Novel Stimuli-Sensitive Telechelic Oligomers. pH and Temperature Sensitivities of Poly(silamine) Oligomers

Yukio Nagasaki,* Eiichi Honzawa, Masao Kato, and Kazunori Kataoka*

Department of Materials Science and Technology, Science University of Tokyo, Noda 278, Japan

Teiji Tsuruta

Research Institute for Biosciences, Science University of Tokyo, Noda 278, Japan

Received March 30, 1994

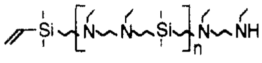
Revised Manuscript Received June 13, 1994

In recent years, studies on polymeric gels (especially ionic gels) have become an attractive field owing to their discrete, reversible transitions in equilibrium volume with certain stimuli such as temperature,[1] electric field,[2] solvent composition,[3] ionic composition,[3b,4] and pH.[3b,5] These stimuli-responsive gels can be applied for switching devices such as drug-releasing matrices[2d,6] and chemical valves.[7]

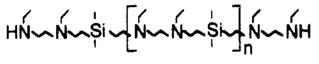
Most of ionic gels investigated so far contained ionic groups in the side chain of the polymers. Volume changes of these gels were considered to be controlled mainly by an internal osmotic pressure and a polymer-network concentration, assuming stiffness of the polymer chains to be unchanged.[8] Recently, Kataoka and his co-workers discovered a new ionic gel system with tremendous volume change in response to a minute change of the environmental pH,[9] using polyamine urea (PAU) gels consisting of cationic diamine groups in the main chain. Since the polyamine telechelic oligomers, as precursor for PAU, were synthesized through anionic polyaddition reactions between *N,N'*-diethylethylenediamine and 1,4-divinylbenzene, the synthetic route of which was first discovered by one of our authors (Tsuruta),[10] the oligomers consist of hydrophilic diamine units and hydrophobic diethylenephenylene units alternatively. Volume changes of the PAU gel were controlled by the protonation extent of amines in the gel with pH change. Due to the presence of ethylenediamine (EDA) units in the main chain,[11] the PAU showed two-step deprotonation with increasing pH value as follows:

In the stage of monoprotonation per chain diamine unit, rotation of the main chain must be much more suppressed than that in the nonprotonated region. Therefore, at the second deprotonation step around pH 5.9, a change in stiffness of the polymer chain itself, in conjunction with a change in the internal osmotic pressure, resulted in a discrete volume change.[12] This way, we considered that polymeric gels with ionic groups, especially diamine units, in the main chain may have an opportunity to open a new field for high-performance stimuli-sensitive materials.

Very recently, we discovered a new synthetic route for end-reactive oligomers with alternative organosilicon and EDA units in the main chain through anionic polyaddition reactions.[13] The resulting oligomers have a reactive vinylsilyl group at one end and a *sec*-amino group at the other end which were defined as poly(silamine) heterotelechelics [I].[14] The vinyl end group in I was easily converted to other functions such as a trimethoxysilyl group for a surface modifier[15] and a *sec*-amino group for homotelechelics [II].[16]



Poly(sil-amine) Heterotelechelics [I]



Poly(sil-amine) Homotelechelics [II]

Since these poly(silamine) oligomers have structural characteristics such as diamine units in the main chain, a hydrophilic/hydrophobic alternating structure, and a flexible chain due to the Si–C bond, several stimuli sensitivities were anticipated. Actually, water solubility of the oligomers changed drastically with environmental pH and also temperature. Thus, these poly(silamine) oligomers are regarded as promising precursors for a poly(silamine) urea gel, surface modification agent, heterolinker for different molecules such as proteins, drugs, etc., with certain stimuli sensitivities. In this paper, we communicate aqueous solution properties of these poly(silamine) oligomers.

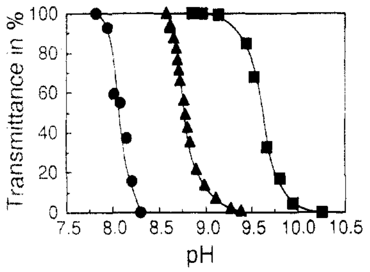


Figure 1. Optical transmittance of a solution of poly(silamine) heterotelechelics [I] at 500 nm. Solution temp: 37 (●); 23 (▲); 4 °C (■).

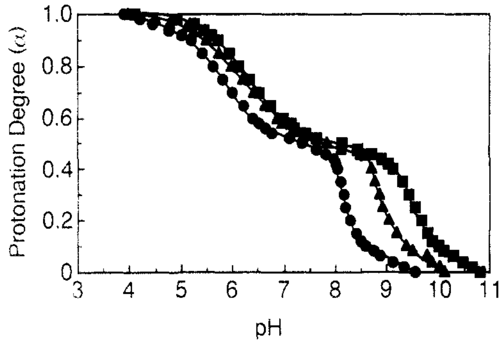


Figure 2. Plots of protonation degree (α) of a solution of **I** versus pH of the solution. Solution temp: 37 (●); 23 (▲); 4 °C (■).

The poly(silamine) oligomers, **I** and **II**, were synthesized according to our previous papers.[13,16] Molecular weights of the oligomers were in the range of 1700–2600. As the poly(silamine) oligomers have diamine repeating units in the main chain, the oligomers were soluble in acidic solution. To investigate an effect of environmental pH on the solubility of the poly(silamine), titrations of the acidic solution were carried out by a 0.1 N aqueous solution of sodium hydroxide as titrant. Figure 1 shows a change in optical transmittance at 500 nm as a function of environmental pH. As can be seen, the transmittance decreased drastically in response to a minute change of the environmental pH in the alkaline region. This may be interpreted in terms of the change in hydrophobicity of the oligomers owing to deprotonations of their amino groups.

With increasing temperature, lower values of pH are required for the onset of turbidity. The α–pH relation (Figure 2) also indicates that the effective pK_a's of the

0024-9297/94/2227-4848$04.50/0

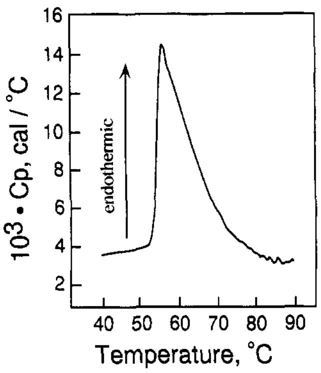


Figure 3. DSC measurement of a solution of poly(silamine) homotelechelics [II] (pH 7.4, 1 mg/mL).

polymer amines increase with temperature. Comparing α–pH curves and turbidity curves shown in Figures 1 and 2, it can be seen that turbidity appears when $\alpha \approx 0.45$, for all temperatures observed.

In the case of potentiometric titrations of polyelectrolytes with phase separation such as poly[2-(dimethylamino)ethyl methacrylate], it is known that the polyelectrolyte solution acts as a very effective buffer when the precipitate is present.[17] This mechanism was explained as follows: In the initial stages all chains are highly charged and prefer to remain in solution. However, when the critical neutralization α_{ppt} is reached, a phase separation, driven by the essential hydrophobicity of the polymer without charge, commences. When a polymer molecule enters the precipitate, it releases all its bound protons, thus neutralizing the added NaOH.

In the case of poly(silamine) titration, $\alpha_{\mathrm{ppt}} \approx 0.45$ may be explained as follows: As monoprotonation per each EDA unit prevents a rotation of the main chain of poly(silamine) and the protonated unit repels with each other cationic unit, the oligomers at $\alpha = 0.5$ presumably take a very rigid and expanded conformation. At around $\alpha = 0.45$, several deprotonated EDA units start free rotation around the main chain to make it more flexible than that at $\alpha = 0.5$, which increases hydrophobic interaction around nonprotonated ethylenediamine units to result in a shrinkage of the oligomer chains from their expanded conformation. Such shrinking releases all its bound protons in conjunction with phase separation.

To get further information about the phase separations, DSC measurements of poly(silamine) oligomer solutions were carried out. As shown in Figure 3, the oligomer solution at pH 7.4 gave an extremely sharp endothermic peak at 57 °C. Under the same conditions, the solution became turbid at the same temperature. This phenomenon can be regarded as the so-called lower critical solution temperature (LCST). The amount of heat was determined using the endothermic peak in the figure to be 26.7 kcal/monomol. It should be noted that the amount of heat in the phase separation stage of the poly(silamine) oligomer solution was ca. 20 times higher than that of poly(*N*-isopropylacrylamide) (poly(NIPAM); ΔH = 1.25 kcal/monomol[18]), the latter of which is well-known as an LCST polymer with a sharp phase transition at around 31 °C. Such a high ΔH at the phase transition stage may be compensated by an entropic term owing to the drastic conformational change of the poly(silamine) oligomers, *viz.*, transition of an expanded rigid chain to a flexible chain by the deprotonation process.

If the deprotonation from the oligomer at around $\alpha = 0.5$ triggered off the phase transition, LCST can be controlled by the environmental pH. Figure 4 shows a relation between the optical transmittances and temperature of poly(silamine) oligomers, **II**, at different pHs. As anticipated, LCST can be controlled by the environmental pH value. Actually, only 0.2 different in pH (7.2–7.4), the turbidity point decreased more than 10 °C. This shows sharp contrast to other ionic polymers with LCST. Kim[19] et al. reported that LCST of the poly[NIPAM-*co*-(dimethylamino)ethyl methacrylate] can be controlled by pH, though the sensitivity of the environmental pH on LCST was not so high [0.8 difference in pH value (7.2–8.0) causes a decreased turbidity point ca. 10 °C (40 to 30 °C)].

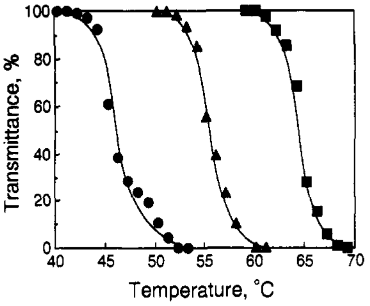


Figure 4. Optical transmittance of a solution of **II** at 500 nm. pH of the solution: 7.8 (●); 7.4 (▲); 7.2 (■).

The poly(silamine) oligomers thus synthesized can be one of the candidates for stimuli-sensitive oligomers with reactive end groups and can be utilized as a precursor for high-performance functional materials.

Acknowledgment. K.K. and Y.N. express their sincere appreciation to *The Ogasawara Foundation for the Promotion of Science & Engineering* (*Tokyo*) for financial support of a part of this study. A part of this study was also supported financially by Grant-in-Aid for Development Scientific Research, the Ministry of Education, Science and Culture, Japan No. 05558118.

References and Notes

(1) (a) Tanaka, T. *Phys. Rev. Lett.* **1978**, *40*, 820. (b) Schild, H. G. *Prog. Polym. Sci.* **1992**, *17*, 163. (c) Katayama, S.; Hirokawa, Y.; Tanaka, T. *Macromolecules* **1984**, *17*, 2641. (d) Hoffman, A. S.; Afrassiabi, A.; Dong, L. C. *J. Controlled Release* **1986**, *4*, 213.

(2) (a) Tanaka, T.; Nishio, I.; Sun, S.-T.; Ueno-Nishio, S. *Science* **1982**, *218*, 467. (b) Shiga, T.; Hirose, Y.; Okada, A.; Kurauchi, T. *J. Appl. Polym. Sci.* **1992**, *46*, 635.

(3) (a) Hrouz, J.; Ilavsky, M.; Ulbrich, K.; Kopecek, J. *Eur. Polym. J.* **1981**, *17*, 361. (b) Ohmine, I.; Tanaka, T. *J. Chem. Phys.* **1982**, *77*, 5725.

(4) (a) Ricka, J.; Tanaka, T. *Macromolecules* **1985**, *18*, 83. (b) Park, T. G.; Hoffman, A. S. *Macromolecules* **1993**, *26*, 5045.

(5) (a) Tanaka, T.; Fillmore, D. J.; Sun, S.-T.; Nishio, I.; Swislow, G.; Shah, A. *Phys. Rev. Lett.* **1980**, *45*, 1636. (b) Siegel, R. A.; Firestone, B. A. *Macromolecules* **1988**, *21*, 3254. (c) Batich, C. D.; Yan, J.; Bucaria, C., Jr.; Elsabee, M. *Macromolecules* **1993**, *26*, 4675.

(6) (a) Siegel, R. A.; Falamarzian, M.; Firestone, B. A.; Moxley, B. C. *J. Controlled Release* **1988**, *8*, 179. (b) Okano, T.; Bae, Y. H.; Jacobs, H.; Kim, S. W. *J. Controlled Release* **1990**, *11*, 255. (c) Kim, C. J.; Lee, P. I. *Pharm. Res.* **1992**, *9*, 195.

(7) Osada, Y.; Ross-Murphy, S. B. *Sci. Am.* **1993**, 82.

(8) Tanaka, T. In *Encyclopedia of Polymer Science and Engineering*, 2nd ed.; Mark, H. F., Bikales, N. M., Overberger, C. G., Menges, G., Kroschwitz, J. I., Eds.; John Wiley & Sons: New York, 1987; Vol. 7, p 514.

(9) Koyo, H.; Kataoka, K.; Tsuruta, T. *Polym. J.* **1993**, *2*, 141.

(10) Tsuruta, T. In *Polymeric Amine and Ammonium Salts*; Goethals, E. J., Ed.; Pergamon Press: Oxford, U.K., 1980; p 163.

(11) Ogino, H. *Inorg. Chem.* **1980**, *19*, 1619.

(12) Kataoka, K.; Koyo, H.; Tsuruta, T. *Macromolecules*, submitted for publication.

(13) Nagasaki, Y.; Honzawa, E.; Kato, M.; Kihara, Y.; Tsuruta, T. *J. Macromol. Sci., Pure Appl. Chem.* **1992**, *A29*, 457.

(14) The term "heterotelechelics" was defined in our previous paper. Yokoyama, M.; Okano, T.; Sakurai, Y.; Kikuchi, A. Ohsako, N.; Nagasaki, Y.; Kataoka, K. *Bioconjugate Chem.* **1992**, *3*, 275.

(15) Nagasaki, Y. Silicon-containing Monomers and Polymers. In *Functional Polymers for Emerging Technologies*; Arshady, R., Ed., to be published.

(16) Nagasaki, Y.; Honzawa, E.; Kato, M.; Kataoka, K.; Tsuruta, T. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)*, **1993**, *34*, 304.

(17) (a) Shatkey, A.; Michaeli, I. *J. Phys. Chem.* **1966**, *70*, 3777. (b) Siegel, R. A.; Cornejo-Bravo, J. M. Hydrophobic Polyelectrolytes: Effect of Hydrophobicity on Buffering and Colloid Osmotic Pressure. In *Polyelectrolyte Gels*; Harland, R. S., Prud'homme, R., Eds.; ACS Symposium Sereis 480; American Chemical Society: Washington, DC, 1991; pp 131–145. (c) Vallin, D.; Huguet, J.; Vert, M. *Polym. J.* **1980**, *12*, 113.

(18) Kubota, K.; Fujishige, S.; Ando, I. *J. Phys. Chem.* **1990**, *94*, 5154.

(19) Feil, H.; Bae, Y. H.; Feijen, J.; Kim, S. W. *Macromolecules* **1993**, *26*, 2496.