# Synthesis and Characterization of Degradable Copoly(ester–amide)s: Poly(*trans*-4-hydroxy-L-proline-*co*-ε-caprolactam)

**Ren-Shen Lee,[1] Jen-Ming Yang[2]**

[1] *Center of General Education, Chang Gung University, Taoyuan, 333, Taiwan, Republic of China*
[2] *Department of Chemical Engineering, Chang Gung University, Taiwan, Republic of China*

Received 19 September 2001; accepted 8 January 2002

**ABSTRACT:** Novel copolyesteramides were synthesized by reacting *trans*-4-hydroxy-*N*-benzyloxycarbonyl-L-proline (*N*-CBz-Hpr) with ε-caprolactam (CLM) in the presence of stannous octoate [Sn(II) Oct.] as a catalyst. Various techniques, including $^1$H-NMR, IR, DSC, and viscosity, were used to elucidate structural characteristics and thermal properties of the resulting copolymers. Data showed that the optimal reaction condition for the synthesis of the copolymers was obtained by using 3 wt % Sn(II) Oct. at 170°C for 24 h. The DSC analysis demonstrated amorphous structure for most of the copolymers. The glass-transition temperature of the copolymers shifts to a higher temperature with increasing Hpr/CLM molar ratio. *In vitro* degradation of these poly(*N*-CBz-Hpr-*co*-CLM)s was evaluated by weight loss measurements. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 86: 1615–1621, 2002

**Key words:** polyesteramides; pseudo(*trans*-4-hydroxy-L-proline); ε-caprolactam; degradation

## INTRODUCTION

Several aliphatic polyesters, exhibiting excellent biodegradability, are now extensively employed for agricultural, biomedical, pharmaceutical, and environmentally related applications.[1] However, low thermal, mechanical, and processing performances greatly restrict the practical use of these materials. Improvement of the mechanical properties can be achieved by introduction of amide linkages in the main chains. For example, ε-caprolactam, adipic acid, and 1,6-hexanediamine have been used as monomers for the synthesis of polyesteramides.[2–5] In general, however, these polymers exhibit low biodegradability because the amide linkages are not sensitive to the attack by enzymes and microbes.

Amino acids are constituents of proteins, and polymers synthesized from amino acids are expected to exhibit biodegradability.[6–12] Polyesteramides containing amino acids, such as phenylalanine, leucine, alanine, and glycine, have been synthesized and were found to be degraded by enzymes. For example, series of polyesteramides were synthesized starting from amino acids, adipic acid, and 1,2-ethanediol.[9,10] However, one of the shortcomings of these polymers is that there are only two reactive groups (amino and carboxylic groups at both chain ends) and no pendant functional groups on the backbone molecules that can be used for covalent bonding of either drugs or biologically active agents.

Pseudopoly(amino acid)s are among the newest classes of biodegradable polymers, having the advantages of being nontoxic, biodegradable, and biocompatible, and possessing functional groups on the backbone.[13] In previous studies,[14–17] we reported on the synthesis of the pseudopoly(amino acid)s of *trans*-4-hydroxy-L-proline (Hpr). In the present work, *trans*-4-hydroxy-*N*-benzyloxycarbonyl-L-proline (*N*-CBz-Hpr) was used with ε-caprolactam (CLM) comonomer to build up a predetermined fraction of amide linkages. The aim of our study was to obtain a series of potentially biodegradable copolyesteramides by hydrolytic melt polymerization of *N*-CBz-Hpr in the presence of different amounts of CLM. Techniques such as $^1$H-NMR, IR, and DSC were used to characterize the structure and thermal properties of the copolyesteramides. The effects of the comonomers on the inherent viscosity ($\eta_{inh}$), and glass-transition temperature ($T_g$) were also examined.

## EXPERIMENTAL

### Materials

Hpr and ε-caprolactam were purchased from Fluka Chemie (Buchs, Switzerland). Benzyloxychloroformate was purchased from Aldrich Chemical (Milwaukee, WI). Stannous octoate was purchased from Strem

*Correspondence to:* R.-S. Lee (lrshen21@yahoo.com.tw).
Contract grant sponsor: National Science Council of the Republic of China.
Contract grant sponsor: Chang Gung University.

Journal of Applied Polymer Science, Vol. 86, 1615–1621 (2002)

Chemical (Newburyport, MA). 6-Aminocaproic acid was purchased from Lancaster Chemicals (UK). Organic solvents (e.g., tetrahydrofuran, methanol, ethyl acetate, and chloroform) and inorganic compounds (e.g., sodium sulfate and sodium bicarbonate) were reagent grade and were purchased from Merck (Darmstadt, Germany).

### Characterization

Infrared spectra were measured on a Jasco IR Report-100 infrared spectrophotometer (Jasco, Tokyo, Japan). Samples were either neat onto NaCl plates or pressed into KBr pellets. $^1$H-NMR spectra were recorded at 500 MHz (WB/DMX-500 spectrometer; Brucker Instruments, Billerica, MA) with tetramethylsilane as an internal standard. Elemental analysis was run on a Perkin–Elmer model 2400 C–H–N analyzer (Perkin Elmer Cetus Instruments, Norwalk, CT). The inherent viscosities were measured with an Ubbelohde viscometer at 30°C. Thermal analysis of the polymer was performed on a DuPont 9900 system differential scanning calorimeter (DSC; DuPont, Boston, MA). The heating rate was 20°C/min. $T_g$'s were read at the middle of the change in the heat capacity and were taken from the second heating scan after quick cooling.

### Synthesis of *trans*-4-Hydroxy-*N*-benzyloxycarbonyl-L-proline (*N*-CBz-Hpr; 1)

Monomer 1 was prepared according to the process described in our previous study.[14] A solution of Hpr (0.02 mol) in 2*N* NaOH (10 mL) was cooled in an ice-water bath and stirred with a powerful magnetic stirrer. Benzylchloroformate (3.16 mL) and 2*N* NaOH (11 mL) were added in about 10 portions, alternately. By design, the reaction mixtures had to remain distinctly alkaline. If necessary, more 2*N* NaOH was added. The temperature of the reaction mixture was kept between 5 and 10°C by the rate of addition of the reactants. Then the ice-water bath was replaced by room-temperature water, and vigorous stirring was continued for 30 min. The alkaline solution was extracted four times with diethyl ether (10 mL each), after which the ether extracted was discarded. The aqueous layer was acidified to Congo Blue by the addition of 5*N* HCl, and the aqueous solution was extracted three times with ethyl acetate (20 mL each). The combined organic layers were dried over $Na_2SO_4$ and concentrated with a rotary evaporator. The residue was purified with silica gel column chromatography by elution with EtOAc to give product **1** as a colorless, viscous oil.

### Synthesis of Copolymer 3

In general, the polymerization was conducted in a round flask with a sidearm. Typically, the purified monomer *N*-CBz-Hpr (**1**; 3.52 mmol) and ε-caprolactam (**2**; 3.52 mmol) as a comonomer were added to the flask. Then, the catalyst Sn(II) Oct. (3 wt %) was added. The flask was purged with nitrogen, and the contents reacted at 170°C for 21 h and, subsequently, under vacuum (60 mmHg) at 170°C for 3 h. The crude polymer was dissolved in tetrahydrofuran and then precipitated into *n*-hexane with stirring. After purification, the polymer was dried *in vacuo* for 24 h and analyzed. Representative $^1$H-NMR and IR spectra of the **3** copolymers are shown in Figures 1 and 2, respectively. Elemental analyses of the representative **3** copolymers indicated that the experimental and calculated elements were approximately matched.

Anal calcd for copolymer **3A**: C, 63.17%; H, 5.45%; N, 5.89%. Found: C, 62.80%; H, 5.72%; N, 5.40%. Anal calcd for copolymer **3B**: C, 63.18%; H, 5.54%; N, 6.02%. Found: C, 63.09%; H, 6.02%; N, 5.30%. Anal calcd for copolymer **3C**: C, 63.22%; H, 5.87%; N, 6.25%. Found: C, 62.83%; H, 5.76%; N, 6.25%. Anal calcd for copolymer **3D**: C, 63.30%; H, 6.56%; N, 7.55%. Found: C, 62.99%; H, 6.27%; N, 6.84%. Anal calcd for copolymer **3E**: C, 63.41%; H, 7.52%; N, 8.97%. Found: C, 62.61%; H, 7.98%; N, 8.58%. Anal calcd for copolymer **3F**: C, 63.50%; H, 8.21%; N, 10.01%. Found: C, 62.34%; H, 8.24%; N, 9.88%.

### Degradation of Copolymer

The N-protected copolymer films were prepared by the pressing technique, in which 40 mg of powder copolymer was pressed into a solid pellet under vacuum for 5 min. For the degradation study, each film (diameter 10 mm; thickness 0.38 mm) was placed in a small bottle containing 5 mL of M/15 phosphate buffer solution (pH 7.4). The bottle was then incubated at 37°C. At time intervals, the specimen was removed, washed with distilled water, lyophilized, and weighed. The degree of degradation was estimated from:

$$\text{Degree of degradation (\%)} = \frac{(D_0 - D)}{D_0} \times 100$$

where $D_0$ is the weight of copolymer before degradation and $D$ is the weight of copolymer after degradation for a certain period.

## RESULTS AND DISCUSSION

### Copolymerization

The copolymerization of *N*-protected *trans*-4-hydroxy-L-proline (*N*-CBz-Hpr) **1** and CLM **2** was investigated over a wide range of compositions by a ring-opening mechanism, where the active hydroxy group of *N*-CBz-Hpr induces a selective acyl-nitrogen cleavage of the lactam ring, thus forming an external amide block (**Scheme 1**). The polymerization was performed in bulk using Sn(II) Oct. as a catalyst, and the results of

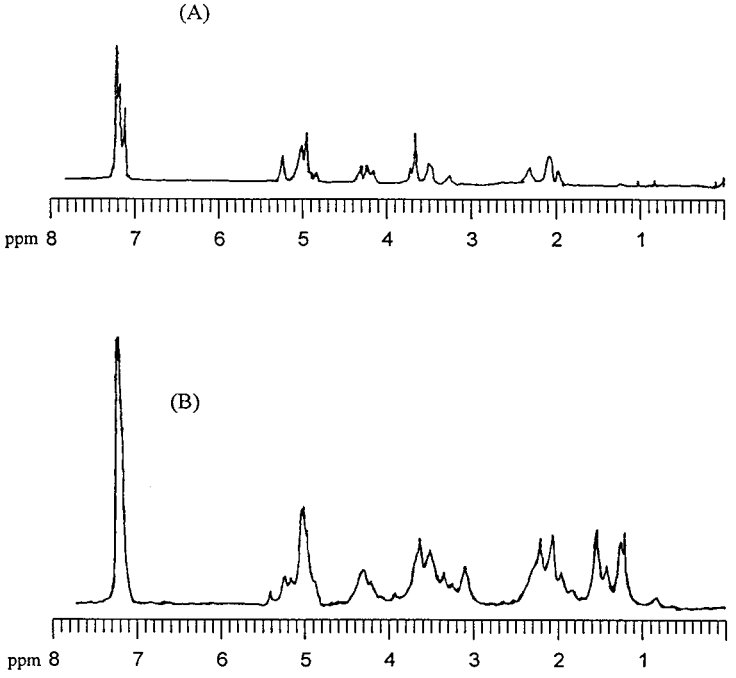



**Figure 1** Representative $^1$H-NMR spectra of (A) poly(*N*-CBz-Hpr) and (B) copoly(*N*-CBz-Hpr-*co*-CLM) (**3D**) with monomer compositions 54/46 mol %.

copolymerization are listed in Tables I–III. To find the optimum copolymerization conditions, the effects of catalyst level, polymerization temperature, and polymerization time on the $\eta_{inh}$ and $T_g$ were investigated. Initially, *N*-CBz-Hpr **1** was polymerized with CLM **2** at an equivalent molar ratio with various amounts of

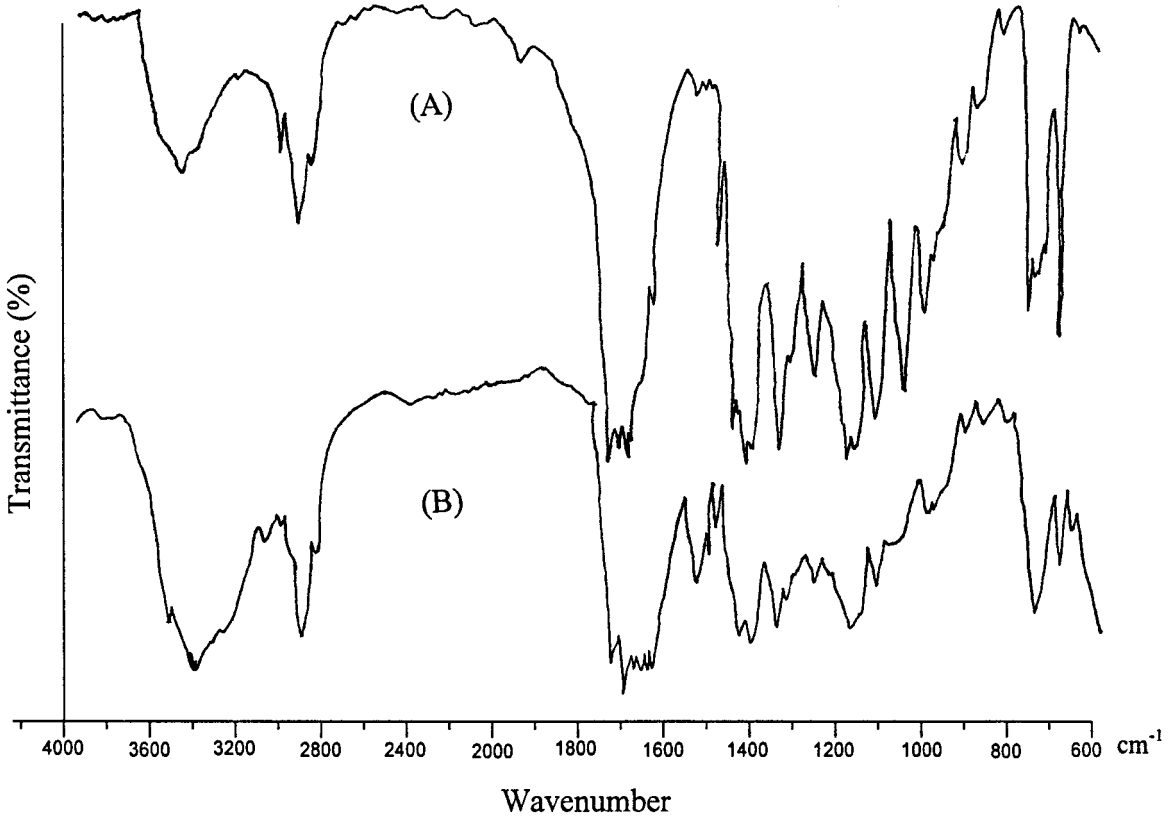
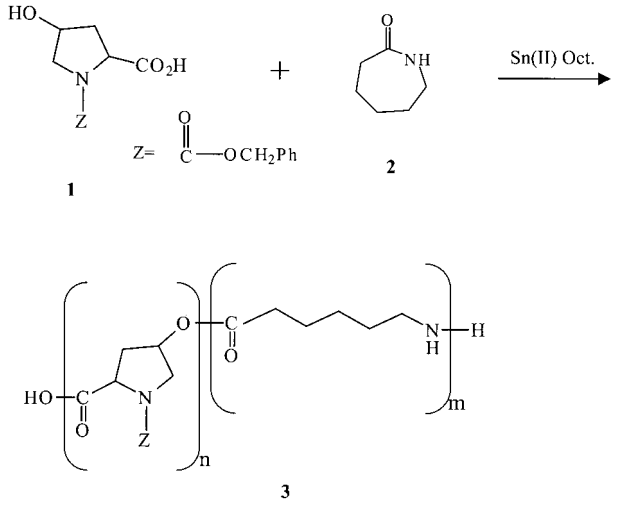



**Figure 2** Representative IR spectra of (A) poly(*N*-CBz-Hpr) and (B) copoly(*N*-CBz-Hpr-*co*-CLM) (**3D**) with monomer compositions 54/46 mol %.




**Scheme 1** Copolymerization of *trans*-4-hydroxy-*N*-benzyloxycarbonyl-L-proline (**1**) and ε-caprolactam (**2**).

catalyst ranging from 0 to 4 wt % at 140°C for 24 h. The results are shown in Table I. The yields were over 80% for all copolymerizations. The $\eta_{inh}$ of the copolymers varied from 0.69 to 1.08 dL/g. The highest $\eta_{inh}$ of the copolymer ($\eta_{inh}$ = 1.08 dL/g, Run **5**) was obtained using 3 wt % Sn(II) Oct. However, the $\eta_{inh}$ of the copolymer decreased to 0.69 dL/g when using 4 wt % Sn(II) Oct, which may be attributed to the anion of the catalyst being incorporated as an octanoyl end group in the polymer, thus limiting the molecular weight. Thus, the optimal catalyst level for the copolymerization was 3 wt % of Sn(II) Oct.

The effect of polymerization temperature on the $\eta_{inh}$ was investigated. *N*-CBz-Hpr **1** was polymerized with CLM **2** with an equivalent molar ratio at the different reaction temperatures of 140, 170, and 200°C, respectively, using 3 wt % Sn(II) Oct. for 24 h. The results are shown in Table II. As the polymerization temperature was increased from 140 to 170°C, the $\eta_{inh}$ increased from 1.08 to 1.54 dL/g (Runs **A** and **B**). However, when the reaction temperature was further increased from 170 to 200°C, the $\eta_{inh}$ decreased from 1.54 to 1.04 dL/g, and the $T_g$ decreased from 62 to 28°C (Runs **B** and **C**). This may be the result of a decomposition of *N*-CBz-Hpr **1** partially occurring during the polymerization.

**TABLE I**
**Effect of the Amount of Sn(II) Oct. Catalyst on the $\eta_{inh}$ and Yield on Polymer 3 Prepared by Polymerization of *N*-CBz-Hpr 1 and ε-Caprolactam 2[a]**

| Run | Sn(II) Oct. (wt %) | $\eta_{inh}$ (dL/g)[b] | Yield (%) |
|---|---|---|---|
| **1** | 0 | 0.75 | 82 |
| **2** | 0.5 | 0.76 | 87 |
| **3** | 1.5 | 0.92 | 88 |
| **4** | 2 | 0.79 | 81 |
| **5** | 3 | 1.08 | 85 |
| **6** | 4 | 0.69 | 88 |

[a] The reaction was performed with equivalent molar ratio of monomers at 140°C in a nitrogen atmosphere for 21 h and subsequently under vacuum (60 mmHg) at 140°C for 3 h.
[b] Measured at a concentration of 0.1 g/dL in $CHCl_3$ at 30°C.

**TABLE II**
**Effect of the Polymerization Temperature and Polymerization Time on the $\eta_{inh}$ and $T_g$ on Polymer 3 Prepared by Polymerization of *N*-CBz-Hpr 1 and ε-Caprolactam 2[a]**

| | Polymerization | | | | |
|---|---|---|---|---|---|
| Run | Time (h) | Temperature (°C) | $\eta_{inh}$ (dL/g)[b] | $T_g$ (°C) | Yield (%) |
| **A** | 24 | 140 | 1.08 | — | 85 |
| **B** | 24 | 170 | 1.54 | 62 | 80 |
| **C** | 24 | 200 | 1.04 | 28 | 42 |
| **D** | 8 | 170 | 0.60 | 49 | 68 |
| **E** | 16 | 170 | 0.87 | 64 | 73 |
| **F** | 40 | 170 | 1.20 | 50 | 71 |
| **G** | 48 | 170 | 0.98 | 61 | 80 |

[a] The reaction was performed with equivalent molar ratio of monomers, using 3 wt % Sn(II) Oct. as a catalyst.
[b] Measured at a concentration of 0.1 g/dL in $CHCl_3$ at 30°C.

To study the effect of polymerization time on the $\eta_{inh}$, *N*-CBz-Hpr **1** was polymerized with CLM **2** at different times of 8, 16, 24, 40, and 48 h, respectively (Table II, Runs **B, D, E, F,** and **G**). The results indicated that the $\eta_{inh}$ of the polymers ranged from 0.60 to 1.54 dL/g. The $\eta_{inh}$ increased from 0.60 to 1.54 dL/g when the reaction time increased from 8 to 24 h (Runs **B, D,** and **E**). The $\eta_{inh}$ of the copolymers reached a maximum at a reaction time of 24 h (Run **B**). However, thereafter the $\eta_{inh}$ gradually decreased with time (Runs **F** and **G**). On the basis of these findings, all the subsequent polymerization reactions were performed with 3 wt % Sn(II) Oct. as catalyst at 170°C for 24 h.

The influence of the feed ratio of the monomers on the copolymerization is summarized in Table III. The copolymerization of *N*-CBz-Hpr **1** and CLM **2** was investigated over a wide range of feed ratios. By increasing CLM feed from 10 to 50 mol %, an increase in $\eta_{inh}$ from 0.83 to 1.54 dL/g was observed (copolymers **3A–3D**). If an amount greater than 50 mol % (from 50 to 80 mol %) of CLM was fed in the polymerization, the resulting copolymers have a decrease in $\eta_{inh}$ from 1.54 to 0.66 dL/g (copolymers **3D–3F**). Similar results have been observed for the *N*-CBz-Hpr/L-lactide system.[18]

The compositions of copolymers were analyzed by $^1$H-NMR. The amounts of comonomer incorporated into the copolymer could be calculated by comparing the integrated areas of the absorption peaks at δ 5.29 ppm of the methine proton ($C_4$–H) of the proline with the absorption peaks δ 1.65–1.20 ppm of the methylene protons ($C_3$, $C_4$, and $C_5$) of the CLM. The mole ratio percentages of the comonomers incorporated into the

**TABLE III**
**Results of the Melt Copolymerization of *N*-CBz-Hpr 1 and ε-Caprolactam 2[a]**

| | *N*-CBz-Hpr/CLM | | | | |
|---|---|---|---|---|---|
| Copolymer 3 | Monomer Composition in Feed (mol %) | $^1$H-NMR Composition Copolymer (mol %) | $\eta_{inh}$ (dL/g)[b] | $T_g$ (°C) | Yield (%) |
| **3A** | 90/10 | 93/7 | 0.83 | 77 | 80 |
| **3B** | 80/20 | 89/11 | 1.35 | 71 | 91 |
| **3C** | 70/30 | 82/18 | 1.29 | 73 | 75 |
| **3D** | 50/50 | 54/46 | 1.54 | 62 | 80 |
| **3E** | 30/70 | 32/68 | 0.66 | 45 | 62 |
| **3F** | 20/80 | 20/80 | 1.05 | 31 | — |

[a] The reaction was performed at 170°C for 24 h with 3 wt % Sn(II) Oct. as a catalyst.
[b] Measured at a concentration of 0.1 g/dL in $CHCl_3$ at 30°C.

copolymers are shown in Table III. These results show that the degree of polymerization of the monomers is close to that of the corresponding feeds. However, the mole fraction of *N*-CBz-Hpr units in the copolymer was higher than that in the monomer feed, which may result from the higher reactivity of *N*-CBz-Hpr compared with that of CLM.

### Thermal Analysis

The thermal properties of the copolymers were investigated by differential scanning calorimetry (DSC). The $T_g$'s of the copolymers are shown in Table III. According to DSC, all the copolymers were amorphous. By increasing the content of CLM incorporated into the copolymers, a decrease in $T_g$ of the copolymers was observed. The values of $T_g$ decreased from 77 to 31°C when the mole ratio percentage of CLM increased from 7 to 80 mol % (copolymers **3A–3F**). This is attributed to the fact that CLM can be considered a soft component compared with *N*-CBz-Hpr. Therefore, when a larger amount of flexible linkages, such as methylene groups, were incorporated into the macromolecular backbone, there was a decrease in the $T_g$. A similar tendency was observed in *N*-CBz-Hpr/ε-caprolactone (ε-CL) copolymers.[19] However, the $T_g$ of the copoly(*N*-CBz-Hpr/CLM) is higher than that of the copoly(*N*-CBz-Hpr/ε-CL), which may be a result of the linkage of the amide being more rigid than that of the ester.

### Structure Characterization

Representative $^1$H-NMR spectra of the copolymer *N*-CBz-Hpr/CLM (with monomer compositions 54/46 mol %, **3D**) and the homopolymer of *N*-CBz-Hpr are shown in Figure 1. Representative characteristic absorption peaks of CLM at δ 1.65–1.20 ppm were observed. Characteristic absorption peaks of copoly(*N*-CBz-Hpr/CLM) at δ 7.28–7.20 ppm (attributed to the protons of aromatic rings of the CBz protecting group), δ 5.29–5.06 ppm (attributed to the $C_4$ methine proton of the Hpr and the benzylic protons of the CBz protecting group), δ 4.41–4.15 ppm (attributed to the $C_2$ methine proton of the Hpr and the proton of nitrogen of the CLM), δ 3.80–3.15 ppm (attributed to the $C_5$ methylene protons of Hpr and the $C_6$ methylene protons of the CLM), δ 2.39–1.80 ppm (attributed to the $C_3$ methylene protons of Hpr and the $C_2$ methylene protons of the CLM), and δ 1.65–1.20 ppm (attributed to the $C_3$, $C_4$, and $C_5$ methylene protons of CLM) were exhibited. The representative IR spectrum of the copoly(*N*-CBz-Hpr/CLM) (with monomer composition 54/46 mol %, **3D**) and poly(*N*-CBz-Hpr) are shown in Figure 2. An absorption band at 1740 $cm^{-1}$ was assigned to the ester carbonyl group. Absorption bands at 1650 and 1543 $cm^{-1}$ were assigned to amide I and amide II, respectively. The spectrum of the copolymer shows characteristic absorptions of the copolyesteramide; that is, the absorption band of the ester carbonyl group is shifted to a lower wavenumber compared with that of poly(*N*-CBz-Hpr) (1745 $cm^{-1}$), whereas the absorption band of the amide groups is shifted to a higher wavenumber compared with that of poly(CLM) (1640 and 1541 $cm^{-1}$).

### Solubility Test

A qualitative survey of the solubilities of the polymers obtained is given in Table IV. Copolymers were soluble in tetrahydrofuran (THF) and chloroform ($CHCl_3$), but insoluble in diethyl ether and water. The behaviors were different with poly(CLM)s (insoluble in THF and $CHCl_3$) and poly(*N*-CBz-Hpr) (soluble in diethyl ether). It can be concluded that the products are copoly(*N*-CBz-Hpr/CLM) and not a blend of homopolymers. In this series, the solubilities in methanol and acetone depend on the composition of the copolymers. In the case of a higher proportion of *N*-CBz-Hpr units, the copolymers were soluble in methanol and acetone because poly(*N*-CBz-Hpr) is soluble in both methanol and acetone.

### Preliminary *In Vitro* Degradation Study

The *in vitro* degradation of the N-protected poly(*N*-CBz-Hpr-*co*-CLM) was evaluated from weight loss of

**TABLE IV**
**Solubility of Copoly(*N*-CBz-Hpr/CLM), Poly(*N*-CBz-Hpr), Poly(CLM), and ε-CLM**

| Solvent | *N*-CBz-Hpr/CLM | | | Poly(*N*-CBz-Hpr) | Poly(CLM) | ε-CLM[c] |
|---|---|---|---|---|---|---|
| | 89/11[b] | 54/46[b] | 20/80[b] | | | |
| Methanol | + | + | − | + | − | ++ |
| Tetrahydrofuran | ++ | ++ | ++ | ++ | − | ++ |
| Chloroform | ++ | ++ | ++ | ++ | − | ++ |
| Acetone | ++ | + | − | ++ | − | ++ |
| Diethyl ether | − | − | − | ++ | − | ++ |
| Water | − | − | − | − | − | ++ |

[a] ++, soluble; +, partially soluble; −, insoluble.
[b] Mole ratio.
[c] See Ref. 5.

the sample. The degradation profile of the protected poly(*N*-CBz-Hpr-*co*-CLM) with monomer compositions of 90/10 mol % at 37°C under physiological conditions (pH 7.4) is shown in Figure 3. The results indicate that the degree of degradation shows a slow increase with time. Comparing the degradation of the copolymers of the poly(*N*-CBz-Hpr-*co*-CLM) with that of poly(*N*-CBz-Hpr-*co*-L-lactide)[18] and poly(*N*-CBz-Hpr-*co*-ε-CL)[19] with the same monomer composition (90/10 mol %), it seems that the order of degradation rate is: poly(*N*-CBz-Hpr-*co*-ε-CL) > poly(*N*-CBz-Hpr-*co*-L-lactide) > poly(*N*-CBz-Hpr-*co*-ε-CLM). The major reason is that the hydrolysis of the ester bonds in the poly(*N*-CBz-Hpr-*co*-ε-CL) is easier than that of the ester bonds in poly(*N*-CBz-Hpr-*co*-L-lactide) and of the ester (or amide) bonds in poly(*N*-CBz-Hpr-*co*-ε-CLM).

## CONCLUSIONS

A series of copolyesteramides [copoly(*N*-CBz-Hpr/CLM)] with various compositions were synthesized from *trans*-4-hydroxy-*N*-benzyloxycarbonyl-L-proline and ε-caprolactam. Properties of the copolymers ($T_g$ and $\eta_{inh}$) were found to be directly dependent on the content of pseudoamino acid added to the polymerization mixture. The $T_g$'s of the copolymers shift to a higher temperature with increasing contents of the pseudoamino acid. These copolyesteramides could be degraded under physiological conditions. The polymers may be promising materials for agricultural or biomedical applications.

The authors are grateful to Huang Shou-Ling and Kao Chung-Shen (Advanced Instrumentation Center, National

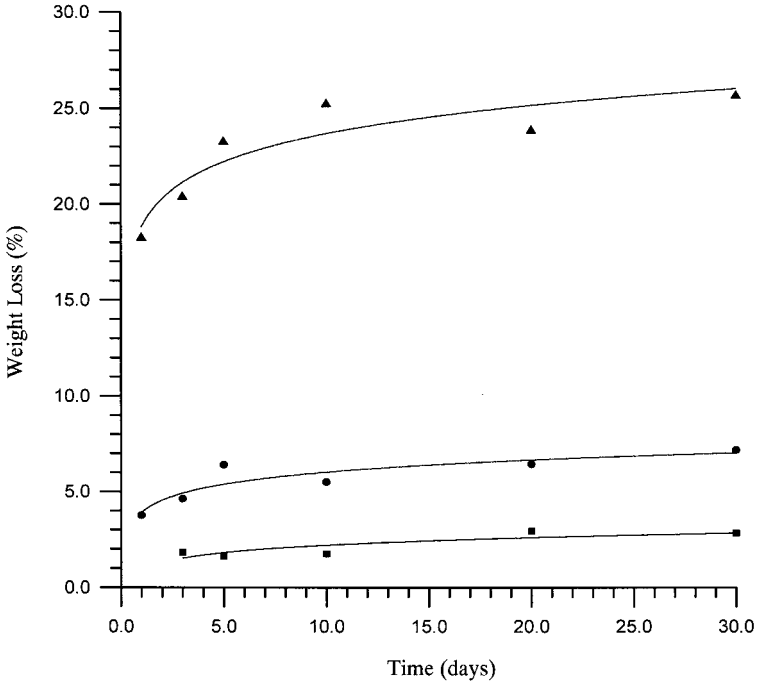



**Figure 3** Weight loss of copoly(*N*-CBz-Hpr/ε-CL) (▲), copoly(*N*-CBz-Hpr/L-lactide) (●), and copoly(*N*-CBz-Hpr/ε-CLM) (■) with molar ratio 90/10 mol %, in which it was treated in M/15 phosphate buffer solution (pH 7.4) at 37°C.

Taiwan University) for obtaining $^1$H-NMR spectra and DSC measurements. They are also thankful for grants from the National Science Council and Chang Gung University.

## REFERENCES

1. Swift, G.; Creamer, M.; Wei, X.; Yocom, K. Macromol Symp 1998, 130, 379.
2. Bera, S.; Jedlinski, Z. J Polym Sci Part A: Polym Chem 1993, 31, 731.
3. Arvanitoyannis, I.; Nakayama, A.; Kawasaki, N.; Yamamot, N. Makromol Chem 1994, 222, 111.
4. Thomas, H. B. in Bioabsorbable Poly(ester-amide)s; Shalaby, W. S., Ed.; Biomedical Polymer Designed-to-Degrade System; Hanser: Munich, 1994; p 97.
5. Kawasaki, N.; Nakayama, A.; Maeda, Y.; Hayaski, K.; Yamamoto, N.; Aiba, S. I. Macromol Chem Phys 1998, 199, 2445.
6. Demicheli, A.; Russo, S.; Mariani, A. Polymer 2000, 41, 1481.
7. Fan, Y.; Kobayashi, M.; Kise, H. Polym J 2000, 32, 817.
8. Nagata, M.; Kiyotsukuri, T. Eur Polym J 1992, 28, 1069.
9. Saotome, Y.; Miyazawa, T.; Endo, T. Chem Lett 1991, 21.
10. Saotome, Y.; Tashiro, M.; Miyazawa, T.; Endo, T. Chem Lett 1991, 153.
11. Paredes, N.; Rodriguez-Galan, A.; Puiggali, J. J Polym Sci Part A: Polym Chem 1998, 36, 1271.
12. Deng, X. M.; Yao, J. R.; Yuan, M. L.; Li, X. H.; Xiong, C. D. Macromol Chem Phys 2000, 201, 2371.
13. Kwon, H. Y.; Langer, R. Macromolecules 1989, 22, 3250.
14. Lee, R. S.; Yang, J. M.; Huang, K. H. Polym J 1999, 31, 569.
15. Lee, R. S.; Yang, J. M. J Polym Sci Part A: Polym Chem 2000, 38, 2445.
16. Lee, R. S.; Yang, J. M. J Polym Sci Part A: Polym Chem 2001, 39, 724.
17. Lee, R. S.; Yang, J. M. J Appl Polym Sci 2001, 81, 1581.
18. Lee, R. S.; Yang, J. M. J Polym Res, to appear.
19. Lee, R. S.; Yang, J. M. Unpublished results, 2002.