Cyclodextrin-Initiated Polymerization of Cyclic Esters in Bulk: Formation of Polyester-Tethered Cyclodextrins

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Cyclodextrins (CDs) attracted much attention of chemists as enzyme models, because of their unique inclusion properties and selective reactivities.[1-3] However, the model reactions of esters catalyzed by CDs have been limited to the hydrolysis of activated esters and there are few reports on the utilization of CDs as synthetic reagents.[4-6] Now we have found that CDs selectively initiated the polymerization of cyclic esters to give polyesters and that the polyesters have CD at the chain end.

Previously we reported that CDs form inclusion compounds with aliphatic polyesters, such as poly(ϵ-CL) (ϵ-CL; ϵ-caprolactone)[7a,b] and poly(ethyleneadipate).[7c] We also found that these polyesters could be easily hydrolyzed into their monomeric state in their inclusion compounds with CDs in water. Later, other researchers reported that some other polyesters are included in CDs.[8,9] Moreover, we found and reported that CDs selectively form inclusion complexes with some lactones (the starting materials of the polyesters) and that the hydrolysis of some lactones is promoted or suppressed according to the sizes of CDs.[10] We suppose that lactones might be polymerized when the reactions are carried out in the presence of CD without water. To the best of our knowledge, the catalytic activities of sugars and CDs on the polymerization of esters have not been reported (eq 1).

(1)
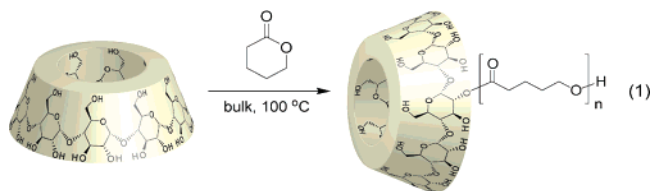
When the mixture of β-cyclodextrin (β-CD) dried at 80 °C in a vacuum and δ-valerolactone (δ-VL) was heated at 100 °C under an argon atmosphere, poly(δ-VL) was obtained in high yield (over 98% after 48 h), although δ-VL did not give any polymers under the same conditions without CDs (Figure 1). γ-Cyclodextrin (γ-CD) also gave a polymer but in a lower yield. By contrast, the activity of α-cyclodextrin (α-CD) was considerably lower under the same conditions. These results suggest that polymerization took place by way of the inclusion of lactone in a CD cavity. A similar tendency was observed in the case of ϵ-CL and CDs but with lower yields than δ-VL (Figure S4), which were due to the differences in reactivity of these lactones. In contrast, the order of the polymer yield of β-butyrolactone (β-BL) with CDs is β-CD (67%) > α-CD (55%) > γ-CD (7%) (Figure S7). A smaller lactone (β-BL) gave higher yields with smaller CD (α-CD), and a larger lactone (δ-VL and ϵ-CL) gave higher yields with a larger CD (γ-CD). These results indicate that the reactions took place via inclusion of cyclic esters in CD cavities.

Figure 2 shows the MALDI-TOF mass spectrum of poly(δ-VL) obtained from the mixture of β-CD and δ-VL. The spectrum shows

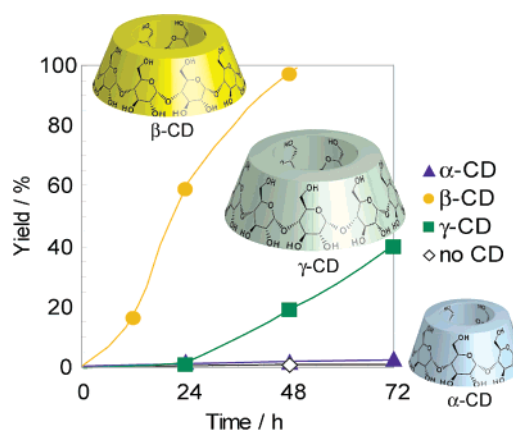**Figure 1.** A dependence of yield on time for polymerization of δ-VL initiated by various cyclodextrin in bulk at 100 °C. [δ-VL]/[CDs] = 5.
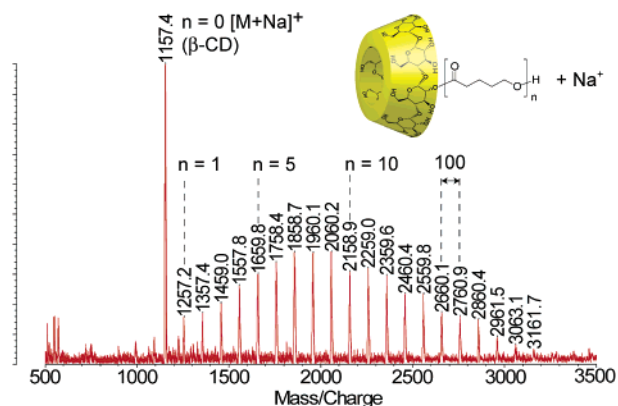
Figure 2. The MALDI-TOF mass spectrum of β-CD attached to poly-(δ-VL) obtained from the mixture β-CD and δ-VL.

that each signal appears at intervals of 100 amu (δ-VL monomer unit) from the signal of β-CD and that there are no other signals at lower molecular weight than β-CD. This indicates that each polymer has a single β-CD at the end of the polymer chain. Poly(ϵ-CL) and poly(β-BL) gave similar results (Figures S5, S6, S8, and S9). The ^{1}H NMR spectrum of the product was shown in Figure 3. Resonances for C2′*H* and C3′*H* of the glucose unit having poly-(δ-VL) appeared at 4.05 and 3.75 ppm, respectively. The chemical shifts have been compared with those of a reference compound, mono-2-*O*-(6-benzoxypentanol)-β-CD, prepared from β-CD and *m*-nitrophenyl 5-benzyloxypentanoate. The structure of the product was confirmed that the polymer chain was attached at C2 as a pendant. The integral values of the glucose residue with poly-(δ-VL) and the other native glucose residue showed the ratio of 1:6, indicating that the product was mono-2-substituted β-CD.

To gain some insights into the mechanism of the polymerization of lactones, we carried out polymerization of δ-VL with some
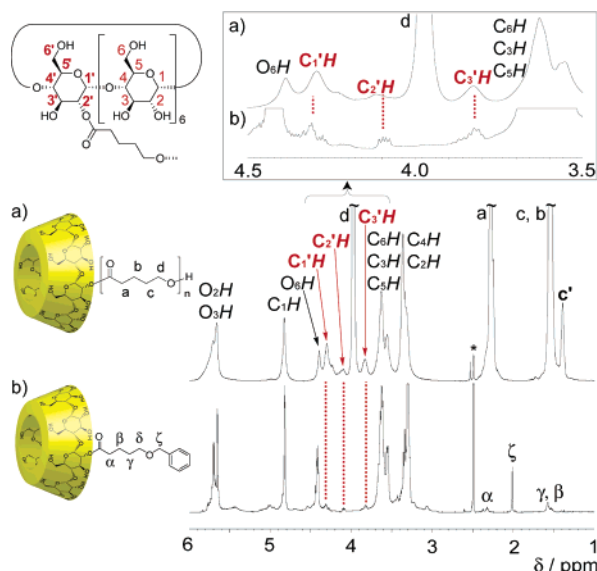
Figure 3. The ^{1}H NMR spectrum of β-CD attached to poly(δ-VL) obtained from the mixture β-CD and δ-VL (a), and the spectrum of mono-2-*O*-(6-benzoxypentanoyl)-β-CD (b) in DMSO-d_6.

Scheme 1
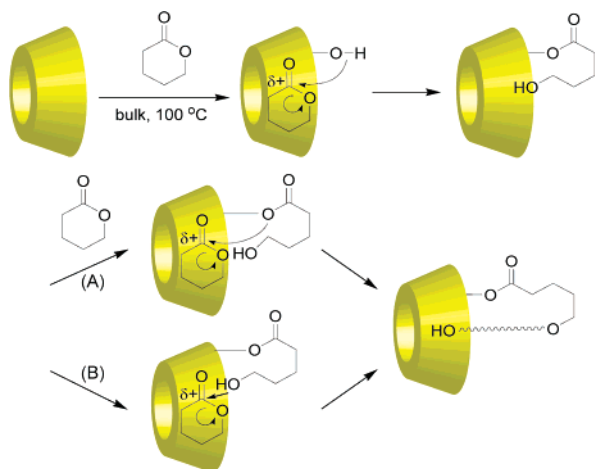
derivatives. First of all, methanol is inactive in polymerization under the same conditions (Figures S10 and S11). 2,6-Di-*O*-methyl-β-CD and 2,3,6-tri-*O*-acetyl-β-CD showed no reactivity for the polymerization of lactones (Figure S12). These results indicate that the inclusion of lactones in the CD cavity and C2 hydroxyl groups play important roles for the initiation of the polymerization. CDs were found to form inclusion complexes at 100 °C without water. Scheme 1 shows possible mechanisms for the polymerization of lactones. The first step is the complex formation of cyclic esters with CD to give a 1:1 inclusion complex. Then OH-2 of CDs should attack the carbonyl carbon of the included cyclic esters, cleaving the C–O bond to form a CD-O(2)-ester. The FT-IR spectra of lactones showed that the guest molecules included were activated by the inclusion in the CDs cavity.

Two plausible routes for the propagation step are shown in Scheme 1. In pathway A, O′-2 of the glucose unit attached to a polymer attacks the carbonyl carbon of the included esters and cleaves the C–O bond. In pathway B, a hydroxyl group at the end of the poly(lactone) attacks the carbonyl carbon of the included cyclic esters. Continuous inclusion and insertion of the cyclic esters yield linear poly(lactone)s with CDs. However, pathway B is unlikely, because mono-2-*O*-(6-benzoxypentanoyl)-β-CD was found to initiate polymerization of δ-valerolactone even when there is no hydroxyl end group (Table S1 and Figure S17). The integral values of the glucose residue with poly(δ-VL) and the other natural glucose residue showed a ratio of 1:6.

In conclusion, a series of CDs were found to initiate the polymerization of cyclic esters selectively without any cocatalysts and cosolvents. The products are polyesters with CD at the end of the chain. Detailed investigation of the polymerization mechanism is now under way using various CD derivatives. This study should contribute to the development of environmentally benign polymers and catalysts using CDs.

Supporting Information Available: Polymerization of ϵ-CL and β-BL with α-CD, β-CD, γ-CD, modified CDs, and methanol. MALDI-TOF MS spectra of β-CD attached poly(δ-VL) and poly(ϵ-CL), γ-CD attached poly(δ-VL) and poly(ϵ-CL), α-CD attached poly(β-BL), and β-CD attached poly(β-BL). Experimental procedures and characterization for mono-2-*O*-(6-benzoxypentanoyl)-β-CD and β-CD attached poly(δ-VL). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) *Comprehensive Supramolecular Chemistry, Vol. 3. Cyclodextrins*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Eds.; Pergamon: Oxford, 1996. (b) Cyclodextrins: Special Issue. *Chem. Rev.* **1998**, *5*.

(2) (a) VanEtten, R. L.; Sebastian, J. F.; Clowes, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242–3253. (b) VanEtten, R. L.; Sebastian, J. F.; Clowes, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3253–3262. (c) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer: Berlin, 1978. (d) Bender, M. L.; Bergeron, R. J.; Komiyama, M. "The Bioorganic Chemistry of Enzymatic Catalysis" Wiley, New York, 1984.

(3) (a) Czarniecki, M. F.; Breslow, R. *J. Am. Chem. Soc.* **1978**, *100*, 7771–7772. (b) Breslow, R.; Czarniecki, M. F.; Emert, J.; Hamaguchi, H. *J. Am. Chem. Soc.* **1980**, *102*, 762–770. (c) Breslow, R.; Trainor, G. L.; Ueno, A. *J. Am. Chem. Soc.* **1983**, *105*, 2739–2744. (d) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 317–324.

(4) (a) Yoshio, T.; Sakuraba, T.; Nakanishi, H. *J. Chem. Soc. Chem. Commun.* **1983**, *17*, 947–948. (b) Sakuraba, H.; Nakai, T.; Tanaka, Y. *J. Inclusion Phenom.* **1984**, *2*, 829–839.

(5) (a) Trost, B. M.; Van Vranken, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 1261–1263. (b) Trost, B. M.; Van Vranken, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444–458.

(6) (a) Harada, A.; Hu, Y.; Takahashi, S. *Chem. Lett.* **1986**, 2083–2084. (b) Hu, Y.; Harada, A.; Takahashi, S. *Synth. Commun.* **1983**, 1051–1052.

(7) (a) Harada, A.; Kawaguchi, Y.; Nishiyama, T.; Kamachi, M. *Macromol. Rapid Commun.* **1997**, *18*, 535–539. (b) Kawaguchi, Y.; Nishiyama, T.; Okada, M.; Kamachi, M.; Harada, A. *Macromolecules* **2000**, *33*, 4472–4477. (c) Harada, A.; Nishiyama, T.; Kawaguchi, Y.; Okada, M.; Kamachi, M. *Macromolecules* **1997**, *30*, 7115–7118.

(8) Huang, L.; Allen, E.; Tonelli, A. E. *Polymer* **1998**, *39*, 4857–4865.

(9) Weickenmeier, M.; Wenz, G. *Macromol. Rapid Commun.* **1997**, *18*, 1109–1115.

(10) Takashima, Y.; Kawaguchi, Y.; Nakagawa, S.; Harada, A. *Chem. Lett.* **2003**, *12*, 1122–1123.

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