

RAPID COMMUNICATIONS

Synthesis of Polyallylamine Derivatives with *N*-Carbamoylguanidine Groups

Keywords: polycationic polymer • poly(allyl-*N*-carbamoylguanidino-*co*-allylamine) • poly(allylguanidino-*co*-allylamine) • potentiometric titration • thermogravimetric analysis

INTRODUCTION

Polyallylamine is a polymer having pendant primary amino groups, and is utilized as the starting material for the synthesis of its derivatives and resins.¹ In our previous article,² the introduction of biguanide groups to this polymer was reported. We also reported that the membranes of this poly(allylbiquanido-*co*-allylamine) hydrochloride/poly(vinyl alcohol) hydrogel promoted cell growth and adhesion.³

The purpose of this communication is to develop another novel polycationic polymer. The introduction of *N*-carbamoylguanidine type base to the primary amine of polyallylamine is described.

EXPERIMENTAL

Materials

Polyallylamine hydrochloride (**1** · HCl) of $M_w = 7,500$ – $11,000$ was purchased from Nitto Boseki Co. (Japan) (sample code PAA-HCl-3S). *N*-carbamoyl-*O*-methylisourea (**2**) was synthesized according to the method developed by Iio et al.⁴ All other chemicals were of reagent grade.

Polymer Synthesis

The synthesis of polyallylamine containing *N*-carbamoylguanidine residues is outlined in Scheme 1. Polymer **1** · HCl [1.96 g (0.02 mol, water content is 5 wt %)] and **2** [2.34 g (0.02 mol)] were dissolved in 20 mL of water, and was stirred for 20 h at 45°C. The solution was acidified with dilute hydrochloric acid to pH 1 to stop the reaction, and a precipitate was filtered off. The solution was poured into an excess amount of acetone to precipitate the product. The precipitated crude polymer **3** · HCl was purified by dissolving in a minimum quantity of water and reprecipitating with acetone. Purified polymer **3** · HCl yielded

2.84 g. The elemental analysis of polymer **3** · HCl, obtained by the reaction for 20 h, was as follows.

ANAL. Calcd for $[(C_3H_8N_1Cl_1)_{0.2}(C_5H_{11}N_4O_1Cl_1)_{0.8}](H_2O)$: C, 30.76%; H, 6.96%; N, 26.51%; Cl, 19.74%. Found: C, 31.80%; H, 6.63%; N, 26.70%; Cl, 18.99%.

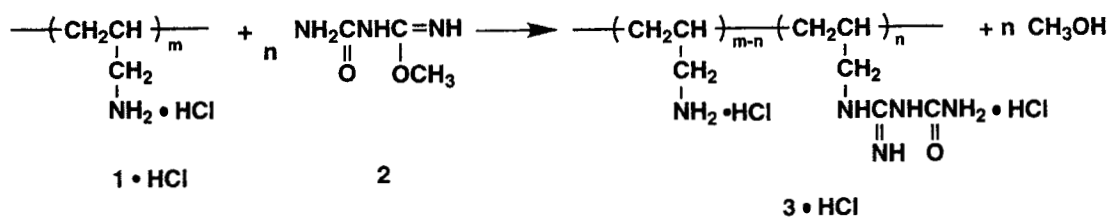
Measurements

Potentiometric titration curves were obtained by using an automatic titrator GT-05 (Mitsubishi Kasei Co.). Polymer **3** · HCl 155.4 mg [0.96 mmol; degree of substitution (DS) = 0.80] and sodium chloride 14.38 mg [2.46 mmol] were dissolved in a mixture of *N*/10 hydrochloric acid ($f = 1.002$) (10.00 mL) and distilled water (about 15 mL) in a 25.00-mL volumetric flask. This solution was titrated with 1N sodium hydroxide ($f = 1.008$) under a nitrogen atmosphere at 25°C. Polymer **1** · HCl was also titrated in a similar manner. Thermogravimetric analysis (TGA) was carried out on a Seiko Instrument TGA/DTA 320, with disk station SSC 5200, at a constant heating rate of 10°C min⁻¹ under a stream of nitrogen or dry air at 300 mL min⁻¹. Each sample (about 20 mg) was preheated for 60 min at 110°C and then cooled to room temperature under a nitrogen or dry air atmosphere. Infrared (IR) spectra were obtained with a Nippon Bunko JASCO FT-IR 5300 spectrometer by the KBr method. Mass spectra were obtained by a Hitachi MS-80B mass spectrometer with perfluorokerosene as a standard.

RESULTS AND DISCUSSION

Polyallylamine (**1**) hydrochloride reacts with *N*-carbamoyl-*O*-methylisourea (**2**) to form poly(allyl-*N*-carbamoylguanidino-*co*-allylamine) hydrochloride (**3** · HCl). Figure 1 shows a degree of substitution that was determined by elemental analysis. The substitution reaction was found to be terminated in about 10 h. The reaction time of 10 h yielded polymer **3** with a degree of substitution (DS) of 0.80.

Figure 2 shows the IR spectra of polymer **1** · HCl, *N*-carbamoylguanidine · HCl and polymer **3** · HCl. The



Scheme 1. Synthesis of polymer 3.

characteristic bands at 1723 and 1680 cm^{-1} for the carbonyl groups were observed in polymer 3 \cdot HCl, and the same bands at 1742 and 1681 cm^{-1} were observed in *N*-carbamoylguanidine \cdot HCl. These results suggest that the carbamoylguanidino groups were introduced to polymer 1, and polymer 3 was obtained.

Figure 3 shows the potentiometric titration curves of polymer 3 and polymer 1. Two equilibrium states of acid-base dissociation at pH 7.4 and 9.7 were observed in polymer 3, though polymer 1 is known as a monoacidic base.^{5,6} These results suggest that the polymer 3 is a diacidic base. It is known that *N*-carbamoylguanidine is a monoacidic

base and has pK_a value at 8.0,⁷ and that *n*-propylamine has pK_a value at 10.5.⁸ The shifts of both pK_a to lower values in polymer 3 can be interpreted in terms of enhanced interactions with the neighboring groups.⁹

Figure 4 shows a typical example of TGA curves of pretreated polymer 3 \cdot HCl (DS = 0.8) and pretreated polymer 1 \cdot HCl measured at a constant heating rate of 10 $^\circ\text{C min}^{-1}$ under the nitrogen or dry air atmosphere with a flow rate of 300 mL min^{-1} . The first weight loss of poly-

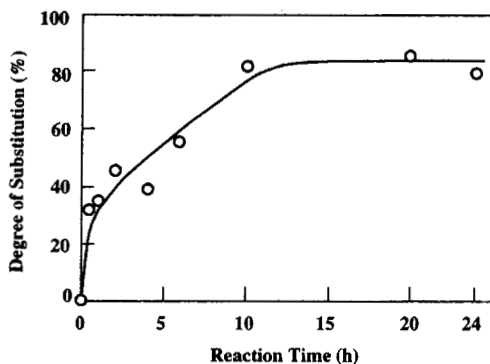
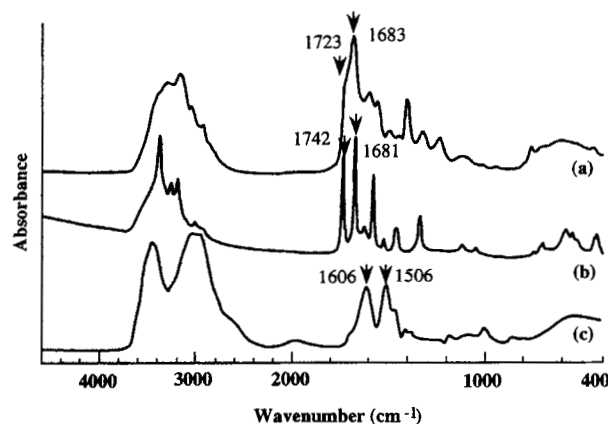
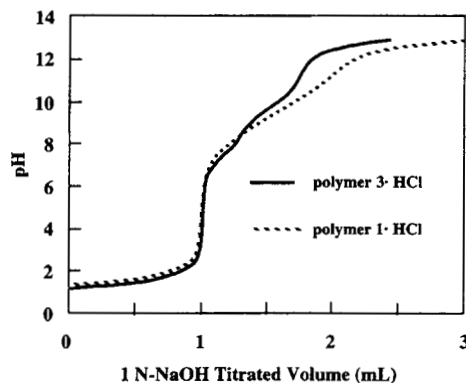
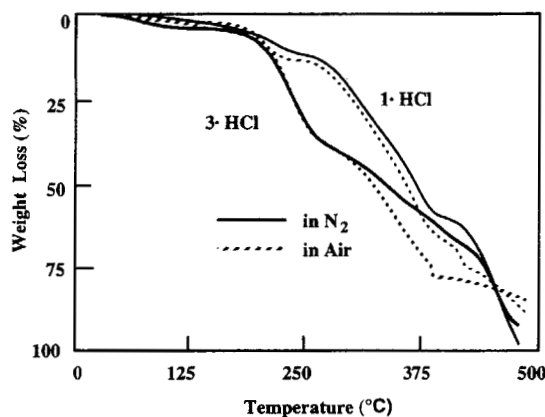
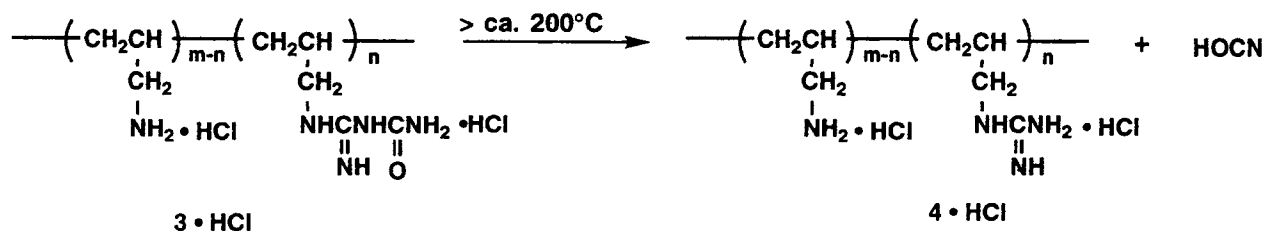


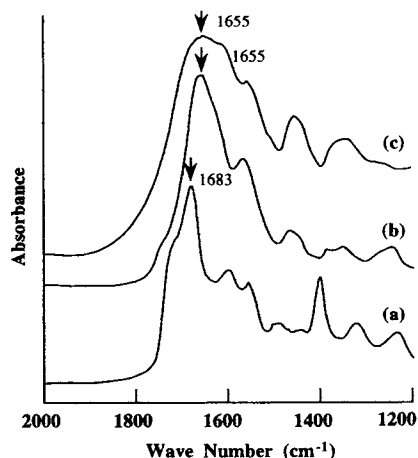
Figure 1. Degree of substitution versus reaction time.

Figure 2. IR spectra of (a) polymer 3 \cdot HCl, (b) *N*-carbamoylguanidine \cdot HCl, and (c) polyallylamine hydrochloride (1 \cdot HCl).Figure 3. Potentiometric titration curves of polyallylamine hydrochloride (1 \cdot HCl) and polymer 3 \cdot HCl.Figure 4. Thermogravimetric analysis of preheated polyallylamine hydrochloride (1 \cdot HCl) and preheated polymer 3 \cdot HCl under a nitrogen or dry air atmospheres. Flow rate, 300 mL min^{-1} ; heating rate, 10 $^\circ\text{C min}^{-1}$.



Scheme 2. Thermal decomposition of polymer 3.

mer **3** · HCl started near 200°C and the second weight loss began near 260°C under the nitrogen and dry air atmospheres. But the weight loss of polymer **1** · HCl occurred near 250°C as already reported.¹⁰ Figure 5 shows the IR of polymer **3** · HCl, thermal-treated polymer **3** · HCl, and poly(allylguanidino-co-allylamine) · HCl (**4** · HCl).¹¹ The thermal-treated polymer **3** · HCl was heated at 260°C for 30 min and washed with a small amount of water. The characteristic band at 1655 cm⁻¹ for the guanidine group was observed in the thermal-treated polymer **3** · HCl and polymer **4** · HCl. Cyanic acid was detected at m/z 43.0047 (HCNO) by means of mass spectrometer at 220°C. It is known that biuret decomposes to urea and cyanic acid¹² and that *N*-carbamoylguanidine hydrolyzes to guanidine.¹³ These results show that polymer **3** · HCl decomposes to polymer **4** · HCl and cyanic acid on the first heating stage (Scheme 2).

Figure 5. IR spectra of (a) polymer **3** · HCl, (b) thermal-treated polymer **3** · HCl, and (c) polymer **4** · HCl.

REFERENCES AND NOTES

1. S. Harada, *Kobunshi Kako*, **33**, 21 (1984).
2. K. Iio and N. Minoura, *J. Polym. Sci. Polym. Chem.*, **30**, 2071 (1992).
3. K. Iio, N. Minoura, S. Aiba, M. Nagura, and M. Kodama, *J. Biomed. Mater. Res.*, **28**, 459 (1994).
4. K. Iio, E. Ichikawa, and K. Odo, *Yuki Gosei Kagaku Kyokashii*, **32**, 513 (1974).
5. Y. Yoshikawa, H. Matsuoka, and N. Ise, *British Polym. J.*, **18**, 242 (1986).
6. S. Kobayashi, M. Tokunoh, T. Saegusa, and F. Mashio, *Macromolecule*, **18**, 2357 (1985).
7. R. C. Hirt and R. G. Schmitt, *Spectrochim. Acta*, **12**, 127 (1958).
8. N. F. Hall and M. R. Sprinkle, *J. Am. Chem. Soc.*, **54**, 3469 (1932).
9. A. Katchalsky, J. Mazur, and P. Spitnik, *J. Polym. Sci.*, **23**, 513 (1957).
10. *Technical Catalog; Polyallylamine*, Nitto Boseki Co. Ltd., 1984.
11. Jpn. Kokai Pat., 87-230806 (1987).
12. J. M. Das Gupta, *J. Indian Chem. Soc.*, **11**, 207 (1934).
13. K. Sugino and M. Yamashita, *Kogyo Kagaku Zasshi*, **45**, 1 (1942).

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