Polycaprolactone-Modified Hydroxyethylcellulose Films Prepared by Lipase-Catalyzed Ring-Opening Polymerization

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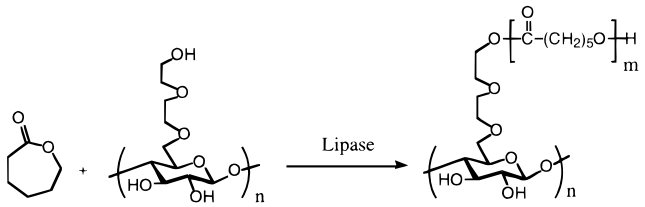
Introduction

Polyesters and polysaccharides represent two traditional and most useful hydrophobic and hydrophilic polymers, respectively. Polysaccharides such as cellulose, in its various forms, constitute about half of all of the polymers consumed industrially in the world. Polyesters such as poly(ϵ-caprolactone) and poly(lactic acids) play important roles in the design of biodegradable and biocompatible polymers[1] in the field of day-to-day-based plastics as well as biomedical materials, for instance, polymer scaffolds for tissue engineering. Synthesis of hydrophobic−hydrophilic biodegradable polymers[2] containing polyesters and polysaccharides will impart novel physical properties to materials which can be used in injection molding operations for shaped articles, biodegradable detergents, compatibilizers for polymer blends, and water-repellent materials or oil absorbents.

There has been a considerable interest in polymerization catalyzed by enzymes as a new methodology for synthesis of well-defined functional polymers.[3] Lipase-catalyzed ring-opening polymerizations of lactones have provided a different array of polyesters in bulk as well as in organic media.[4−10] Recently, this special type of ring-opening polymerization for regioselective acylation of monosaccharides such as glucoside and galactoside has presented a unique method to incorporate hydrophilic sugar headgroups with hydrophobic polyester chains.[11,12] Unlike monosaccharides, polysaccharides are a difficult class of materials for chemical and enzymatic processing because of the presence of many reactive hydroxy groups and the class's poor solubility in non-aqueous solvents. Although chemical modification of cellulose derivatives using graft copolymerization has been extensively studied,[13,14] few studies have been reported on the enzymatic modification of polysaccharides in organic solvents. A recent report representing the first attempt for the modification of solvent-insoluble polymer using enzymes such as subtilisin Carlsberg in organic solvents provides a new approach for polysaccharide modification.[15]

In the present paper, we demonstrate that hydroxyethylcellulose (HEC) as an organic solvent-insoluble polysaccharide derivative, when deposited as a film, can be grafted by ϵ-caprolactone in bulk using lipases derived from porcine pancreas (PPL) and from a thermophilic CLONEZYME ESL-001 library which was previously shown to be effective for the formation of optically active (*R*)-enriched poly(3-hydroxybutyrate)[10] (Scheme 1).

Scheme 1. Proposed Structure of Polycaprolactone-Modified HEC via Lipase-Catalyzed Lactone



Experimental Section

Materials. Chemicals were purchased from Aldrich and Sigma and were reagent grade. Natrosol hydroxyethylcellulose 250LR was from Hercules, Inc. Porcine pancreatic lipase (PPL) (E.C.3.1.1.3) (Sigma Chemical Co.) and a thermophilic CLONEZYME ESL-001 lipase library (Diversa, Inc., San Diego, CA) were dried in a vacuum desiccator before use. ϵ-Caprolactone (99+%) was obtained from Aldrich and used as received. An HEC film was prepared by depositing HEC 7% (w/w) aqueous solution (250 μL) on the bottom of a 20-mL vial and casting by spinning and using high vacuum followed by drying in an oven.

Graft Polymerization of ϵ-Caprolactone on HEC To a 20-mL vial with a film of HEC deposited on the bottom was added pre-dried enzyme, as well as ϵ-caprolactone which was 100-fold molar excess to the HEC hydroxyl groups. The reaction vial was capped tightly and placed still or shaken in an incubator at 60 °C (in the presence of PPL) for 3−5 days or at 75 °C (in the presence of CLONEZYME library) for 3 days. All of the reactions were stopped by removing the solid film and washing it with chloroform. The solid film was extracted with chloroform in a Soxlet reflux apparatus for at least 24 h to remove any homopolymer that may have formed.

Characterization and Analysis. FT-IR spectra of the films were recorded on NaCl plates using a Perkin-Elmer 1600 series spectrometer at ambient temperature. High-resolution ^{1}H and ^{13}C NMR spectra were obtained using a Varian VMR 400-MHz NMR spectroscopy at ambient temperature in D_2O. Thermal analysis of the graft copolymers was carried out using V5.1A thermogravimetric analysis (TGA) (DuPont 2200) under either a nitrogen or compressed air atmosphere. The heating rate was 10 °C/min.

Results and Discussion

FT-IR spectroscopy was used to identify whether enzymatic grafting of HEC occurred. A comparison of the spectrum of PPL lipase-treated HEC (3 days) to that of parent HEC at the same reaction condition without lipase shows a new peak in the region around 1730 cm^{-1} corresponding to a C═O group in ester in the enzymatic treated film (Figure 1). In proton NMR spectra, two obvious signals at 2.33 and 4.18 ppm were corresponding to α-H next to carbonyl group and alkoxyl H next to ester (Figure 2). The signals between 20 and 40 ppm in the ^{13}C NMR spectra indicated the presence of alkyl groups from lactone (Figure 3). The approximate sub-

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Table 1. Degree of Substitution Resulted from Lipase-Catalyzed ϵ-Caprolactone Ring-Opening Polymerization on Hydroxyethylcellulose (HEC) Backbone[a]

	ESL-01	ESL-02	ESL-03	ESL-04	ESL-05	ESL-02	PPL
degree of substitution (DS)	0.17	0.32	0.21	0.23	0.10	0.16	0.18

[a] All of the reactions were carried out for 3 days at 75 °C except PPL at 60 °C.

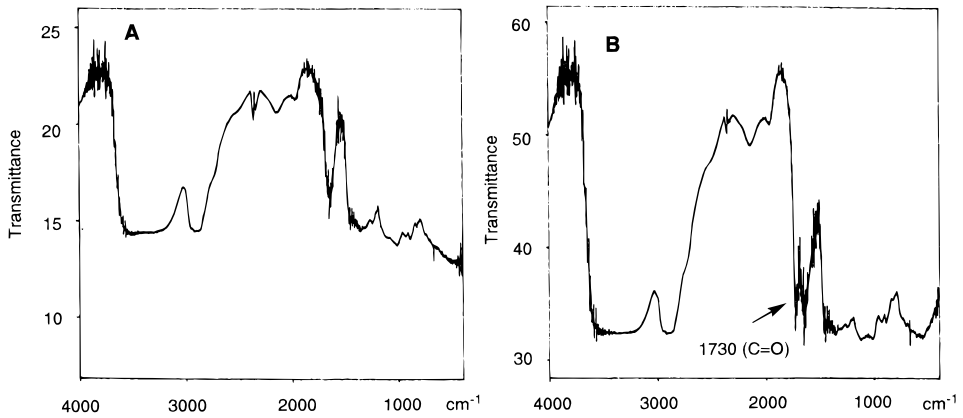

Figure 1. FT-IR spectra of (A) native HEC and (B) polycaprolactone-modified HEC.

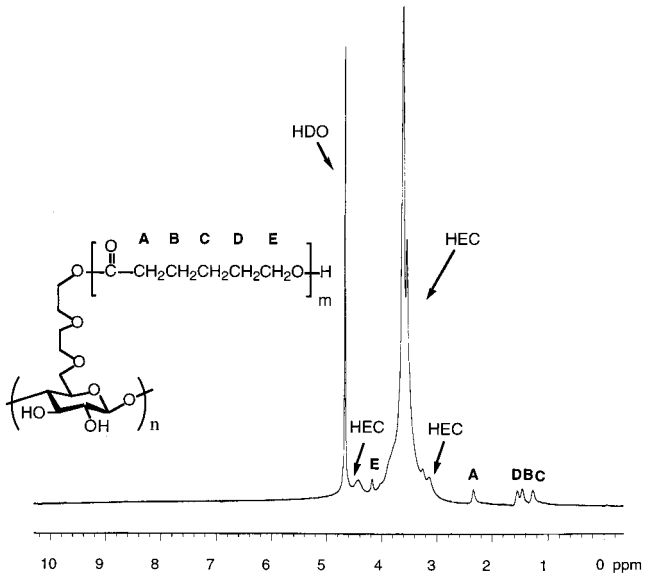

Figure 2. Proton NMR spectrum (400 MHz) of polycaprolactone-modified HEC in D_2O at room temperature.

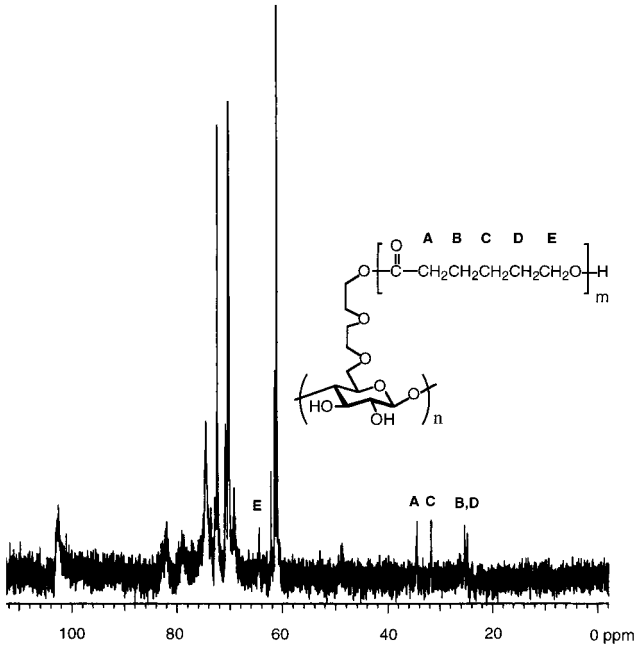

Figure 3. ^{13}C NMR spectrum (100 MHz) of polycaprolactone-modified HEC in D_2O at room temperature.

stitution was also calculated from the proton NMR integration ratio between the protons such as α-H from lactone and the total protons from HEC. The degree of substitution (DS) designated the average number of hydroxyl groups on the anhydroglucose ring that have been reacted with ϵ-caprolactone. The DS value was determined by taking the integration of all of the nonexchangeable protons of each anhydroglucose unit (7 H for a pyranose ring and 10 H for ethylene oxide units with degree of substitution of 2.5 in parent HEC 250LR) and comparing it to the two α-H designated as proton A in ϵ-caprolactone.

For HEC modified in the presence of PPL at 60 °C for 3 days, 74 monomeric ϵ-caprolactone units were grafted on the HEC. That indicated ca. 0.18 monomers were associated with each anhydroglucose unit. The degree of substitution is comparable to that of a recent study on subtilisin-catalyzed acylation of insoluble amylose in organic solvent, in which DSs of 0.15 and 0.30 were reported.[15] The low substitution was due to the small amount of accessible hydroxyl groups on the surface of the films exposed to enzymes. Graft copolymerization of ϵ-caprolactone was screened against six enzymes in a thermophilic CLONEZYME lipase library. The reactions for thermophilic enzymes were carried out at their optimal temperature around 75 °C. The DS values were comparable to PPL-catalyzed graft reactions (Table 1).

The materials prepared by model reaction using PPL were also characterized by thermogravimetric analysis that further confirmed the presence of polycaprolactone (Figure 4). The decomposition of native HEC under compressed air atmosphere was shown by a weight loss starting at 200 °C and ending at 365 °C. It clearly indicated that polycaprolactone-modified HEC had a weight loss around 430 °C under air atmosphere, which was characteristic of the degradation of polycaprolactone backbone and was absent in native HEC. The degree of the substitution in the HEC film was further deter-

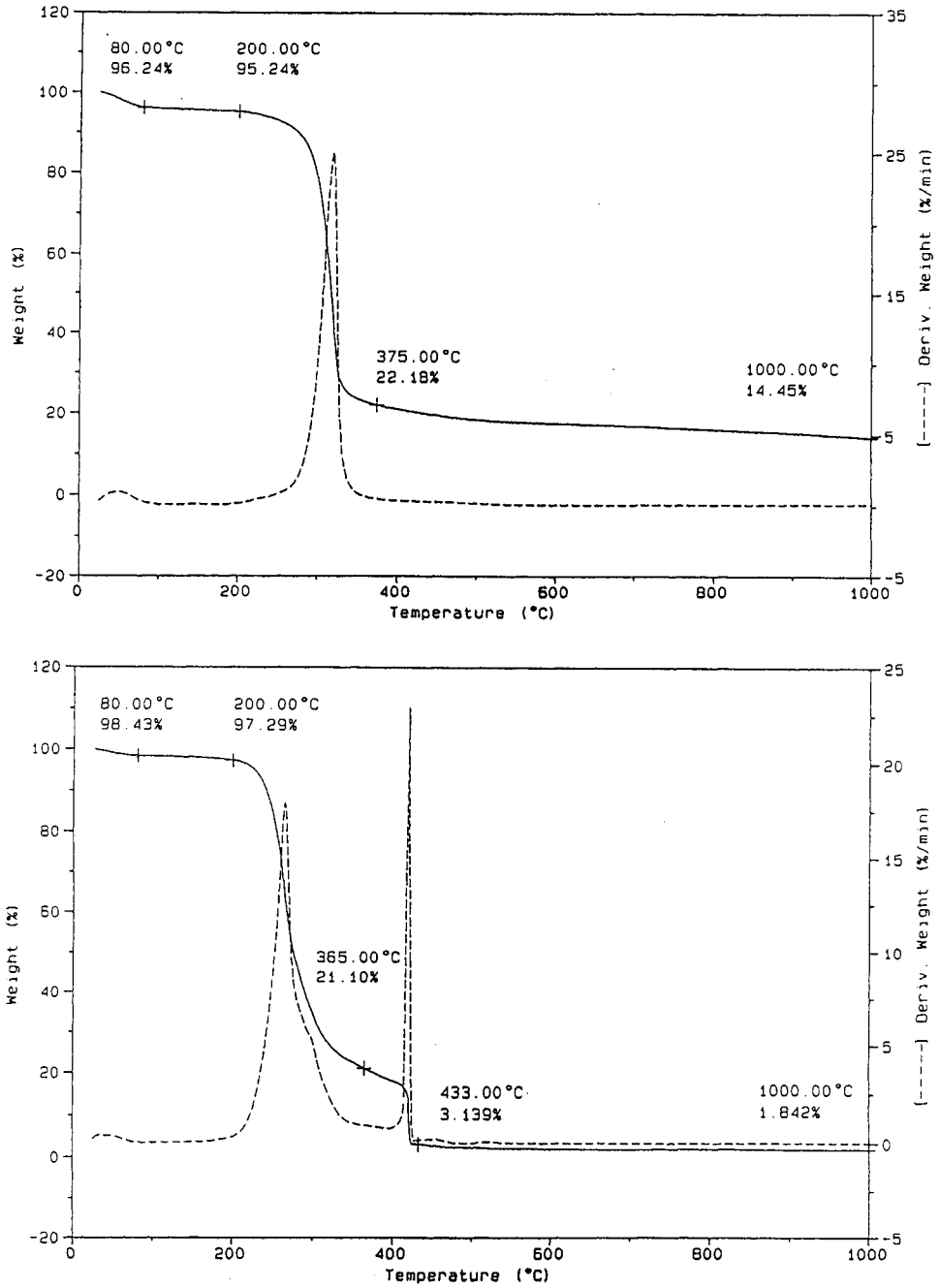

Figure 4. Thermogravimetric analysis of (top) native and (bottom) polycaprolactone-modified HEC. Programmed scan at 10 °C/min under compressed air atmosphere.

mined by TGA. From the TGA profile of caprolactone-grafted HEC, quantification of the weight loss resulted in a DS value of ca. 0.35.

In summary, this work demonstrates that lipase-catalyzed ring-opening graft copolymerization can be employed to graft hydrophobic polyesters onto hydrophilic cellulose-based polymers. The reaction resulted in polyester grafted HEC with DSs between 0.10 and 0.32 in terms of per anhydroglucose unit. This polyester-modified HEC films may find a variety of practical applications.

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References and Notes

(1) Li, S.; Vert, M. *Biodegradation of Aliphatic Polyesters.* in *Degradable Polymers, Principles & Applications* Scott, G., Gilead, D., Ed.; Chapman & Hall: London, 1995 and references herein.

(2) Huang, S. J.; Onyari, J. M. *J. Macromol. Sci., Pure Appl. Chem.* **1996**, *A33* (5), 571.

(3) Kobayashi, S.; Shoda, S.; Uyama, H. *Adv. Polym. Sci.* **1995**, *121*, 1.

(4) Knani, D.; Gutman, A. L.; Kohn, D. H. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1221.

(5) Uyama, H.; Kobayashi, S. *Chem. Lett.* **1993**, 1149.

(6) Uyama, H.; Kikuchi, H.; Kobayashi, S. *Chem. Lett.* **1995**, 1047.

(7) MacDonald, R. T.; Pulapura, S. K.; Svirkin, Y. Y.; Gross, R. A.; Kaplan, D. L.; Akkara, J.; Swift, G.; Wolk, S. *Macromolecules* **1995**, *28*, 73.
(8) Hendersson, L. A.; Svirkin, Y. Y.; Gross, R. A.; Kaplan, D. L.; Swift, G. *Macromolecules* **1996**, *29*, 7759.
(9) Bisht, K. S.; Hendersson, L. A.; Gross, R. A.; Kaplan, D. L.; Swift, G. *Macromolecules* **1997**, *30*, 2705.
(10) Xie, W.-H.; Li, J.; Chen, D.-P.; Wang, P. G. *Macromolecules* **1997**, *30*, 6997.
(11) Bisht, K. S.; Deng, F.; Gross, R. A.; Kaplan, D. L.; Swift, G. *J. Am. Chem. Soc.* **1998**, *120*, 1363.
(12) Cordova, A.; Iversen, T.; Hult, K. *Macromolecules* **1998**, *31*, 1040.
(13) Narayan, R.; Tsao, T. G. Anionic Graft Polymerization onto Cellulose. *Cellulose Structure, Modification and Hydrolysis*; Young, R. A., Rowell, R. M., Eds.; John Wiley and Sons: New York, 1986; p 177.
(14) McCormick, C. L.; Dawsey, T. R. *Macromolecules* **1990**, *23*, 3606.
(15) Bruno, F. F.; Akkara, J. A.; Ayyagari, M.; Kaplan, D. L.; Gross, R.; Swift, G.; Dordick, J. S. *Macromolecules* **1995**, *28*, 8881.

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