Macromolecules

Volume 26, Number 5 March 1, 1993

Synthesis and Redox Gelation of Disulfide-Modified Polyoxazoline

Yoshiki Chujo,* Kazuki Sada,[1] Akio Naka, Ryoji Nomura, and Takeo Saegusa[2]

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-01, Japan

Received May 1, 1992; Revised Manuscript Received November 9, 1992

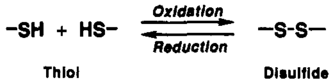
ABSTRACT: A polyoxazoline hydrogel having a disulfide bridge was prepared by the reduction-oxidation of thiol-protected poly(*N*-acetylethylenimine) (PAEI) (anthracene-SS-modified PAEI) or by the cross-linking reaction of the partially hydrolyzed PAEI with bifunctional disulfide compounds. As a disulfide cross-linking agent, dithiodi-2,1′-ethanediyl diisocyanate/1,8-diazabicyclo[5.4.0]undec-7-ene or 3,3′-dithiodipropanoic acid/dicyclohexylcarbodiimide gave good results. The reduction of thiol-protected PAEI produced the thiol-modified PAEI, which was susceptible to air oxidation to form the networks. These gels based on highly hydrophilic PAEI were stable and swollen in water as a hydrogel. A series of PAEIs having varying amounts of the functional groups were prepared and subjected to cross-linking reactions by reduction–oxidation. The degree of swelling in water increased with a decrease of the degree of substitution in the prepolymer. The disulfide-bridged PAEI gel became soluble to form the linear polymer by the treatment with reducing agents such as sodium hydrosulfite, sodium borohydride, or triphenylphosphine. This solubilization of gel was caused by the reductive cleavage of the disulfide bridge at the cross-linking points. This interconversion from a hydrogel to a soluble polymer can be regarded as a novel redox-reversible hydrogel system by means of reversible conversion between disulfide and thiol groups.

Introduction

Poly(*N*-acetylethylenimine) (PAEI) prepared by ring-opening polymerization of 2-methyl-2-oxazoline is highly hydrophilic and well compatible with commodity organic polymers such as poly(vinyl chloride) or polyamides.[3] Previously, we prepared the nonionic hydrogels based on PAEI using two methods, a cross-linking reaction of partially hydrolyzed PAEI[4] and copolymerization between 2-methyl-2-oxazoline and bis(oxazoline).[5] Recently, the thermally reversible hydrogel system based on the thermal equilibrium of the Diels–Alder reaction[6] and the photoreversible hydrogel system by photodimerization of coumarin-modified polymer[7] were also reported. Thus, it should be of interest to explore a new reversible hydrogel system based on PAEI.

The chemically reversible cross-linking in the modified fibers including natural wool has been of interest from both theoretical and practical viewpoints.[8] It is well-known that the disulfide (e.g., cystine residues of the protein) can be ruptured by reduction to form two thiol groups (e.g., cysteine residues of the protein), and the cross-linkings were reformed by mild oxidation (Scheme I). Several modified cotton fabrics[8] and cellulose[8,9] derivatives containing disulfide cross-linkages have been prepared and studied as an analogue of wool fibers. More recently, this reversible system was extended to the polymerized–depolymerized vesicle one.[10–12]

Scheme I



$$-SH + HS- \underset{\text{Reduction}}{\overset{\text{Oxidation}}{\rightleftharpoons}} -S\text{-}S-$$

A thiol-bearing polymer was previously prepared by Nakahama et al. during their studies on the polymerization of functional monomers protected by trialkylsilyl groups.[13] Endo reported the preparation and catalytic activity of a polymer-supported lipoamide ferrous complex.[14] On the other hand, Wulff reported the cross-linked polymer prepared from styrene, bis(*p*-vinylbenzyl) disulfide, and divinylbenzene and discussed the redox properties of the thiol groups in the styrene networks in relation to the cooperativity and site separation of the functional groups.[15] In these cases, the thiol groups were not recognized as a reversible cross-linker to give the networks by oxidation and to return to the linear polymer by reduction of the networks.

In this article, we describe the redox-reversible hydrogel system on the basis of reversible interconversion between disulfide (SS) groups and thiols (SH). The thiol-modified PAEIs were prepared by condensation of a thiol-protected carboxylic acid with the partially hydrolyzed PAEIs or by reduction of the disulfide-bridged PAEI gel. These thiol-PAEIs were redox-active to form the networks by oxida-

0024-9297/93/2226-0883$04.00/0

tion, and the disulfide-bridged gel became soluble by reduction to give the original linear polymer (PAEI). The change of the swelling property of the disulfide-bridged gel by partial reduction was also observed. In the present study, a useful candidate for the functional polymers would be provided in a series of our reversible gel systems based on PAEI.

Experimental Section

General Procedure. IR spectra were recorded on a Hitachi 260-50 grating spectrophotometer and Perkin-Elmer FT-IR 1600. ^{1}H NMR spectra were obtained on a Hitachi R-600 (60 MHz) or on a JEOL JNM-JX-400 (400 MHz) spectrometer. All NMR spectra were recorded in deuterated solvents relative to the internal standard tetramethylsilane. UV spectra were measured on a Hitachi 200 UV-vis spectrophotometer. GPC analysis was carried out on a Tosoh CCPD (TSK gel, G4000) after calibration with standard polystyrene samples.

Materials. All solvents and reagents were used as supplied except the following cases. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride. Nitromethane or dichloromethane was distilled from phosphorus pentoxide under nitrogen. According to the previous method,[4] poly(*N*-acetylethylenimine) (PAEI) was prepared by ring-opening polymerization of 2-methyl-2-oxazoline in the presence of methyl *p*-toluenesulfonate as an initiator and was partially hydrolyzed by the treatment with aqueous sodium hydroxide.

Synthesis of (9-Anthracenyl)methyl Hydrogen 3,3′-Dithiodipropanoate (5). To a THF solution of 3,3′-dithiodipropanoic aicd (1) (6.1 g, 29.0 mmol) and 9-anthracenemethanol (4) (3.0 g, 14.5 mmol) were added 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (0.205 g, 1.7 mmol) and dicyclohexylcarbodiimide (DCC) (4.0 g, 19.0 mmol) rapidly under nitrogen. The reaction mixture was stirred for 3 days. The white solid (dicylohexylurea, DCUrea) was removed by filtration, and the filtrate was concentrated to dryness. The residue was dissolved in a small portion of dichloromethane and cooled in a refrigerator. After filtration of the insoluble part, the solvent was removed in vacuo. The yellow solid was dissolved in chloroform, and the organic layer was extracted with saturated aqueous sodium bicarbonate. The aqueous layer was acidified (pH = 4-5) by concentrated hydrochloric acid and then extracted several times with chloroform. The combined organic layers were dried over anhydrous sodium sulfate. After the evaporation of the solvent, the yellow solid was obtained, which was recrystallized from methanol giving 1.91 g of 5 (32.8% based on 4). ^{1}H NMR ($CDCl_3$): δ 2.50-3.05 (m, 4 H), 6.10 (s, 2 H), 7.08-8.50 (m, 9 H). IR (KBr): 2931, 1736, 1714, 1248, 1177, 729 cm^{-1}. UV ($CHCl_3$): $\lambda_{max} = 386$ ($\epsilon = 8000$), 370 ($\epsilon = 9100$), 348 nm ($\epsilon = 6600$). MS: $M^+ = m/z$ 400.

Synthesis of Anthracene-SS-Modified PAEI 7. A typical procedure is as follows. To a solution of **5** (0.586 g, 1.46 mmol) in 10 mL of dry dichloromethane was added DCC (0.55 g, 2.66 mmol) at 0 °C under nitrogen, and the reaction mixture was stirred for 30 min (after DCC dissolved, the deposition of DCUrea was soon observed). A solution of 10.2%-hydrolyzed PAEI **6** (0.723 g, 0.90 mmol equiv NH) in 10 mL of acetonitrile was added. After the reaction mixture was kept stirring at room temperature for 3 days, the precipitate was filtered off, and the solvent was removed in vacuo. The polymeric residue was extracted with the mixed solvent (dichloromethane-methanol = 1/1), and the solution was poured into diethyl ether. After purification by the repeated reprecipitations (dichloromethane-diethyl ether) and freeze-drying in vacuo, 1.632 g (77% based on hydrolyzed PAEI) of the anthracene-SS-modified PAEI (**7**) was obtained as a slight yellow powder. ^{1}H NMR ($CDCl_3$): δ 1.60-2.30 (brd s), 2.46-2.92 (brd s), 3.03-4.13 (brd s), 6.08 (s), 7.10-8.57 (m). IR (KBr): 3448, 1736, 1648, 1459, 1421 cm^{-1}. UV (methanol): $\lambda_{max} = 386$, 370, 348 nm.

Redox Gelation of 7. A typical procedure is as follows. *Anthracene-SS-modified* (6.5% modification) PAEI (**7**) (107 mg) was dissolved in 1.5 mL of ethanol, and dry nitrogen was bubbled through the solution for more than 30 min. To this solution was added 15 mg (0.40 mmol) of sodium borohydride. After the solution was kept stirring for 2 h, 0.5 mL of degassed methanol was added. The white mass was removed by filtration under nitrogen. The filtrate was concentrated in vacuo and then poured into degassed diethyl ether (100 mL). The white precipitate was collected and dissolved in a small portion of degassed methanol. The solution was poured into a Petri dish, and kept overnight under air. The formed gel was immersed in methanol, washed with several portions of methanol, and collected. After drying in vacuo, 55.4 mg (63%) of PAEI gel **8** was obtained.

Quenching of Thiol-Modified PAEI. Anthracene-SS-modified (2.8% modification) PAEI (**7**) (160 mg, 0.047 mmol equiv for disulfide group) was dissolved in 4.0 mL of degassed ethanol. Sodium borohydride (32 mg, 0.84 mmol) was added to this solution under nitrogen. After the stirring was continued for 2 h, degassed methanol (1.0 mL) was added through a syringe during 30 min. 2,2′-Dithiodipyridyl (55 mg, 0.25 mmol) was added and the resulting mixture was kept stirring overnight. The polymer solution was concentrated in vacuo and purified by gel filtration (Sephadex LH-20, methanol as an eluent). After the solvent was removed in vacuo, 153.2 mg (95%) of polymer **9** was recovered.

Cross-Linking Reactions Using Bifunctional Disulfide Compounds. A typical procedure is as follows. To a solution of partially hydrolyzed PAEI **6** (24%-hydrolyzed, $M_n = 14\,000$, 0.308 g, 0.99 mmol equiv NH) and triethylamine (0.125 g, 1.23 mmol) in 0.70 mL of dry DMF was added dropwise 122 mg (4.9 mmol) of 3,3′-dithiodipropanoyl dichloride (**2**) under nitrogen. The gelation was observed within 30 s, and the reaction mixture was kept stirring for 30 min. The gel was purified by washing with methanol (10 mL) and then dried in vacuo. A total of 135 mg of the gel **8** was obtained. Gel **10** was prepared by the same procedure for **8**.

Swelling Property. The equilibrium swelling properties in water were examined as follows. The carefully dried and weighed gel (**8** or **10**) was immersed in ca. 100 mL of deionized water (the resistance was more than 12 MΩ) for 24 h at room temperature. The weight of the swollen gel was measured after filtration by 1G4 glass filter under reduced pressure (ca. 17 mmHg, 2 min). The degree of swelling was calculated by the following equation: $\{W_{g(s)} - W_{g(d)}\}/W_{g(d)}$, where $W_{g(s)}$ is the weight of the swollen gel and $W_{g(d)}$ is the weight of the dry gel.

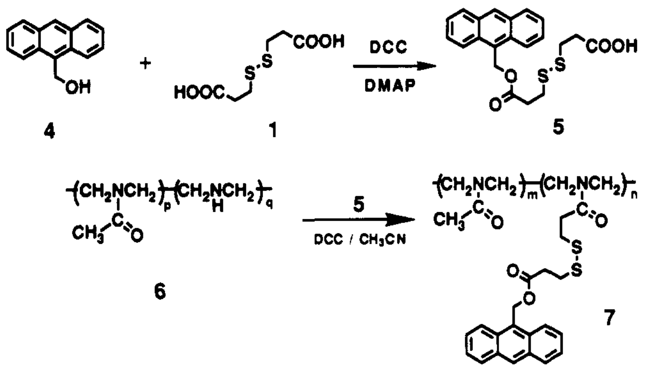
Reductive Cleavage of Disulfide-Bridged PAEI Gel. In a typical method, disulfide-bridged gel **8** (4.6%-modified, 52 mg) was suspended in 6 mL of ethanol, and dry nitrogen was passed through the solution for 30 min. Under nitrogen, 39 mg of sodium borohydride was added, and the solution was kept stirring for 2 h at room temperature. Degassed methanol (3 mL) was added through a syringe, and 88 mg of 2,2′-dithiodipyridyl was added. After the white solid was filtered off, the solution was concentrated under reduced pressure and poured into diethyl ether. The slightly yellow polymer was collected and further purified by gel filtration (Sephadex LH-20, methanol as an eluent). After drying in vacuo, 42.1 mg (81%) of polymer **9** was obtained.

Partial Cleavage of Disulfide-Bridged PAEI Gel by Reduction. A typical experiment is as follows. The disulfide-bridged gel **10** (100 mg) prepared from 10% partially hydrolyzed PAEI **6** ($M_n = 24\,000$) and dithiodi-2,1′-ethanediyl diisocyanate (**3**) was placed in a dialysis tube, which was immersed in 30 mL of dioxane-water (2/1). After the gel was swollen for 1 day in this solvent, the dialysis tube was transferred to the fresh solvent (30 mL of dioxane and 15 mL of water) containing 0.1 g of triphenylphosphine with slow stirring at room temperature. After incubation for 4 h, the gel was collected by filtration, washed with the same solvent and methanol, and then treated with 80 mg of *N*-ethylmaleimide (NEM) as a quenching reagent for thiol groups. After washing with methanol, drying in vacuo gave 52.2 mg (52%) of the gel.

Results and Discussion

Synthesis of Anthracene-SS-Modified PAEI 7. The preparation of anthracene-SS-modified PAEI (**7**) is outlined in Scheme II. A series of partially hydrolyzed PAEIs **6** with various degrees of hydrolysis were prepared by the modified method from the previous report.[6,7] The degree of polymerization could be controlled by the feed ratio of

Scheme II



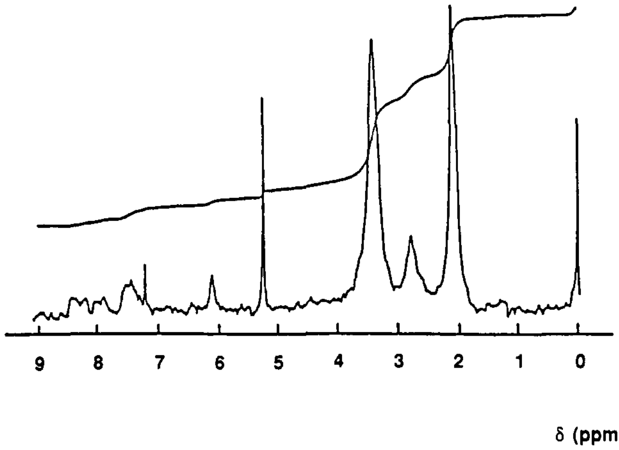


Figure 1. ^{1}H NMR spectrum of anthracene-SS-modified PAEI (7) in CDCl$_3$.

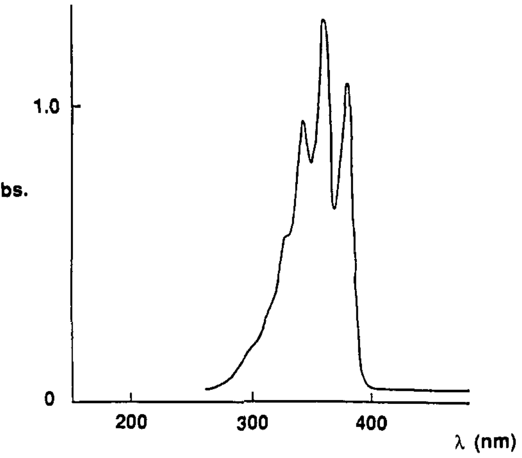


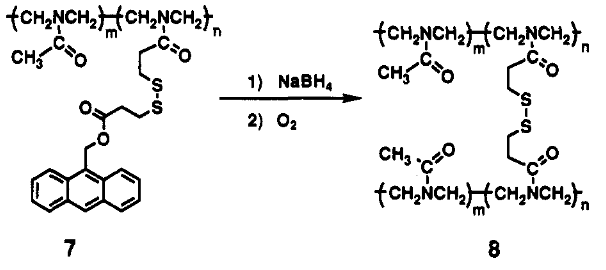
Figure 2. UV absorption spectrum of anthracene-SS-modified PAEI (7) in methanol.

Table I
Synthesis of Anthracene-SS-Modified PAEIs (7)

run	partially hydrolyzed PAEI (6)		7	
	$\bar{M}_n$[a]	$q/(p+q)$[b,c]	yield (%)	$n/(m+n)$[c,d]
1	24 500	4.7	77	2.7
2	19 900	5.8	76	4.6 (4.5[e])
3	24 500	10.2	84	6.5
4	19 900	12.4	99	9.4 (8.7[e])

[a] Determined by GPC (PSt standard). [b] Calculated by titration. [c] The numbers of repeating units, p, q, m, n, are shown in Scheme II. [d] Determined by UV (λ_{max} = 386 nm, ϵ = 8000). [e] Determined by ^{1}H NMR.

Scheme III



monomer to initiator, and the degree of hydrolysis could be successfully regulated by the amount of alkali.

These polymers having various degrees of hydrolysis were treated with (9-anthracenyl)methyl hydrogen 3,3′-dithiodipropanoate (5) in the presence of a few equivalents of dicyclohexylcarbodiimide (DCC) as a condensing agent. Figure 1 illustrates the ^{1}H NMR spectrum of anthracene-SS-modified PAEI (7) (9.4%-modified, determined by UV). The peak of the methylene protons adjacent to the secondary amino group in the starting partially hydrolyzed PAEI 6 (12.4%-hydrolyzed) disappeared completely, and aromatic protons and singlet methylene protons were observed in the spectrum of the modified PAEI. This result is taken to support almost quantitative introduction of anthracene and disulfide groups in PAEI. The degrees of substitution of anthracene groups were calculated by the integral ratio of aromatic protons to acetyl protons.

The UV spectrum of the obtained anthracene-SS-modified PAEI (7) in methanol is represented in Figure 2. The absorption maxima of the anthracene group are shown at 386, 370, and 348 nm. The starting compound 5 has a similar absorption, λ_{max} = 386 nm (ϵ = 8000). From the UV spectrum of the anthracene-SS-modified polymer (7), the degree of substitution could be estimated on the basis of the molecular absorptivity (ϵ) for the starting compound (5). Table I summarizes the results of the preparation of anthracene-SS-modified PAEIs (7) together with their degrees of substitution.

The degrees of substitution estimated by UV spectra were found to be close to those from ^{1}H NMR. These values also corresponded well to the degrees of hydrolysis of the starting partially hydrolyzed PAEIs. This result confirms a completion of condensation reaction for the preparation of 7. The swelling properties of the obtained gels can be controlled by the values of degrees of substitution (vide infra), that is, by the degrees of hydrolysis in 6.

From GPC analysis, no significant change of the molecular weight of 7 was observed in comparison with that of the parent polymer. The molecular weight distribution of 7 was also similar to that of the starting polymer. The GPC trace using the UV detector at 391 nm supported the fact that the anthracene group was introduced to the PAEI. These results indicate that no significant chain degradation or cross-linking reaction took place during the condensation step for the preparation of these functionalized PAEIs. It should be also noted here that no low molecular weight impurity was contaminated in 7 from the results of GPC analysis.

Redox Gelation of Anthracene-SS-Modified PAEI. The preparation of PAEI gel by the reduction–oxidation of disulfide groups is shown in Scheme III. The reduction of disulfide was carried out in the presence of an excess amount of sodium borohydride in deaerated ethanol to liberate thiol groups in the polymer chain. The thiol groups are known to be unstable under air to form a disulfide bond by oxidation. Thus, it should be difficult to isolate the thiol-modified PAEI. After the removal of the reducing agent, in situ oxidation of thiol in a pendant group of the polymer took place in air to afford the formation of networks at the high concentration or in bulk.

Table II
Redox Gelation of Anthracene-SS-Modified PAEIs (7)

	7		gel (8)	
run[a]	$\bar{M}_n$[b]	$n/(m+n)$[c]	yield (%)	deg of swelling[d]
1	24 500	2.7	45	44.8
2	19 900	4.6	68	17.3
3	24 500	6.5	63	15.2
4	19 900	9.4	75	10.7
5	24 500	0[e]	0[f]	

[a] After reduction by $NaBH_4$, then oxidation under air. [b] Determined by GPC (PSt Standard). [c] Determined by UV (λ_{max} = 386 nm, ϵ = 8000). [d] g of H_2O/g of dry gel. [e] Hydrolyzed or not hydrolyzed PAEI was used. [f] No gelation was observed.

Scheme IV

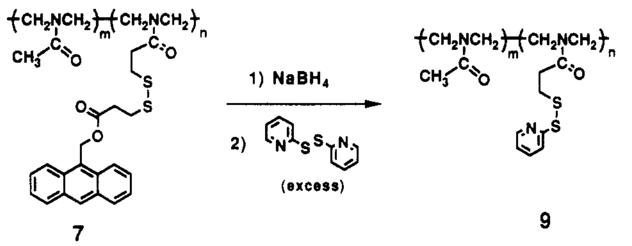


Table II shows the results of gelation by in situ reduction–oxidation of anthracene-SS-modified PAEI (7) with a variety of degrees of the substitution together with degrees of swelling. The PAEI gel 8 film was obtained in good yield, which was swollen in water to form a stable hydrogel. No gelation was observed in the absence of disulfide group in the polymer pendant, i.e., in the cases of hydrolyzed PAEI 6 and of nonhydrolyzed parent polymer by the treatment with the reducing agent and then exposure to air (run 5). As shown in Scheme IV, the quenching of the liberated thiol groups from the anthracene-SS-modified (2.7%) PAEI (7) in the presence of an excess amount of 2,2′-dithiodipyridyl was carried out under a rather diluted condition to avoid the cross-linking. The content of the anthracene moiety in the regenerated polymer 9 was found to be less than 0.1% estimated by its UV spectrum. From GPC analysis monitored by the UV detector at 391 nm, no peak was observed in the region that the original polymer had. These results may indicate that the intermolecular cross-linking by the formation of the disulfide bonds caused the formation of networks. With increasing degrees of substitution of the anthracene-SS-modified PAEIs, the decrease of degrees of swelling of the resulting gel in water was observed. Thus, the average distance between the nearest two branches could be controlled by the content of the disulfide groups in 7.

Cross-Linking Using Bifunctional Disulfide Compounds. An alternative method for the preparation of disulfide-bridged PAEI gel is the reaction of the secondary amino groups in the partially hydrolyzed PAEI 6 with the bifunctional disulfide compounds as the cross-linking agents (Scheme V). Commercially available 3,3′-dithiodipropanoic acid (1) was employed as the starting material. Diacid 1 was converted to diacid dichloride 2 by the treatment with thionyl chloride in good yield. Diisocyanate 3 was prepared from the diacid dichloride (2) by the Curtius reaction according to the reported procedure.[16] In the case of diacid 1, the condensation reagent or the activating system for the carboxylic acid group such as DCC, 2-ethoxy-1-(ethoxycarbonyl)-1,2-dihydroquinoline (EEDQ), triphenylphosphine (PPh_3)–pyridine, or 1,1′-carbonyldiimidazole (CDI) was required to form the amide linkage with partially hydrolyzed PAEI 6. Diacid dichloride 2 or diisocyanate 3 was used to form the cross-linking points in the presence of triethylamine as a base and DBU as a catalyst, respectively. Table III shows the results of condensation reactions of the partially hydrolyzed PAEI 6 (M_n = 14 000, 24%-hydrolyzed) using these bifunctional disulfides (1–3) together with the swelling properties. When diacid 1 or diacid dichloride 2 was used as a cross-linking agent to form the gel with the amide linkage, the molecular structure of the resulting gel (8) was same as that of the product prepared by the reduction–oxidation method described before. In the case of diisocyanate 3, the resulting gel (10) had the urea linkage at the cross-linking points.

Scheme V

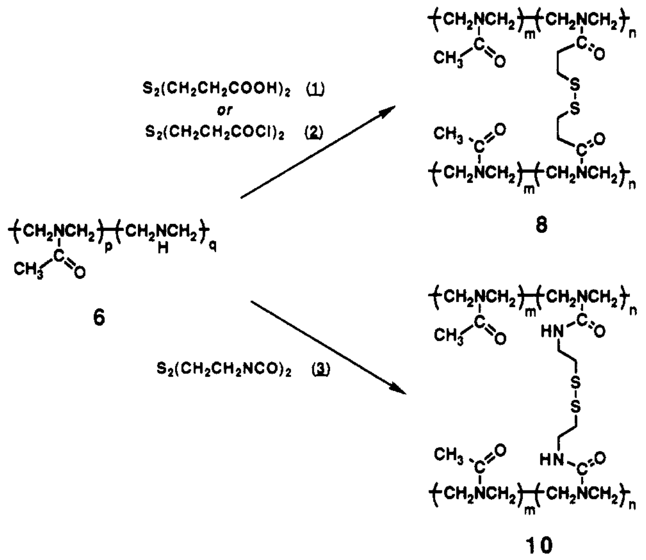


Table III
Cross-Linking Reactions Using Various Cross-Linkers[a]

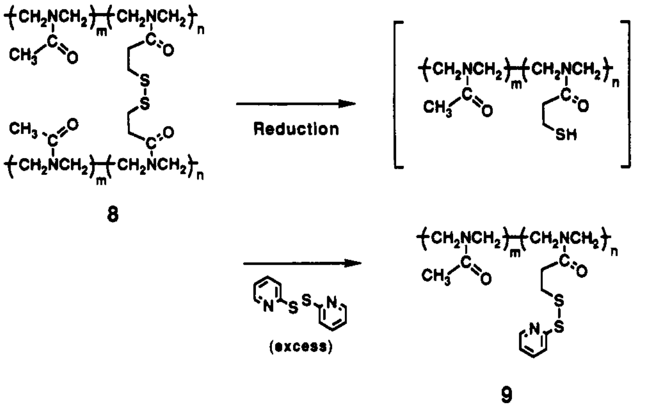
run	S–S cross-linker	yield (%)	deg of swelling[b]
1	1/DCC	73	4.0
2	1/$(PhO)_3P$-Py	0	
3	1/EEDQ	76	24.1
4	1/CDI	0	
5	2/Et_3N	30	13.6
6	3/DBU	80	8.0

[a] Prepolymer ($\bar{M}_n$ = 14 000 by GPC PSt standard, 24% hydrolyzed) 300 mg, DMF 0.7 mL, 30 min, room temperature. [b] g of H_2O/g of dry gel.

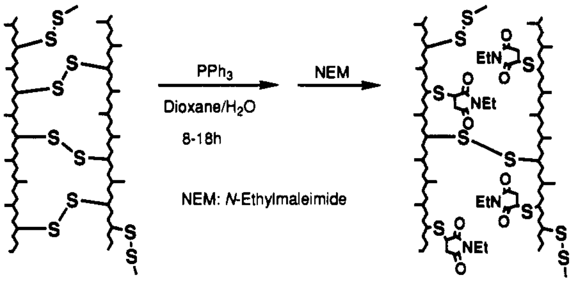
In run 2 of Table III, triphenyl phosphite–pyridine was used as a cross-linking agent to the amide linkage, but this compound is also known to be a reducing agent for the disulfide group. Thus, the reaction was complicated, and no gelation was observed. On the other hand, in the case of run 4, the addition of the solution of CDI-activated carboxylic acid to the polymer solution caused an increase of viscosity. However, enough cross-linking to form a stable network was not observed. In other cases, the gelation occurred within a few minutes after the addition of the cross-linking agent or the solution of the corresponding activated carboxylic acid. Especially in the case of the diacid dichloride (run 5), the gelation took place too fast to maintain a homogeneous solution, which caused the low yield. Other condensation systems provided the PAEI gels in good yields (runs 1, 3, and 6).

Swelling Property. The PAEI gels (8 or 10) prepared by the cross-linking reactions using bifunctional disulfide compounds were also swollen in water to form the stable hydrogels as were those prepared from the reduction–oxidation method or by conventional cross-linking agents such as diisocyanates.[4] In the case of the gel having the urea linkage (10) prepared by diisocyanate 3, the structure of the product should be different from that of the gel

Scheme VI



Scheme VII



from the diacid (1) or the diacid dichloride (2). However, the swelling property of the PAEI gel did not depend on these differences of the linkages but mainly on the degrees of hydrolysis or on the content of the remaining secondary amino groups.[4]

Reductive Cleavage of Disulfide-Bridged PAEI Gel. These disulfide-bridged PAEI gels (8 and 10) were subjected to reduction of the disulfide groups to form the linear polymers (Scheme VI). The reduction of the gel was carried out in the presence of excess amounts of various reducing agents such as sodium borohydride (in ethanol), triphenylphosphine (in dioxane–water), or sodium hydrosulfite (in water–methanol). The activities of these reducing agents to the disulfide groups in the networks were almost same. The gel became soluble and was found to be homogeneous within 1 day to give a linear polymer. Without reducing agent, these disulfide-bridged gels were not soluble in each medium, but only swollen. The previously reported[4] PAEI gels having no disulfide group at the cross-linking points were not cleaved by the reduction. These blank experiments showed that the cleavage of the networks to the soluble polymer was caused by breaking the disulfide bonds. Thus, the disulfide-bridged gel became soluble by the reduction of disulfide bonds. To avoid reoxidation by air, the generated thiol-modified PAEI was quenched by 2,2′-dithiodipyridyl or *N*-ethylmaleimide. As a result, the anthracene-SS-modified PAEI (7) is demonstrated as a redox-sensitive reversible hydrogel through the covalent cross-linking by means of the reversible conversion between disulfide and thiol groups.

Partial Cleavage of Disulfide-Bridged PAEI Gel. The partial cleavage of the disulfide-bridged PAEI gel (8 or 10) was carried out in the presence of PPh_3 as a reducing agent in dioxane–water = 2/1 (Scheme VII). The gel was swollen in this mixed solvent more and more by the reduction of the disulfide cross-linkages. Table IV shows the results of the partial cleavage and the swelling properties of the obtained gels. In the case that the reaction time was longer than 12 h, the gel was completely dissolved, and no apparent insoluble part was recovered. With increasing the reaction time, the yield of PAEI gel was decreased and its swelling property in water was increased. This means that the cleavage of the cross-linking of disulfide bonds by reduction caused an increase of the degree of swelling. The swelling property of the gel could be controlled both by the degree of hydrolysis, i.e., the degree of substitution, and also by the reaction time for the reduction of the disulfide-bridged gel.

Table IV
Partial Cleavage of SS-Bridged Gel

run[a]	time (h)	yield (%)	deg of swelling[b]
1	0[c]	100	9.6
2	3	57	11.6
3	8	52	16.6
4	10	30	29.5
5	12	0[d]	

[a] 100 mg of dry gel, 0.1 g of PPh_3, dioxane/water = 2/1. [b] g of H_2O/g of dry gel. [c] Without reducing agents. [d] No apparent insoluble part.

References and Notes

(1) Present address: Department of Applied Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-11, Japan.
(2) Present address: KRI International Inc., Chudoji, Shimogyo-ku, Kyoto 600, Japan.
(3) Reviews of the polymerization of cyclic imino ethers: (a) Kobayashi, S.; Saegusa, T. In *Ring-Opening Polymerization*; Ivin, K. J., Saegusa, T., Eds.; Elsevier Applied Science Publishers: Essex, U.K., 1984; Vol. 2, p 761. (b) Saegusa, T.; Kobayashi, S. *Encyclopedia of Polymer Science and Technology*; Wiley: New York, 1976; Suppl. Vol. 1, p 220. (c) Saegusa, T.; Kobayashi, S. In *Macromolecular Science, International Review of Science, Physical Chemistry Series 2*; Butterworth: London, 1975; Vol. 8, Chapter 4. (d) Saegusa, T.; Chujo, Y. *Frontiers of Macromolecular Science*; Blackwell Science Publications: Oxford, U.K., 1989; p 119.
(4) Chujo, Y.; Yoshifuji, Y.; Sada, K.; Saegusa, T. *Macromolecules* **1989**, *22*, 1074.
(5) Chujo, Y.; Sada, K.; Matsumoto, K.; Saegusa, T. *Macromolecules* **1990**, *23*, 1234.
(6) Chujo, Y.; Sada, K.; Saegusa, T. *Macromolecules* **1990**, *23*, 2636.
(7) Chujo, Y.; Sada, K.; Saegusa, T. *Macromolecules* **1990**, *23*, 2693.
(8) Sakamoto, M.; Yamada, Y.; Tonami, H. *J. Appl. Polym. Sci.* **1969**, *13*, 1845 and references cited therein.
(9) Sakamoto, M.; Takeda, J.; Yamada, Y.; Tonami, H. *J. Appl. Polym. Sci.* **1970**, *14*, 865.
(10) Samuel, N. K. P.; Singh, M.; Yamaguchi, K.; Regen, S. L. *J. Am. Chem. Soc.* **1985**, *107*, 42.
(11) Regen, S. L.; Czech, B.; Singh, A. *J. Am. Chem. Soc.* **1980**, *102*, 6638.
(12) Regen, S. L.; Singh, A.; Oehme, G.; Singh, M. *J. Am. Chem. Soc.* **1982**, *104*, 791.
(13) Yamaguchi, K.; Kato, T.; Hirao, A.; Nakahama, S. *Makromol. Chem., Rapid Commun.* **1987**, *8*, 203.
(14) Nambu, Y.; Kijima, M.; Endo, T. *Macromolecules* **1987**, *20*, 962.
(15) Wulff, G.; Schulze, I. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 537.
(16) Lwowski, W.; Tisue, G. T. *J. Am. Chem. Soc.* **1965**, *87*, 4022.