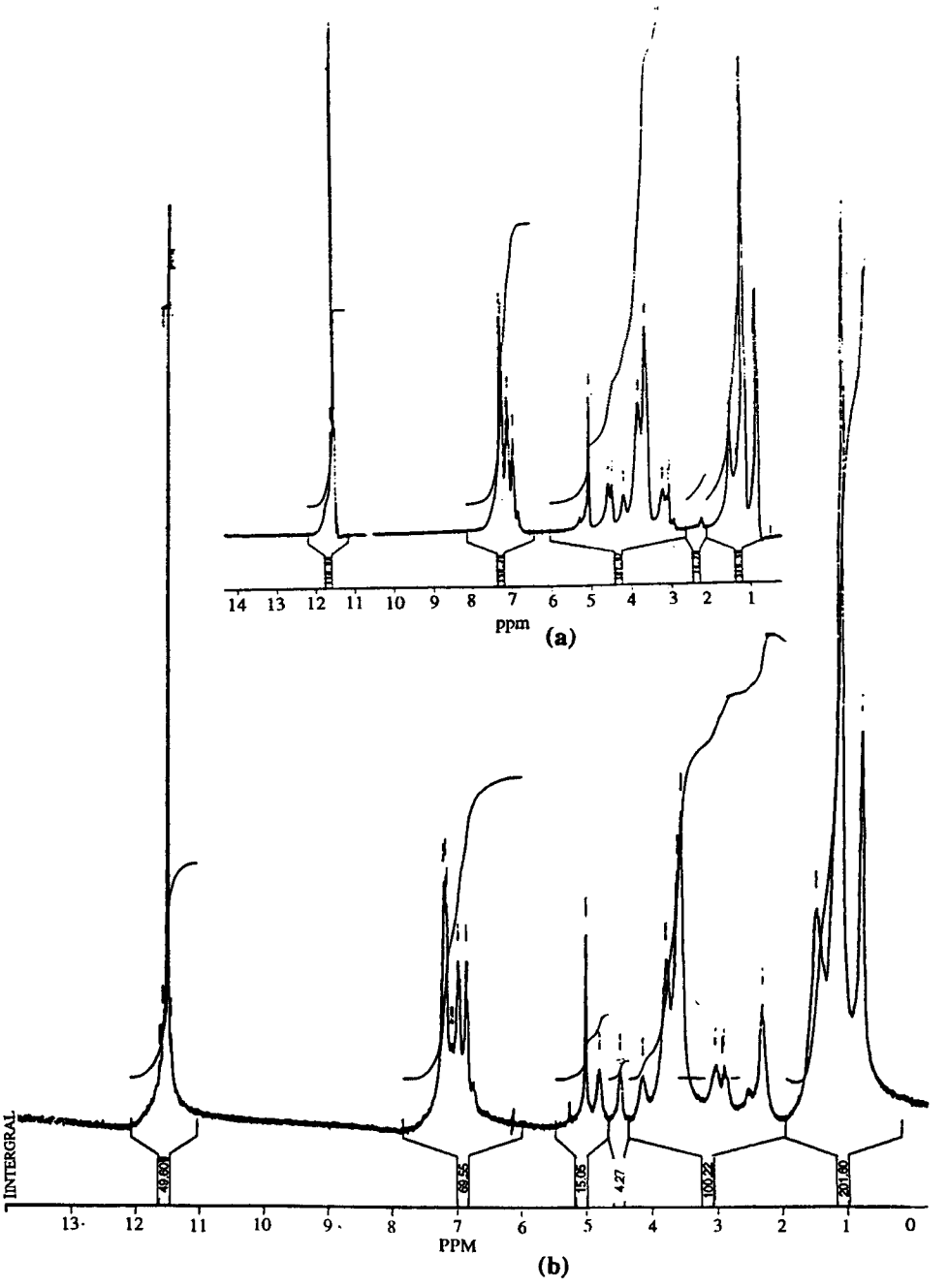


FIG. 1. Proton NMR of Jeffamine containing (a) monomer **I** and (b) polymer **1**.

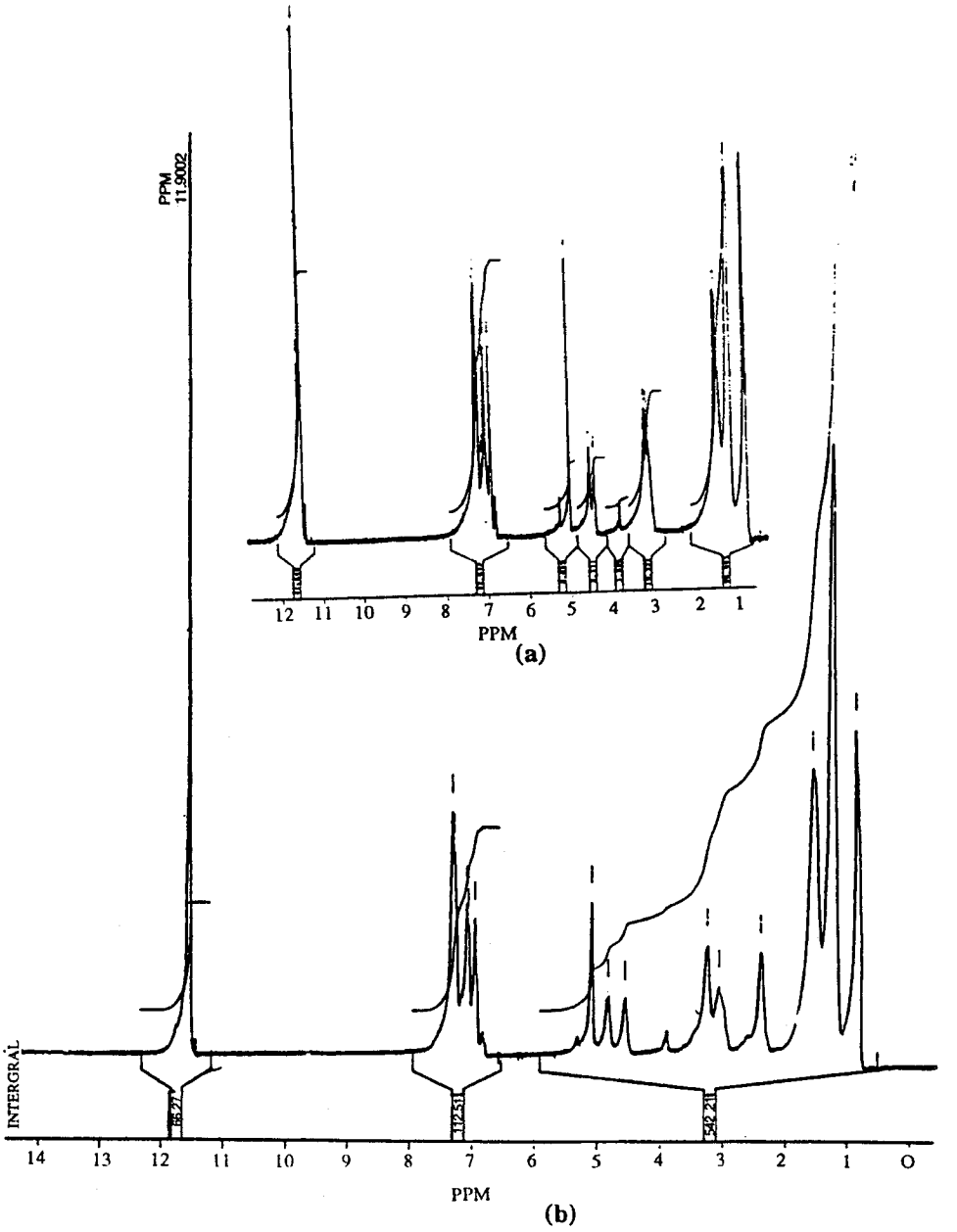


FIG. 2. Proton NMR of dodecanediamine-containing compounds (a) monomer **II** and (b) polymer **2**.

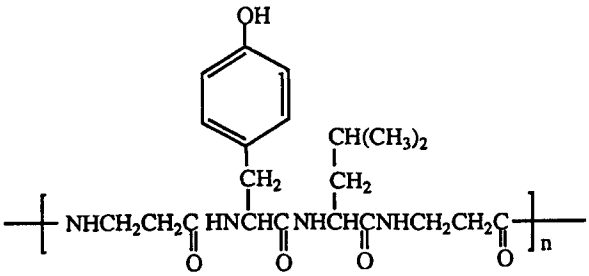


FIG. 3. Structure of poly(β-alanyltyrosylleucyl-β-alanine), **PATLA, 3.**

tion. The polymers **1a** (0.67 g, yield, 48.6%) and **1b** (0.60 g, yield 44%) had M_w/M_n of 47,600/26,700 and 32,000/23,700, respectively. The polymers had the same off-white color as the monomer. They were characterized with IR and NMR. The IR spectrum (Fig. 4) shows the characteristic peaks for the amide I and amide II at 1643 and 1541 cm^{-1}, respectively. The NMR in CF_3COOD (Fig. 1) was similar to that of the monomer except for the CH_2CO peak at 2.4 ppm due to the sebacoyl moiety. Another notable difference is in the peak integration between 1.2–1.5 ppm, with the polymer showing the presence of CH_2 from the sebacoyl group.

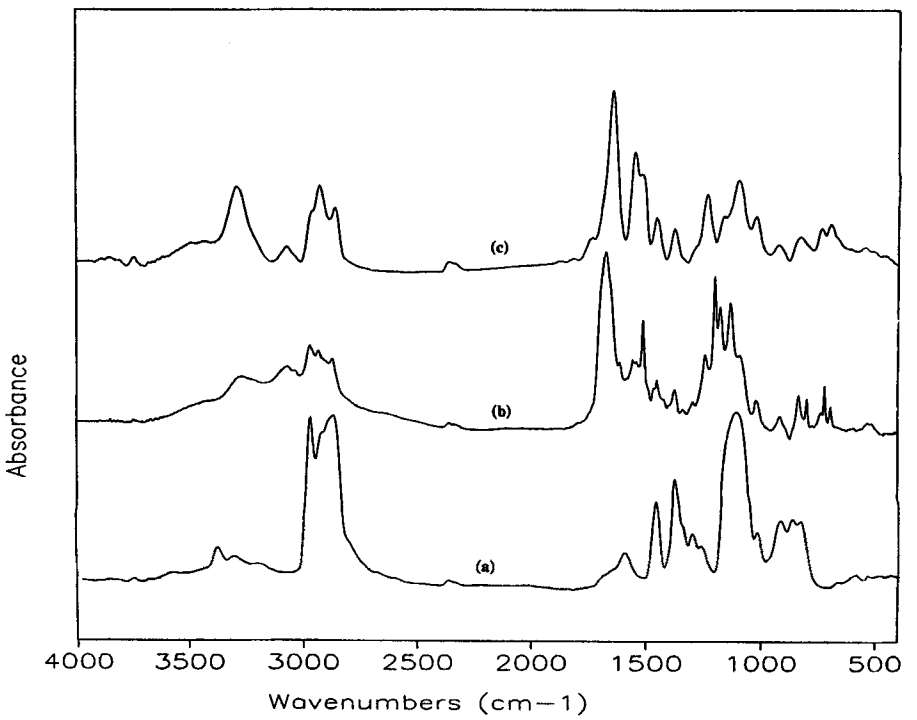


FIG. 4. Infrared spectra of Jeffamine-derived compounds: (a) Jeffamine, (b) Jeffamine-containing monomer **I**, (c) polymer **1**.

Dodecanediamine-Containing Polymer, 2

The polymer containing dodecanediamine spacer, **2**, was synthesized in a similar manner as **1** described above (Scheme 1) and was found to have an M_w/M_n of 47,000/2,600. The NMR spectrum is presented in Fig. 2 and shows the CH_2CO peak at 2.33 ppm, as in the case of **1**, and the presence of additional CH_2 from the diacyl unit between 1.2 and 1.5 ppm. The IR of **2**, shown in Fig. 5, is identical to that of monomer **II**. The spectrum has characteristic amide peaks as observed in polymer **1**.

Physical Properties of Polymers

Tables 1 and 2 give some of the physical properties of the polymers. Polymers containing spacers Jeffamine (**1a** and **1b**) and dodecanediamine (**2**) gave relatively high molecular weights. There are two plausible explanations for the observed molecular weights. The first is the solubility factor. Generally, polymers that are relatively soluble in the reaction medium have a higher probability of reacting to form a higher molecular weight material as the probability of molecular collision is high [13]. On the contrary, polymers that precipitate out very quickly do not achieve high molecular weight because molecular collisions are much more hindered in the suspension compared to the solution. It was observed that the reaction leading to Jeffamine polymer took some time before becoming viscous unlike the case of

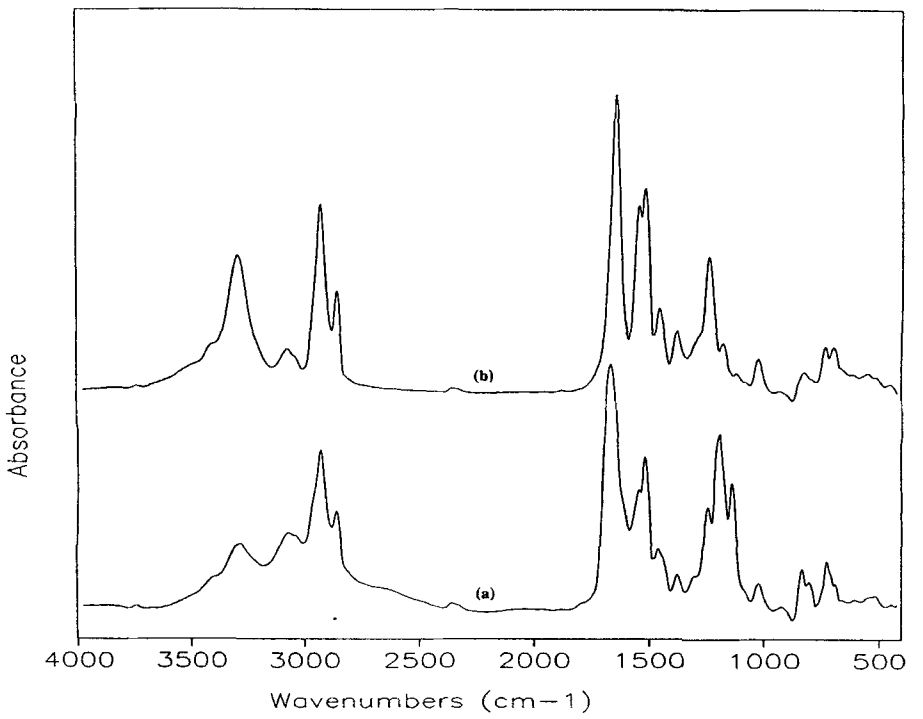


FIG. 5. Infrared spectra of dodecanediamine-derived compounds (a) dodecanediamine containing monomer **II** and (b) polymer **2**.

TABLE 1. Yields, T_m, and GPC Data of the Tyr-Leu Polymers

	Sample			
	1a	**1b**	**2**	**3**
Yield, %	48.6	44	88.3	55.3
M_w	47,600	32,000	47,000	16,500
M_n	26,700	23,700	26,000	5,700
M_w/M_n	1.78	1.35	1.81	2.89
T_m (°C)	178	[a]	216	270
T_g (°C)	51	[a]	77	80

[a]Not determined.

previously synthesized **PATLA, 3**, where the solution became viscous after only a few minutes. In the case of polymer **2**, the reaction behaved in a manner similar to that of polymer **3**. Apparently a relatively high molecular weight was obtained in case of polymer **2**, therefore, solubility cannot be the only factor affecting the molecular weight. The effect of solubility is clearly reflected from the difference in the molecular weights of polymers **1a** and **1b** synthesized in DMF and $CHCl_3$. DMF, which is a better solvent for a relatively polar polymer, gives a higher molecular weight product. Notable from the molecular weight data is a slight difference in the polydispersity of the two polymers. The higher molecular weight polymer has a higher polydispersity, which can be explained as due to the larger extent of the reaction. Another factor found to greatly influence molecular weight is chain flexibility. Polymers made from flexible chains generally give higher molecular weights [13]. Flexibility increases the chain motion, thus increasing the chances of molecular collision. This factor can explain the observed high molecular weight of polymer **2** despite its low solubility in the reaction medium. The relatively large and flexible spacer derived from dodecanediamine increases chain flexibility. The same argument is applicable to the polymer derived from Jeffamine, which is a polymer with ether linkages and hence is relatively more flexible.

Table 1 also shows the T_m and T_g values of the polymers containing the different spacers. The polymers containing large and more flexible spacers show

TABLE 2. Solubility of the Tyr-Leu Polymers[a]

	Solvent					
	m-Cresol	NMP	DMAc	DMF	DMSO	MeOH
1a	+	+	+	+	+	−
1b	+	+	+	+	+	−
2	+	±	±	±	±	−
3	+	±	±	±	±	−

[a]+ = Soluble at room temperature, ± = soluble after heating, − = insoluble.

relatively lower T_m and T_g values as compared to their counterparts with a shorter, more rigid spacer [13]. The chain flexibility probably lowers the T_m by disrupting the crystalline phase of the molecule. Similarly, flexible chains have a high segmental motion which leads to a decrease in T_g. These two effects are more pronounced in Jeffamine-containing polymers, and this can be attributed to the more flexible nature of the ether linkage as opposite to the carbon—carbon bond in dodecanediamine.

The solubility data of the polymers is presented in Table 2. The results show **1a** and **1b** to be more soluble in a wide range of solvents as opposed to the other two polymers. These results can be attributed to the ether linkage in Jeffamine. The presence of these soft segments disrupts the intermolecular H-bonds associated with solubility difficulties in polyamides. Films cast from solvents were found to be much stronger and flexible, in the case of Jeffamine polymers as compared to those of polymers **2** and **3** which were brittle. The difference in the film properties can also be attributed to the flexible soft segment from ether linkages in the Jeffamine spacer. The films obtained from these polymers, including the ones from Jeffamine-containing polymers, were, however, weaker relative to those obtained from polyamides without pendant groups such as nylon 26 and 266 [14]. The reason for this behavior could be the nature of the amino acids in the dipeptide. Tyrosine and leucine have bulky side chains which can greatly affect the molecular order of the polymers, resulting in brittle material. The effect of the two groups can have an adverse effect on the material properties because there are four such groups per spacer molecule in the case of polymers derived from Jeffamine and dodecanediamine. Thus the contribution of the dipeptide unit to the overall properties of the polymers is bound to be significant.

Enzymatic Degradation

The results for the enzymatic degradation of **PATLA, 3**, are given in Table 3. Degradation using *thermolysin* gave higher values of soluble total organic carbon (TOC), thus indicating that it degraded the polymer more than the other proteases. Since the proteases were subjected to the same polymer material, the difference in

TABLE 3. Total Organic Carbon (TOC) Results for Poly(β-Ala-Tyr-Leu-β-Ala), **3**

Sample	TOC, mg/L
Thermolysin + sample	473
Thermolysin alone	73
Subtilisin + sample	157
Subtilisin alone	103
Chymotrypsin + sample	152
Chymotrypsin alone	140
Aspergillopeptidase A + sample	112
Aspergillopeptidase A alone	100

the results can only be explained in terms of specificity of the enzyme. It can be argued that the endopeptidase metalloenzyme, *thermolysin* [15], is able to bind with the polymer substrate and initiate the degradation reaction. Enzymatic degradation by thermolysin has been found to be more efficient compared to other related proteases, especially in the hydrolysis of polypeptides contaning aromatic amino acid acids such as Tyr [15]. Similar results as for polymer **3** have been obtained from other polymers having the same dipeptide linkage that we synthesized with a hexamethylenediamine spacer and polycondensed with adipoyl chloride [5]. Similar TOC results have also been obtained by Saotome and coworkers in their determination of enzymatic degradation of poly(ester amides) containing α-L-amino acids [7]. The results of degradation of the polymer as a factor of time are given in Fig. 6. This part of the test was done using *thermolysin* since it gave better results in the TOC screening test. As seen in the figure, degradation increases with time up to about 12 hours when it essentially stops. This point in the graph may indicate the onset of enzyme inhibition, probably due to the presence of the degradation by-products [16].

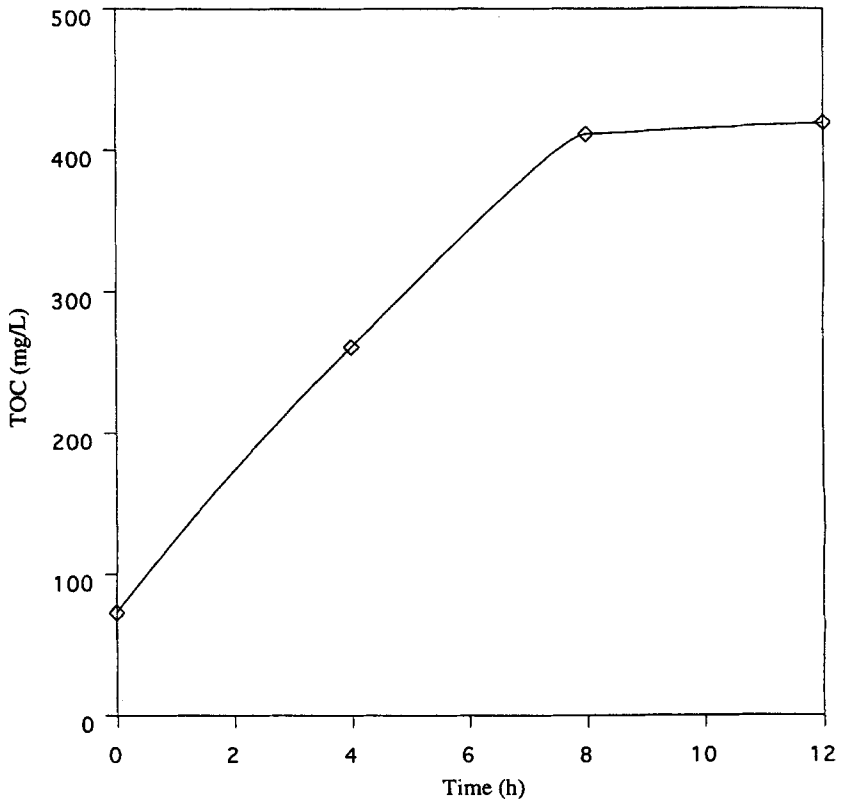


FIG. 6. Graph of total organic carbon (TOC) vs time for thermolysin degradation of **PATLA, 3.**

CONCLUSIONS

These studies demonstrate the versatility of DPPA reagent in synthesizing oligomeric diamine monomers containing enzymatically hydrolyzable bonds such as tyrosine-leucine. The oligomeric diamines were utilized in polycondensation reactions with diacyl chlorides to give polymers with a relatively higher molecular weight. It has been demonstrated that it is feasible to alter the properties of the Tyr-Leu polyamides by changing the functionality or varying the chain extenders or spacers, e.g., β-alanine, dodecanediamine, and poly(oxypropylenediamine) used as spacers gave polymers with different properties. This difference in properties due to structural changes can be utilized to make materials for specific applications. The inclusion of Jeffamine soft segment as a spacer in polymers greatly improved the nature of the films relative to the ones obtained from polymers containing the rigid C—C linkages. It is worth pointing out that the polymers have hydroxyl group masked by the benzyl group. This group can be deblocked to give polymers with a reactive side chain. This has the potential of being reacted, for example, with a drug molecule for drug-controlled release. The enzymatic degradation results with proteases indicate that polymers containing the Tyr-Leu dipeptide bond are degradable, with *thermolysin* being the most effective. It has also been shown that degradation is time-dependent. Degradation of polymer **3** in *thermolysin* showed that the degradation ceased after about 12 hours.

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