Macromolecules 1993, 26, 5611–5614

Photogelation and Redox Properties of Anthracene–Disulfide-Modified Polyoxazolines

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Received February 19, 1993; Revised Manuscript Received July 23, 1993®

ABSTRACT: Polyoxazoline having both anthracene and disulfide groups was prepared by the reaction of partially hydrolyzed poly(*N*-acetylethylenimine) (PAEI) with (9-anthracenyl)methyl hydrogen 3,3′-dithiodipropanoate in the presence of dicyclohexylcarbodiimide (DCC) as a condensing agent. This photosensitive PAEI was irradiated with a 450-W high-pressure Hg lamp ($\lambda > 300$ nm) to produce a PAEI gel, which was swollen in water and showed characteristic hydrogel properties. The equilibrium swelling degree in water was controlled both by the irradiation time and by the degree of substitution of the anthracene moieties. The water uptake was up to 20 times the weight of the dry gel. The photo-cross-linked PAEI gel became soluble by the reductive cleavage of disulfide cross-links. The gelation by photoreaction and the cleavage by reduction constitute a novel photosensitive and redox-sensitive hydrogel system.

Introduction

Poly(*N*-acetylethylenimine) (PAEI) prepared by the ring-opening polymerization of 2-methyl-2-oxazoline is known to be highly hydrophilic and compatible with other organic commodity polymers.[4] On the basis of these characteristic properties of PAEI, we have previously reported that nonionic hydrogels based on PAEI can be prepared by several methods: cross-linking reaction of partially hydrolyzed PAEI,[5] copolymerization between 2-methyl-2-oxazoline and a bisoxazoline,[6] Diels–Alder reaction between maleimide- and furan-modified PAEIs,[7] and cross-linking of star-shaped PAEI.[8]

Recently, we also explored the preparation of hydrogel by photo-cross-linking of coumarin-modified PAEIs and the interconversion between hydrogel and soluble polymer by light irradiation.[9] A redox-reversible hydrogel was also described recently based on the reversible redox cross-linking of disulfide groups.[10] It is well-known that a disulfide can be ruptured by reduction to form two thiol groups and that cross-links are re-formed by mild oxidation (e.g., a cystine residue and two cysteine residues of proteins).[11,12]

In the present paper, a hydrogel system that is both redox sensitive and photosensitive is described on the basis of a reversible redox interconversion between disulfide (SS) and thiols (SH) and the photoreversibility of the photodimerization of an anthracene moiety. Anthracene is known to form [4 + 4] dimer upon light irradiation. It should be noted that λ_{max} of the anthracene moiety is near the visible region (around 380 nm).[13-15] Thus, light of a longer wavelength can be used for the photodimerization of anthracene than for coumarin derivatives. The splitting of the anthracene dimer by light or heat was also reported.[14] Thus, the anthracene moiety has a potential for a multiresponse hydrogel system by using covalent cross-linkings (thermo- and photosensitive system).

Scheme I

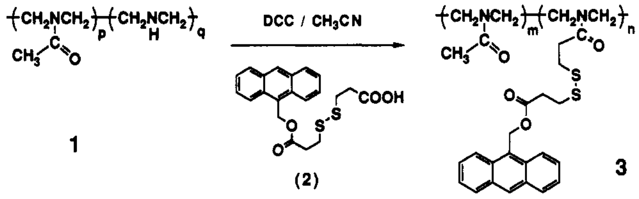


Table I. Synthesis of Anthracene–Disulfide-Modified PAEIs (3)

	partially hydrolyzed PAEI (1)		anthracene–SS PAEI (3)	
run	$\bar{M}_n$[a]	$q/(p+q)$[b]	yield (%)	$n/(m+n)$[c]
1	24 500	4.7	77	2.7
2	19 900	5.8	76	4.6
3	14 000	7.4	100	5.0
4	19 900	12.4	99	9.4 (8.7)[d]

[a] Determined by GPC (Pst standards). [b] Determined by titration. [c] Determined by UV analysis ($\lambda_{max} = 386$ nm, $\epsilon = 8000$). [d] Determined by ^{1}H NMR analysis (aryl protons vs acetyl protons).

Polymers bearing anthracene moieties and their photochemistry were reported by Tazuke et al.,[13] and the formation of polymer by the dimeric anthracene compound in the crystalline state was investigated by Yamamoto et al.[14] These studies were mainly concerned with the macromolecular photophysics. However, little is known about the preparation of hydrogel by photo-cross-linking of water-soluble polymer molecules. The only example is a water-soluble photo-cross-linkable poly(vinyl alcohol), which was employed as a matrix for immobilizing enzymes.[16,17]

It is shown here that the multiresponse PAEI gel system was prepared by photoreaction of the anthracene moiety and the gel was converted to the soluble polymer by reduction of disulfide cross-links.

Results and Discussion

Synthesis of Anthracene–Disulfide-Modified PAEI (3). The preparation of anthracene–disulfide (SS)-modified PAEI (3) is outlined in Scheme I. A series of partially hydrolyzed PAEIs (1) with various degrees of hydrolysis were prepared, and the introduction of the anthracene moiety to PAEI was carried out by a slightly modified method from the previous report.[10] The degrees of substitution of the anthracene groups could be calculated both from the integral ratio of the protons in the aromatic region to the acetyl protons in the ^{1}H NMR spectra and from the UV absorption spectra ($\lambda_{max} = 386$ nm, $\epsilon = 8000$). Table I summarizes the results of the preparation of anthracene–SS-modified PAEIs (3) together with their degrees of substitution.

® Abstract published in *Advance ACS Abstracts*, September 15, 1993.

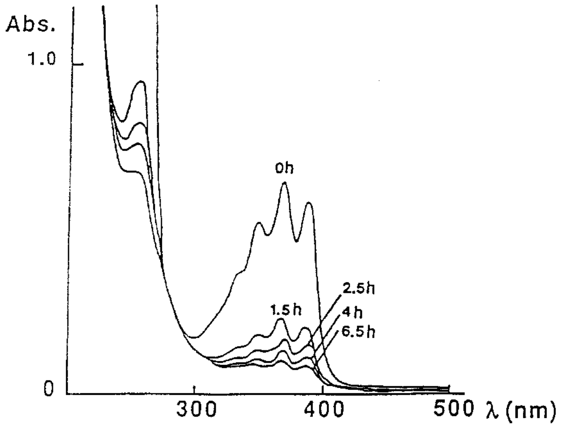
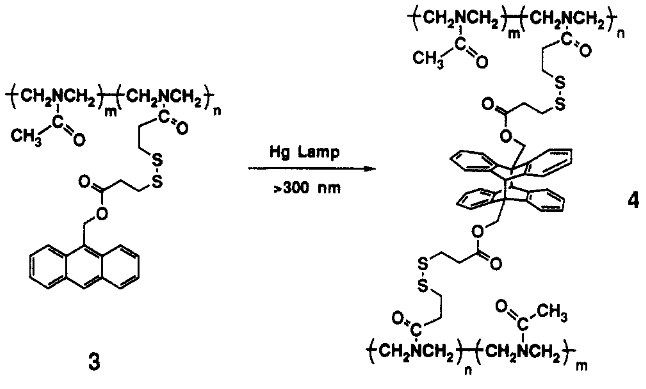


Figure 1. UV absorption spectral change of anthracene–disulfide-modified (9.4 mol %) PAEI (3) by irradiation with a 450-W high-pressure Hg lamp.

Scheme II



As can be seen in Table I, the degrees of substitution in 3 estimated from the UV spectra were found to be close to those from the ^1H NMR spectra. These values also corresponded to the degrees of hydrolysis of the starting partially hydrolyzed PAEIs (1). This result confirms a completion of condensation reaction for the preparation of 3. The swelling properties of the obtained gels from 3 can be controlled by the degree of substitution (*vide infra*), that is, by the degree of hydrolysis in 1.

From GPC analysis, no significant change of the molecular weights of 3 was observed in comparison with that of the parent polymer. The molecular weight distribution of 3 was also similar to that of the starting polymer. The GPC trace (UV detection at 391 nm) supported that the anthracene group was introduced to the PAEI. These data 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 also be noted that the GPC results show that no free photosensitive compounds contaminated 3.

Photogelation of Anthracene–Disulfide-Modified PAEI (3). The preparation of polyoxazoline gel (4) by the photodimerization of anthracene groups is shown in Scheme II. The photocoupling reaction was carried out in a bulk film (cast from methanol solution on a glass slide) at room temperature by using a 450-W high-pressure mercury lamp at λ > 300 nm. The reaction could be monitored by the UV absorption change of the cast film of PAEI on a quartz plate. As shown in Figure 1, the absorption around 380 nm decreased with increasing time of irradiation, which showed the disappearance of the longer conjugated anthracene moiety. Anthracene is known to form two isomeric dimers (head-to-head or head-to-tail) upon light irradiation. However, these two isomers in 4 were not identified in this study.

Table II. Photogelation of Anthracene–Disulfide-Modified PAEI (3)[a]

run	prepolymer (3) $\bar{M}_n$[b]	$n/(m+n)$[c]	irrad time (h)	gel yield (%)	degree of swelling[d] in H_2O
1	19 900	0.094	9.0	76	2.0
2	14 000	0.050	0.5	37	5.5
3	14 000	0.050	1.0	67	4.1
4	14 000	0.050	3.0	74	3.5
5	14 000	0.050	6.0	79	3.2
6	19 900	0.046	6.0	52	6.0
7	24 500	0.027	1.0	trace	
8	24 500	0.027	3.0	26	25.8
9	24 500	0.027	6.0	31	17.2
10[e]	24 000	0	6.0	0	

[a] Irradiated in the bulk film at room temperature under air. [b] Determined by GPC (PSt standards). [c] Determined by UV analysis. [d] Grams of H_2O/gram of dry gel. [e] Prepolymer (20% hydrolyzed or not hydrolyzed) without the anthracene moiety formed no gel.

Swelling Property in Water. Table II shows the results of photogelation and the swelling properties of the obtained films. When the degree of substitution was fixed at 5.0 mol % (runs 2–5 in Table II) or 2.7 mol % (runs 7–9 in Table II), the yield of photo-cross-linked PAEI gel (4) was increased and the swelling in water decreased with increasing reaction time. Thus, the swelling property of the obtained gel could be controlled by the time of irradiation.

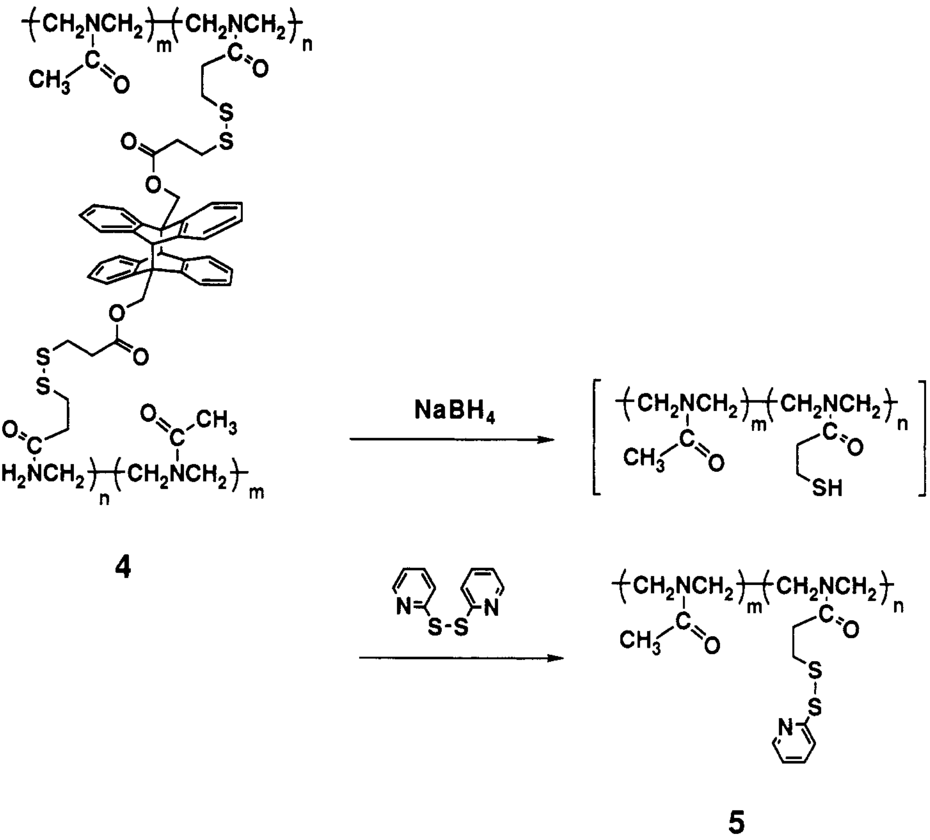
When the reaction time was fixed at 1 h (runs 3 and 7 in Table II), the PAEI gel (4) was obtained in 67% from 5.0 mol % modified PAEI, but the 2.7 mol % modified PAEI gel gave only a trace amount of insolubles. Thus, the more substituted PAEI tended to form more stable cross-linked products. No gelation was observed in the absence of pendent photosensitive groups in the polymer, i.e., in the cases of hydrolyzed PAEI and nonhydrolyzed parent polymer (run 10).[9] These results indicate that the intermolecular cross-linking by [4 + 4] photodimerization of the anthracene moieties in 3 caused the formation of the stable hydrogel.

As shown in Table II, the degree of swelling in water was increased on decreasing the content of photo-sensitive groups in the polymer. For example, the gel (4) prepared from PAEI containing 2.7 mol % anthracene took up water more than 25 times its own weight. The swelling property could be controlled also by the degree of functionalization of PAEI.

Reductive Cleavage of Photo-Cross-Linked PAEI Gel (4). These photo-cross-linked PAEI gels (4) were subjected to reduction of the disulfide groups to form linear polymers (see Scheme III). The reduction of the gel was carried out in the presence of an excess of sodium borohydride in ethanol. Photo-cross-linked PAEI gel (4) was initially swollen and then gradually dissolved in the solvent. It was found to be homogeneous within 1 day to yield soluble polymer. In the absence of the reducing agent, 4 was not soluble in this medium and was only swollen. The gel prepared from PAEI having no SS–anthracene moiety was not cleaved by the reduction and was stable under the same conditions. These blank experiments showed that the cleavage of the network to the soluble polymer was caused by breaking of disulfide bonds. Thus, 4 prepared by a photoreaction was soluble by reduction of S–S bonds.

To avoid reoxidation by air, the generated thiol-modified PAEI was quenched with 2,2′-dithiodipyridyl. The GPC

Scheme III



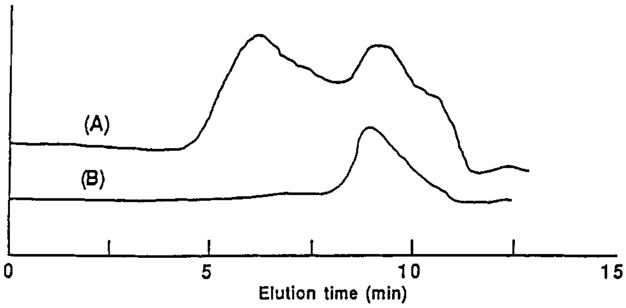


Figure 2. GPC traces of (A) the regenerated polymer (5) after the reduction of the gel (4) and (B) the starting PAEI.

trace of the regenerated polymer treated with the quenching reagent is illustrated in Figure 2 together with that of the original polymer. The molecular weight distribution of the regenerated polymer (5) after one polymer–gel–polymer cycle was bimodal, and the molecular weight of the peak at the shorter retention time was more than 100 000 (polystyrene standards). This peak is, therefore, due to microgel. The molecular weight of the peak at the longer retention time was almost that of the original polymer. This shows that the reduction of the disulfide group was not complete, and some microgel remained. A part of the soluble polymer obtained from the photo-cross-linked PAEI gel (4) by the reduction of the disulfide groups had a molecular weight and a molecular weight distribution similar to those of the starting PAEI. Thus, the conversion from PAEI gel (4) to the linear polymer by the reduction has been accomplished.

It should be noted that the present anthracene–SS-modified PAEI (3) has potential as a redox-sensitive and photosensitive hydrogel by means of reversible conversion between disulfides and thiols and the photodimerization of anthracene moieties. This multiresponse hydrogel can be applied as a functional polymeric material.

Experimental Section

General Procedure. IR spectra were recorded on a Hitachi 260-50 grating spectrophotometer. ^{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 solvent relative to the internal standard tetramethylsilane. 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 under nitrogen. Nitromethane or dichloromethane was distilled from P_2O_5 under nitrogen. According to the previous method, poly(*N*-acetylethylenimine) (PAEI) was prepared by the ring-opening polymerization of 2-methyl-2-oxazoline in the presence of methyl *p*-toluenesulfonate as an initiator and was partially hydrolyzed by treatment with aqueous sodium hydroxide.[5] Anthracene–SS-modified PAEI (3) was prepared by the previously described method.[10]

Photogelation of Anthracene–Disulfide-Modified PAEI (3). A typical procedure is as follows: A solution of 3 (18.8 mg) in dichloromethane (ca. 1 mL) was cast upon a slide glass (76 mm × 26 mm) at room temperature under air. The polymer film was irradiated with a 450-W high-pressure Hg lamp for 6 h. After the irradiation, the film was immersed in methanol to remove the unreacted polymer. After repeated washing with fresh methanol, the gel was dried in vacuo. The yield of PAEI gel (4) was 9.8 mg (52%).

Swelling Property. The equilibrium swelling properties in water were measured by using the previous method,[5-10] and 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 Photo-Cross-Linked PAEI Gel (4). In a typical method, photo-cross-linked PAEI gel (4, 5.0% modified, 52 mg) was suspended in 6 mL of ethanol, and dry nitrogen was passed through the solution for 30 min. Under a stream of nitrogen, 39 mg of sodium borohydride was added, and the solution was stirred 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 was further purified by gel filtration (Sephadex LH-20, eluent: methanol). After drying in vacuo, the polymer (**5**) was obtained quantitatively.

References and Notes

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