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New Thermosensitive Rubbery Polymers. Synthesis of Poly(siloxyethylene glycol) and Its Aqueous Solution Properties

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ABSTRACT: Poly(siloxyethylene glycol) (PSEG), which consists of alternating oligo(dimethylsiloxane) and oligo(ethylene glycol) (OEG) units in the main chain, was synthesized through polycondensation reactions between oligosiloxane having two diethylamino groups and OEG. The molecular weight of the polymer was in the range 3500−17 700 g/mol with a monomodal molecular weight distribution. The glass transition temperature of the polymer thus obtained was controlled by changing the silicon content in the polymer. Actually, with increasing Si content, the T_g of the polymer decreased from −53 (PEG) to −100 °C. PSEG having a silicon content of <15 wt % was soluble in aqueous media. With increasing solution temperature, phase separation occurred and the solution become turbid. The temperature at the phase separation is known as a lower critical solution temperature (LCST). The LCST was controlled by the silicon content in the polymer. The hydrolytic stabilities of the PSEG in aqueous solution were also examined.

Introduction

There are many kinds of synthetic polymers which respond to environmental conditions. For example, poly(*N*-isopropylacrylamide) [poly(NIPAAM)] shows a phase transition with temperature (LCST).[1] The characteristics such as solubility and conformation of such polymers vary with changing surrounding conditions such as temperature,[2] solvent composition,[3] pH,[3b,4] ionic strength,[3b,5] and electric field.[6] Hydrogels prepared from stimuli-sensitive polymers have recently been of increasing interest in the field of drug delivery systems[7] as well as chemomechanical systems.[8] The volumetric transition of the hydrogels with a minute change in the environmental conditions permits controlled drug release from the hydrogel and controlled chemomechanical systems.

However, because most of the stimuli-sensitive polymers prepared so far are vinyl polymer homologues, their mobility is not very high. Even if the properties of the polymer change sufficiently rapid in response to environmental conditions, the volumetric transition of the hydrogels is governed by the restricted mobility of the vinyl polymer chains. This slow motion of the gel networks limits the application of the hydrogel to some extent.

Most recently, unique approaches have been reported by two different groups. Hoffman and co-workers reported the synthesis and characterization of a new heterogeneous, thermally reversible hydrogel prepared from mixtures of NIPAAM monomer and vinyl-terminated poly(dimethylsiloxane) (PDMS) macromonomer.[9] They reported that with a higher PDMS branch the polymer exhibits an enhanced rate of shrinking when heated through the LCST. This is explained by the extremely high mobility of PDMS due not only to the flexibility of the chain but also to the flexible branching of the PDMS. The branching effect of the polymer in the hydrogel on the rate at volumetric transition was confirmed by Okano and co-workers.[10] They prepared the poly(NIPAAM) hydrogel with poly(NIPAAM) branches from the network, and the rate of shrinking of the gel increased significantly when heated through the LCST. Therefore, the introduction of branching from the networks of the hydrogels enhances the rate at volumetric transition. However, the introduction of branching generally causes lowering of the mechanical strength of the gel.

The objective of this work is to develop new polymers having both stimuli-sensitivity and higher flexibility than vinyl polymers. If such a polymer can be obtained, its gel will have a higher rate of volume change than that of hydrogels prepared with the vinyl polymer even with no branching.

Schild[11] reproted that the thermosensitivity of poly(NIPAAM) in aqueous solution is due to the alternating hydrophilic/hydrophobic hydration cluster surrounding the polymer molecule. If a polymer having hydrophilic/hydrophobic alternating segments in a suitable balance can be prepared, a new LCST polymer can be anticipated. To achieve this objective, we designed a new polymer, PSEG, which consists of alternating oligo(dimethylsiloxane) and OEG units in the main chain. By changing the extent of the silicone moiety, both the mobility and LCST of the polymer could be controlled.

There has been a significant amount of low molecular weight (MW) siloxane polyether copolymers in the last 20 years.[12] The objective of these materials was mainly for controlling surface activity and wetting properties. Oligosiloxane with oligo(ethylene glycol) graft(s) and oligosilioxane−oligo(ethylene glycol) diblock copolymers are two major commercially available products for these purpose (Sylagard and Silwet). However, these materials are too low in MW to prepare functional polymeric materials such as hydrogels. Also, there is not enough information on the characteristics such as solubility, temperature dependency, flexibility, hydrolytic stability, etc.

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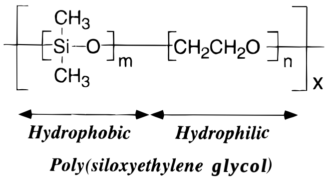
This paper describes the new synthesis of poly(siloxyethylene glycol) and its properties in aqueous media in detail.

Scheme 1



Experimental Section

Materials. Commercial THF (Wako) was purified in the following way. After THF was predried with KOH for several days, reflux was carried out over lithium aluminum hydride for 5 h, followed by distillation. The fraction at 68 °C was collected and stored under an Ar atmosphere. Oligo(ethylene glycol)s were dried at 110 °C for 2 days in vacuo. Diethylamine (Wako), dichlorodimethylsilane (Shin-etsu Chemical Co. Ltd.), and 1,3-dichlorotetramethyldisiloxane (Shin-etsu Chemical Co. Ltd.) were used as received. Bis(diethylamino)dimethylsilane (DAS) and 1,3-bis(diethylamino)tetramethyldisiloxane (DADS) were prepared by the reaction of diethylamine with dichlorodimethylsilane and 1,3-dichlorotetramethyldisiloxane, respectively.[13] The boiling points of DAS and DADS were 30−31 °C/1 mmHg and 79 °C/3 mmHg, respectively. Other materials were used as received.

Polymer Synthesis. A typical polymerization was performed in a 100-mL round-bottomed flask with a three-way stopcock. After 6.19 g of OEG ($M_n = 300$) (20.6 mmol) was weighed into the flask, the inside of the reactor was degassed sufficiently and filled with Ar gas. THF (20 mL) and DAS (4.17 g, 20.6 mmol) were then added to the flask via syringe and allowed to react for 24 h at 60 °C. After THF and liberated diethylamine were removed by evaporation in vacuo, the obtained polymer was analyzed by GPC. The ^{1}H NMR of the obtained polymer was recorded after the sample was purified by GPC fractionation.

Hydrolytic Stability Test. The stability of PSEG against hydrolysis in aqueous media was estimated as follows: A polymer sample was dissolved in phosphate buffer (1.5 wt %; pH = 7.0; $I = 0.05$) at 4 °C. Every few hours, an aliquot of the solution was subjected to measurement of its turbidity after the sample was heated above the LCST. The turbidity was monitored as a normalized attenuance using the following equation.

$$\text{normalized attenuance} = \log(I_R/I_{s,t})/\log(I_R/I_{s,\min})$$

where, I_R and $I_{s,t}$ denote the intensities of reference (phosphate buffer) and sample after t hours of reaction, respectively. $I_{s,\min}$ represents the minimum intensity of the sample during the experiment.

Measurement. GPC measurements were performed on a Tosoh CCPE with a RI detector and TSK-Gel GMH6 × 2 + GMHXL × 2 columns. The ^{1}H spectra (^{1}H: 399.65 MHz; ^{13}C: 100.53 MHz) were determined on a JEOL EX400 spectrometer using $CDCl_3$ as a solvent at room temperature. Chemical shifts relative to $CHCl_3$ (^{1}H: $\delta = 7.26$) were employed. Glass transition temperatures of the polymers were determined using a differential scanning calorimeter (DSC) (Mettler TA4000 system) at a heating rate of 20 °C/min from −170 to +200 °C. The turbidity of the polymer solution was recorded using a Photorode Mettler DP 550. The absorption at 550 nm was monitored.

Results and Discussion

Polymer Synthesis. The polymerization employed in this study involved polycondensation reactions between hydroxyl groups and the silyl compound. There are several choices of leaving groups from the silicon atom as an electrophile such as halogen, amine, isocyanate, etc. Silyl halide, especially silyl chloride, is the most common electrophile for the coupling reaction with hydroxyl groups.[14] However, if silyl chloride is employed for the synthesis of PSEG, the liberated acid may induce some side reactions such as acid hydrolysis of the polymer chain. Actually, though Watanabe and coworkers[15] prepared the PSEG by the polycondensation reaction between OEG and dichlorodimethylsilane, the molecular weight and hydrolytic stability of the obtained polymer were extremely low.[16] Therefore, we employed a dimethylamino group as a leaving group in the silicon compound (Scheme 2).

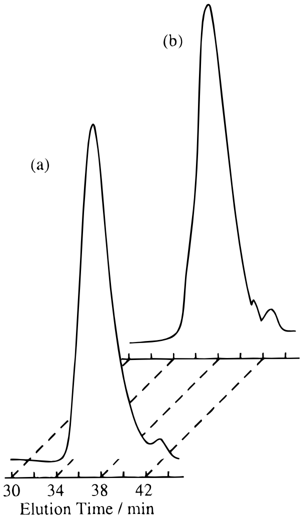
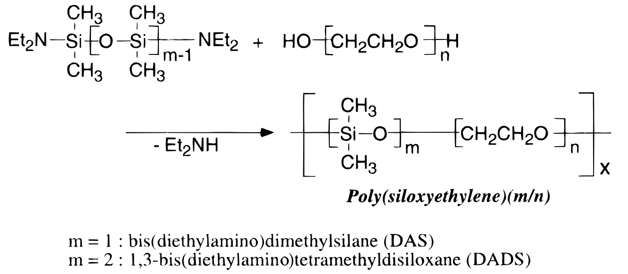


Figure 1. GPC profiles of poly(siloxyethylene glycol)(1/7) (a) and -(2/7) (b).

Scheme 2



Polycondensation between OEG and bis(diethylamino)silane compounds proceeds homogeneously to form a viscous liquid. Figure 1 shows the GPC profiles of the products of the polycondensation reaction of OEG ($M_n = 300$ g/mol) with DAS (a) and DADS (b). As can be seen in the figure, the MWs of the products have a monomodal distribution and were more than 10 000 g/mol. The results of the polycondensation reactions under several conditions are summarized in Table 1. The MWs of the obtained polymers were in the range of 3700−18000 g/mol under these reaction conditions. Figure 2 shows the ^{1}H NMR spectra of the obtained polymers. In Figure 2a, two main signals appear at 0.13 and 3.65 ppm; these are assignable to $OSi(CH_3)O$ and OCH_2CH_2O protons, respectively. In Figure 2b, the signal assignable to the two methyls adjacent to a disiloxane unit appears at 0.10 ppm along with an oxyethylene signal at 3.65 ppm. A sole singlet signal at 0.13 ppm in Figure 2a indicates no contamination of disiloxane linkages in the polymer obtained by the polycondensation with DAS. The integral ratios of the silylmethyl and the oxyethylene signals agreed well

Table 1. Results of Synthesis of Poly(siloxyethylene glycol) through Polycondensation Reactions between Bis(dimethylamino)siloxanes (BAS) and Oligo(ethylene glycol)s (OEG)[a]

polymer code	*m* in BAS	$[BAS]_0$ (mmol)	*n* in OEG	$[OEG]_0$ (mmol)	THF	temp (°C)	time (h)	$10^{-3}M_n$[b]	M_w/M_n[b]
PSEG(1/2)	1	20.0	2	20.0	20	reflux	36	14.0	1.50
PSEG(1/3)	1	22.4	3	22.5	20	reflux	36	4.7	1.42
PSEG(1/4)	1	20.8	4	20.8	20	60	24	17.7	1.52
PSEG(1/7)	1	11.1	7	11.1		60	48	11.8	1.41
PSEG(1/9)	1	6.5	9	6.4	20	60	24	5.9	1.25
PSEG(1/13)	1	10.0	13	10.0	20	60	24	3.7	1.17
PSEG(2/2)	2	9.9	2	10.0	20	60	24	10.8	1.28
PSEG(2/3)	2	9.9	3	9.7	20	60	24	8.4	1.47
PSEG(2/4)	2	6.2	4	6.1	20	60	24	7.7	1.52
PSEG(2/7)	2	11.2	7	11.1		60	48	13.2	1.47
PSEG(2/9)	2	6.5	9	6.4	20	60	24	11.5	1.21
PSEG(2/13)	2	3.7	13	3.8	20	60	24	3.5	1.20

[a] THF was used as solvent. [b] Determined from GPC results.

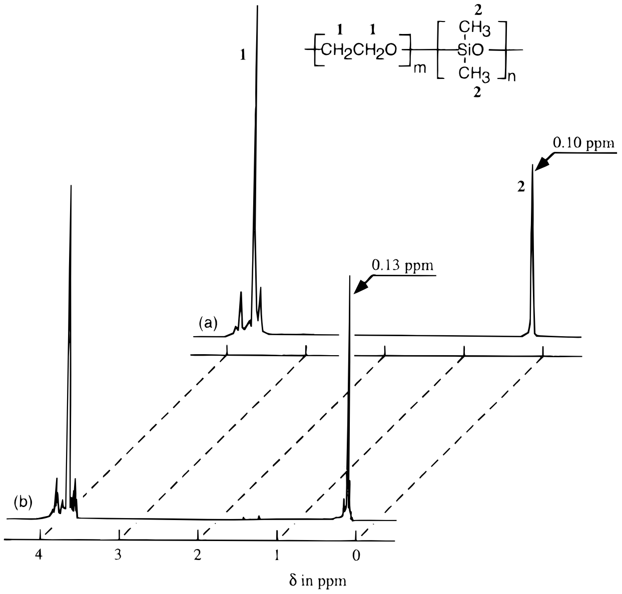


Figure 2. ^{1}H NMR spectra of poly(siloxyethylene glycol)(1/7) (a) and -(2/7) (b).

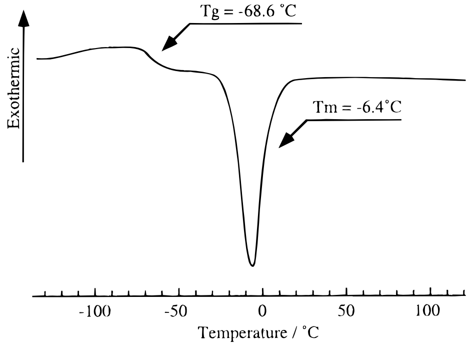


Figure 3. DSC profile of poly(siloxyethylene glycol)(1/9).

Table 2. Glass Transition Temperatures and Melting Points of Poly(siloxyethylene glycol)s[a]

polymer code	T_g (°C)	T_m (°C)
PSEG(1/2)	−81.3	
PSEG(1/3)	−78.4	
PSEG(1/4)	−74.7	
PSEG(1/7)	−72.2	−30.4
PSEG(1/9)	−68.6	−6.4
PSEG(1/13)	−64.0	16.6
PSEG(2/2)	−95.4	
PSEG(2/3)	−88.9	
PSEG(2/4)	−85.3	
PSEG(2/7)	−78.6	−33.2
PSEG(2/9)	−73.1	−12.1
PSEG(2/13)	−67.2	10.7

[a] T_g and T_m were determined by DSC at a heating rate of 20 °C/min from −170 to 200 °C.

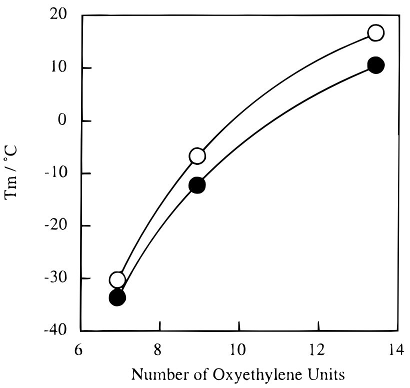


Figure 4. Plots of melting point of poly(siloxyethylene glycol) versus number of oxyethylene units in OEG repeating units: (○) PSEG(1/*n*); (●) PSEG(2/*n*).

with that calculated by the segment lengths from the monomers employed. On the basis of these results, it is concluded that PSEGs having various segment lengths of oligo(oxyethylene) units and oligosiloxane units in each repeating unit in the main chain could be synthesized. The polymers are thus expressed by PSEG(*m*/*n*), where *m* and *n* respectively denote repeating units of siloxane and oxyethylene in each repeating unit.

Thermal Properties of PSEG. The thermal properties of PSEG were evaluated by means of DSC analysis. Figure 3 shows a typical example of a DSC profile of PSEG(1/9). The inflection at −68.6 °C is assignable to the glass transition temperature, and the endothermic peak at −6.4 °C is based on the melting. The glass transition temperature (T_g) and the melting temperature (T_m) are summarized in Table 2. Polymers having repeating units of OEG of less than 5 show no melting peak under these conditions. Both poly(siloxyethylene glycol)(1/7) and -(2/7) showed an exothermic peak just before the melting peak. In these cases, crystallization occurred during the heating process in the DSC measurements. The polymers having repeating units of OEG of more than 8 show no exothermic peak in the DSC measurements, indicating that the crystallization rate increases with increasing number of oxyethylene units.

Figure 4 shows the change in melting temperature as a function of oxyethylene units of the PSEG. At higher oxyethylene units, a higher T_m was observed, indicating the effect of the siloxane unit at both ends of

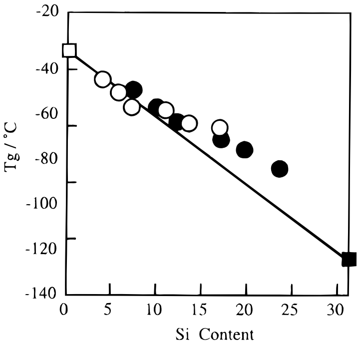


Figure 5. Plots of glass transition temperature versus silicon content in the poly(siloxyethylene glycol): (○) PSEG(1/*n*); (●) PSEG(2/*n*); (□) PEG;[17] (■) PDMS.[16]

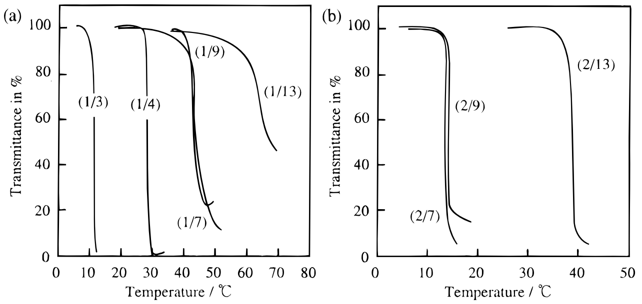


Figure 6. Change in transmittance of poly(siloxyethylene glycol) aqueous solution (1.5 wt %) in phosphate buffer (pH = 7.0; *I* = 0.05): (a) PSEG(1/*n*); (b) PSGE(2/*n*) (number in parentheses denotes *m*/*n* in PSEG).

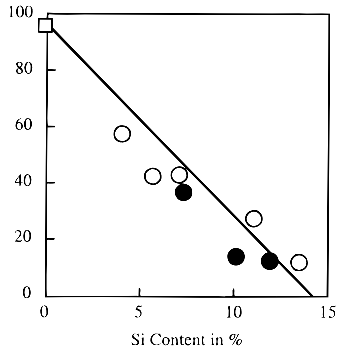


Figure 7. Plots of the LCSTs of poly(siloxyethylene glycol) versus silicon content in the polymer: (○) PSEG(1/*n*); (●) PSEG(2/*n*); (□) PEG.[17]

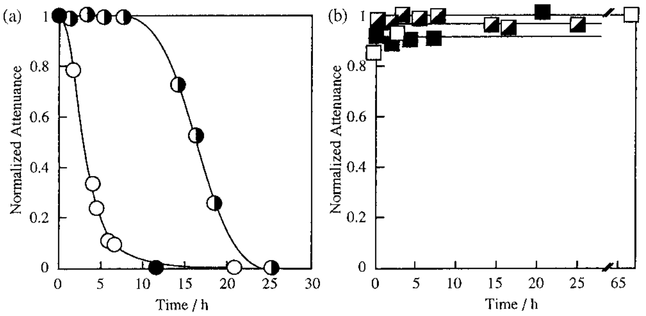


Figure 8. Time course of the normalized attenuance of PSEG in phosphate buffer (see text for experimental conditions): (a) PSEG(1/*n*), (◑) (1/3), (○) (1/7), (●) (1/9); (b) PSEG(2/*n*), (■) (2/7), (□) (2/9), (◨) (2/13).

OEG; viz., a flexible siloxane linkage at both ends of the OEG chain influenced the stability of the crystal. Actually, the melting points (T_m) of PSEG(2/*n*) homologues were lower than those of the corresponding PSEG(1/*n*) homologues due to the higher flexibility of the disiloxane linkage between the OEG chains than that of the monosiloxane. Therefore, the melting point of PSEG was dependent on both the length of the oxyethylene and siloxane units. The glass transition temperature (T_g) of the PSEG, however, was governed only by the silicon content in the polymer. Figure 5 shows the relation between T_g and Si content of PSEG. Because the T_g of PDMS is very low (−127 °C[17]), a relatively lower T_g was observed on the introduction of a siloxane linkage in the polymer. As can be seen in the figure, the T_g of PSEG can be controlled between the T_gs of PEG (−53 °C[18]) and PDMS (−127 °C), though at a Si content higher than 10 wt %, the plots slightly deviated to the higher temperature side than the linear line across the T_gs of PEG and PDMS. It should be noted that no difference was observed between the monosiloxane linkage and the disiloxane linkage in the T_g of PSEG. The Si content is only the factor controlling their T_gs, which indicates that, in the amorphous region, the OEG and siloxane segments were mixed completely.

Phase Separation Behavior of PSEG Aqueous Solution. As mentioned above, polymers having hydrophilic−hydrophobic moieties in a suitable balance in each repeating unit show a temperature dependency in solubility in aqueous media. Because the OEG segment is hydrophilic, PSEG with a relatively higher OEG content is soluble in water. For example, PSEG(1/4) was soluble in water at 4 °C and the solution became transparent. This solution became turbid when heated above 30 °C. Figure 6 shows the turbidity change in PSEG in phosphate buffer (pH = 7.0; *I* = 0.05) at elevated temperatures. In a series of PSEGs having monosiloxane linkage (1/*n*), the polymers with more than 2 oxyethylene units were soluble in the buffer at low temperature. With increasing solution temperature, the solution became turbid at 10.5 °C in the case of PSEG(1/3). A higher LCST was observed for PSEGs with more oxyethylene units. PSEG(2/*n*) with *n* greater than 6 also shows an LCST under the same conditions. As can be seen in Figure 6, the phase separation occurred very sharply in the case of an LCST lower than 40 °C. Above 40 °C, however, the phase separation range became broader than 40 °C. It is known that the siloxy group is susceptible to hydrolysis.[19] Above 40 °C, the hydrolysis of PSEG may occur during the phase separation measurements (see below). Figure 7 shows plots of LCST vs the Si content of PSEG. It can be seen in the figure that the LCST decreases linearly with increasing Si content. Again, no difference was apparent between mono- and disiloxane linkages in the polymers.

Hydrolytic Stability of PSEG in Aqueous Media. As stated above, there was concern about the hydrolytic stability of PSEG in aqueous media. The hydrolytic stabilities were estimated by the phase separation ability as follows: First, the polymer sample was dissolved in phosphate buffer (pH = 7.0, *I* = 0.05) with stirring at 4 °C. Every few hours, an aliquot of the solution was subjected to measurement of its turbidity after the sample was heated above the LCST. If hydrolysis occurs, the MW of the polymer decreases and the solution retains a high transmittance even above the LCST. Figure 8 shows the time course of the transmittance change. In the case of PSEG(1/*n*)s, the rate of the hydrolysis reaction depends on their hydrophobicity; viz., a polymer having a relatively higher hydrophobicity showed a lower rate of hydrolysis. For example, PSEG(1/3) aqueous solution started to increase in transmittance after ca. 10 h of reaction, while PSEG-

(1/7) started to hydrolyze within an hour. After 8 h, the solutions were almost transparent even above the LCST. It is rather surprising that in the case of PSEG(2/*n*), no transmittance change was observed under the present conditions. The higher stability of PSEG(2/*n*) compared to PSEG(1/*n*) may be attributable to the hydrophobicity of the disiloxane segment. Namely, the higher hydrophobicity of the disiloxane segment than that of the monosiloxane prevents the attack of water molecules on the siloxane linkage.

Conclusions

The polycondensation reactions of OEG with DAS and DADS proceeded smoothly to give PSEG with a MW of a few thousand to 18 000 g/mol. The crystallinity of the PSEG was influenced by the length of both the OEG and siloxane units. The T_g of the polymer was controlled between −53 and −127 °C by changing the Si content of the polymer. PSEG having relatively higher OEG content was soluble in cold water and its aqueous solution showed phase separation when heated above the LCST. The LCST was also controlled by changing the Si content of the polymer. For example, PSEG with a Si content of 8 wt % showed an LCST of ca. 37 °C. PSEG having a disiloxane linkage showed a high hydrolytic stability in aqueous media, though PSEG with a monosiloxane linkage in phosphate buffer hydrolyzed within a few hours at 4 °C. Such stimuli-sensitive PSEGs having high flexibility are promising as new functionality materials.

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