SHORT COMMUNICATIONS

The Polymerization of γ-Methyl-L-glutamate-N-carboxyanhydride Initiated with Acetic Acid

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The rate of polymerization of *N*-carboxyanhydrides (NCAs) of α-amino acids and the molecular weight of polypeptides formed vary widely with the characteristic of reaction medium and initiator[1-3]. We have found that for the polymerization of γ-methyl-L-glutamate-NCA, acetic acid which has little or no initiating ability in one solvent, does act as an initiator in another solvent. Thus, when the NCA was dissolved in chloroform (1.07×10^{-1} mol. l^{-1}) containing acetic acid (5.35×10^{-2} mol. l^{-1}), rapid polymerization occurred, and completed within 130 min., while in dioxane solution no appreciable reaction was observed. Addition of dioxane (10% by volume) to the chloroform solution of the NCA caused an induction period of approximate 70 min. and a depression in rate (See Fig. 1). The evolution of carbon dioxide upon dissolution of the NCA in acetic acid was much slower than in the system chloroform-acetic acid. From the reaction mixture in acetic acid we were able to isolate only terminal-free low molecular weight peptide, which, according to the results of elementary analysis and optical rotation in dichloroacetic acid, had no acetyl group and was composed of 3 units of γ-methyl-L-glutamate residue. Found: C, 47.1; H, 6.71; N, 9.53. Calcd. for $(C_6H_9O_3N)_3\cdot H_2O$: C, 48.3; H, 6.49; N, 9.40%. $[\alpha]_D^{23}=17°$ (*c* 1.9). So far, no other products such as acetylated derivatives, diketopiperazine or cyclic peptide have been detected.

The fact that the degree of polymerization of the final polymer obtained in the polymerization in chloroform is much higher ($[\eta]=0.98$, $\overline{DP}=500\sim600$) than that expected from the initial NCA-initiator ratio of 2 indicates that only a small part of acetic acid was utilized as a true initiator. Therefore, the behavior of acetic acid as an initiator in chloroform solution seems to resemble somewhat that of tertiary amine.

Fig. 2 shows that two successive propagation rates exist. Similar change in propagation rate was observed in polymerizations of other NCAs[3-8] and explained either by conformational change (random or β-form to α-helix)

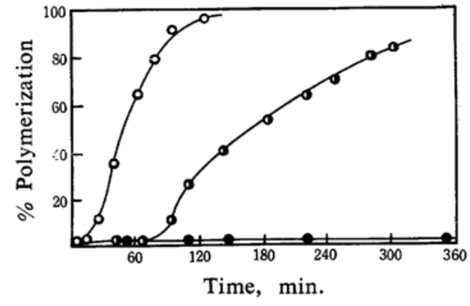

Fig. 1. Time-conversion curves for polymerization of γ-methyl-L-glutamate-NCA (1.07×10^{-1} mol. l^{-1}) indicated with acetic acid (5.35×10^{-2} mol. l^{-1}) in solution at 30°C. —○—: In chloroform, —◑—: in chloroform-dioxane (9 : 1 by volume), —●—: in dioxane.

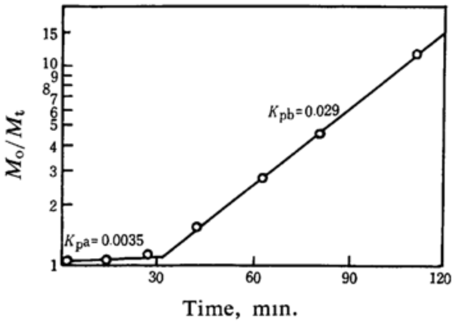

Fig. 2. The polymerization of γ-methyl-L-glutamate-NCA in chloroform at 30°C, initiated with acetic acid under the condition given in Fig. 1. The values of [NCA] initially and at time *t* are denoted by M_0 and M_t, respectively.

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in the growing polypeptide chain[4,7], or by gel effect due to precipitation of polymer or gelation[6]. In the present case, after a slow propagation rate, when about one-tenth of the NCA had been consumed the propagation shifted to a faster rate. Since the average DP of the polymer was found to be 500～600, the transition occurred when the growing polypeptide chain had reached a $\overline{\mathrm{DP}}=50\sim60$. Because this value exceeds the one necessary for the conformational transition of poly-γ-methyl-L-glutamate (15～25 residues[5]) the gel effect might be more responsible for occurrence of the two successive propagation rates.

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