

Study on pH-Sensitive and Thermosensitive Polymer Networks Containing Polyacetal Segments

JUAN DU, YUXING PENG, TINGTING ZHANG, XIAOBIN DING, ZHAOHUI ZHENG

Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610065, China,

Received 17 November 2000; accepted 5 March 2001

ABSTRACT: A series of pH-sensitive and thermosensitive polymer networks were first obtained by copolymerization of telechelic poly(1,3-dioxolane) (PDXL) with acrylic acid (AA), acrylamide (AM), and *N*-isopropylacrylamide (NIPAM), respectively. The copolymerization of PDXL diacrylate (PDXLDA) with AA, AM, or NIPAM is expected to lead to polymer networks in which homopolymeric segments of the monomer are connected by polyacetal segments. As a combination of these two parts, these polymer networks can have some interesting physical properties. For example, the copolymer networks of poly(AA-*b*-DXL) showed pH sensitivity, and both the copolymer networks of poly(AM-*b*-DXL) and poly(NIPAM-*b*-DXL) showed temperature sensitivity. Moreover, because of the low ceiling temperature of polyDXL, the networks containing polyacetal segments (PDXL) can degrade by treatment with a trace of appropriate cationic initiator. The polymer networks prepared were characterized by Fourier transform infrared, differential scanning calorimetry, and swelling data. © 2002 John Wiley & Sons, Inc. *J Appl Polym Sci* 83: 3002–3006, 2002; DOI 10.1002/app.2329

Key words: polymer networks; degradation; poly(1,3-dioxolane)

INTRODUCTION

The pioneering work of Goethals and coinvestigators^{1–5} on the preparation of poly(1,3-dioxolane) (PDXL) bismacromonomers provided the possibility of preparing well-defined polymer networks containing PDXL segments. Among the reports, three methods were used in the synthesis of PDXL bismacromonomers.

1. By end-capping the bifunctionally living polyDXL with triethylamine, followed by nucleophilic substitution of the ammonium groups by a methacrylate anion.
2. By the end-blocker method, in which the polymerization of DXL is carried out in the

presence of diacryloylformals as chain transfer agent.

3. By synthesis of linear, well-defined dihydroxylated PDXL bismacromonomer, as reported by Franta et al.⁶

However, few polymer networks have been synthesized since then.

In recent years, more interest has focused on the synthesis of polymers containing polyacetal segments because of the ease of degradation of these polymers under mild conditions by treatment with a trace of acid.⁷ Such networks are interesting from at least two standpoints: (1) solubilization of crosslinked polymers under mild conditions may be useful in itself and (2) the possibility of studying the soluble residual linear polymer chains may be used to obtain more insight into the copolymerization behavior. Until now, Goethals' group prepared polymer networks by copolymerization of PDXL bismacromonomer

Correspondence to: J. Du (dujuan98@263.net)
Contract grant sponsor: National Nature Sciences Foundation of China; contract grant number: 59773019.

Journal of Applied Polymer Science, Vol. 83, 3002–3006 (2002)
© 2002 John Wiley & Sons, Inc.

with methyl methacrylate (MMA), butylacrylate, and styrene.⁸ However, no studies are based on the intelligent polymer networks containing PDXL. In this investigation, pH-sensitive and thermosensitive polymer networks containing polyDXL segments were prepared. According to Hoffman and Tanaka,^{9–12} the polyacrylamide (PAA) gels proved to be pH sensitive and both poly(*N*-isopropylacrylamide) (PNIPAM) and polyacrylamide (PAM) were temperature sensitive. The copolymers of PDXL with the three monomers AA, AM, and NIPAM, respectively, possessed corresponding sensitivity. Because of the ease of degradation, these polymer networks tend to have potential applications in intelligent drug delivery systems. In the future, we hope more attention will be paid to this kind of materials.

EXPERIMENTAL

Reagents

1,3-Dioxolane (Acros Organics) was purified by distillation over CaH₂ and dried on sodium wire under reflux in the presence of a trace of benzophenone, until a blue color was obtained. The monomer was distilled just before use (bp 74°C). Dichloromethane was distilled twice over CaH₂. The solvent was distilled just before use. Triflic acid was purified by distillation. Acrylic acid was distilled in a trace of benzoquinone. Dried pyridine was obtained by distillation in KOH.

Synthesis of OH–PDXL–OH Macromonomer (I)

CF₃SO₃H (15 μL) in 10 mL of CH₂Cl₂ solution was placed in a 50-mL flask provided with stirring and an inlet for dry nitrogen, after which 0.2 mL ethylene glycol was added to the bottle. With stirring, 20 mL dioxolane was added dropwise to the system. The mixture was stirred for 3 h and was thermostated at 50°C; finally, an excess amount of *tert*-butylamine was added to stop the reaction. The reaction mixture was poured out into a beaker and precipitated in cold ether and washed several times with ether. The precipitate was then dried under vacuum. A 15.5-g sample of **I** (yield 80%; $M_n = 2950$) was obtained.

Synthesis of PDXL Bismacromonomer

OH–PDXL–OH (10 g; $M_n = 2950$) and pyridine (10 mL) were placed in a flask provided with stirring and an inlet for dry nitrogen, after which 1 mL acrylic acid was introduced. Then 2 g of

dicyclohexcarbodiimide in 5 mL CH₂Cl₂ solution was added dropwise to the mixture, which was then thermostated at 25°C for 2 h. The mixture was washed with cold ether several times. The precipitate was dried under vacuum. An 8.5-g sample of PDXL diacrylate (PDXLDA; yield 85%) was obtained.

Synthesis of Networks

Toluene (10 mL), PDXLDA (1 g), 2,2'-azobis(2-methylproprionitrile) (5 mg), and a certain amount of comonomer were placed in a 20-mL test tube, which was sealed under vacuum at 70°C for 16 h. A piece of gel was obtained.

Degradation in Acid Solution

A 0.2-g sample of each polymer network was placed in 10 mL of a 0.01 mol/L triflic acid solution in CH₂Cl₂ or other solvents. The degradation time was measured as the time necessary to completely dissolve the material.

RESULTS AND DISCUSSION

Synthesis of PolyDXL Bismacromonomer

Recently, Franta and Reibel¹³ established that, when 1,3-dioxolane is polymerized by strong protonic acids, such as triflic acid, in the presence of a diol, the polymer formed is essentially linear and carries –OH groups at both chain ends. In this way, by changing the ethylene glycol content, a series of OH–PDXL–OH (**I**) macromonomers with different molecular weights (M_n) were obtained. Figure 1 shows that the number-average molecular weights of polymer **I** as measured by GPC can be controlled by the content of ethylene glycol. With the increase of ethylene glycol concentration, the number-average molecular weight of polydioxolane decreased.

I can be esterified with acrylic acid, as shown in **Scheme 1**. The reaction is one of the standard methods of peptide synthesis. The DCCI is used for the reaction of the acid with an alcohol to form an ester, whereby it becomes a substituted urea. Pyridine is used as the catalyst. This esterification reaction is carried out quantitatively, so no side reaction can be found. According to this, the PDXL bismacromonomer **II**–PDXL diacrylate (PDXLDA) was produced.

Synthesis and Swelling Behavior of the Copolymer Networks

PDXLDA can copolymerize with different monomers that determine the properties of networks.

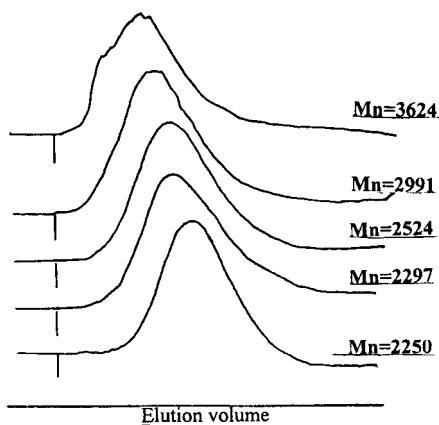
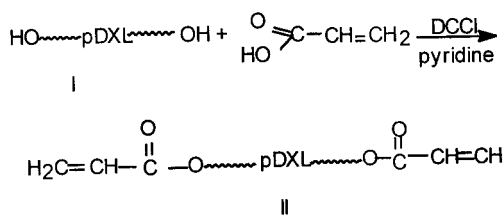


Figure 1 GPC analysis of PDXL macromonomer with different ethylene glycol (EG) contents: 0.625 mol/L ($M_n = 3624$); 1.210 mol/L ($M_n = 2991$); 1.815 mol/L ($M_n = 2524$); 2.420 mol/L ($M_n = 2297$); 6.050 mol/L ($M_n = 2250$).

In this study, comonomer acrylic acid (AA), acrylamide (AM), and *N*-isopropylamide (NIPAM) were selected. The reactions were conducted in toluene at 70°C with 2,2'-azobis(2-methylpropanitrile) as initiator. The polymerization was continued for 16 h. The end products were either transparent polymer networks [poly(AA-*b*-DXL) and poly(NIPAM-*b*-DXL)] or a translucent polymer network [poly(AM-*b*-DXL)] with good elasticity. Figure 2 shows the FTIR spectra of PDXL, PDXLDA, poly(AA-*b*-DXL), poly(NIPAM-*b*-DXL), and poly(AM-*b*-DXL). The difference appears in 1638 and 1720 cm^{-1} , which is attributed to the stretching of C=C and C=O of the ester structure, respectively. In polyDXL, no peaks appear, whereas in PDXLDA, both peaks appear. Evidently, PDXLDA was an ester product of polyDXL. In IR spectra of polymer networks [poly(AA-*b*-DXL), poly(NIPAM-*b*-DXL), and poly(AM-*b*-DXL)], the stretching of C=C was weakened and C=O was greatly strengthened compared to



DCCl: dicyclohexylcarbodiimide

Scheme 1

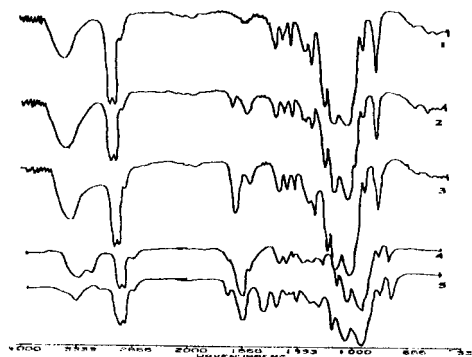


Figure 2 FTIR spectra of PDXL macromonomer and copolymer networks: 1, PDXL; 2, PDXLDA; 3, poly(AA-*b*-DXL); 4, poly(NIPAM-*b*-DXL); 5, poly(AM-*b*-DXL). [PDXL] : [AA] = 1 : 3 mol/mol; M_n (PDXL) = 2950.

those of PDXLDA. This shows that the radical copolymerization of PDXLDA with AA, NIPAM, and AM does occur.

Polyacrylic acid (PAA) is well known as a pH-sensitive hydrogel because of the -COOH groups. The polymer networks with homopolymeric segments of acrylic acid should also be expected to have pH sensitivity. Figure 3 supports this result. The swelling degree of the poly(AA-*b*-DXL) networks is greatly influenced by pH values of water. At pH = 1.5, the networks swell slowly, start to degrade after 10 h, and finally dissolve in water after 24 h; whereas at pH ≥ 7.0 , the networks swell rapidly because the -COOH groups can be easily ionized by reaction with OH^- , and the swelling degree remains at equilibrium thereafter.

The degree of swelling is calculated from the following expression: $\text{SD} = [(W_s - W_d)/W_d] \times 100$, where W_s is the swelling sample and W_d is the dried gel sample.

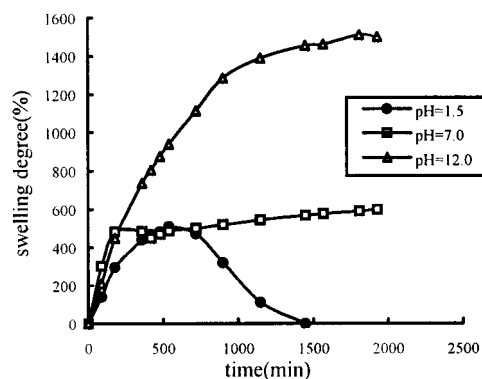


Figure 3 Swelling kinetics of the hydrogel in water at different pH polymer networks. [PDXL] : [AA] = 1 : 3 mol/mol; M_n (PDXL) = 2950.

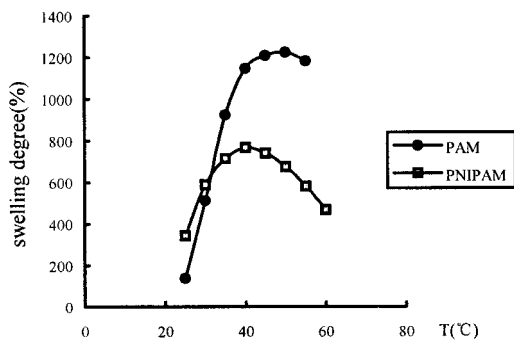
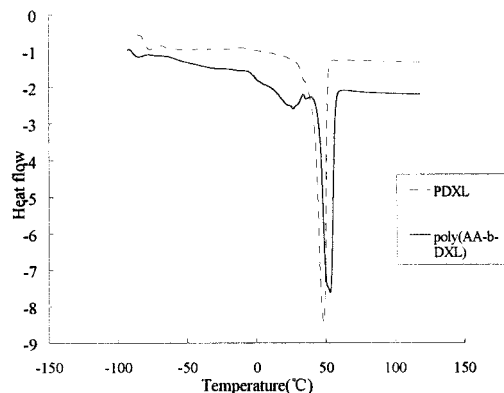
Table I Swelling Behavior of Poly(AA-*b*-DXL) Networks [M_n (PDXL) = 2950] with Different Compositions

Poly(AA- <i>b</i> -DXL) [PDXL]/[AA] (mol/mol)	Degree of Swelling (%) in 20 h			
	CH ₂ Cl ₂	H ₂ O	THF	CH ₃ OH
1 : 1.5	1400	1139	309	18
1 : 15	1252	507	437	125
1 : 30	243	101	229	170

The polymer networks prepared can swell in organic solvents. It was found that the swelling degree of the networks is both solvent dependent and composition dependent. For example, the poly(AA-*b*-DXL) networks swell rapidly in CH₂Cl₂ and reach swelling equilibrium in no more than 0.5 h. However, it takes more than about 20 h to reach equilibrium in CH₃OH. Table I shows that the swelling behavior of poly(AA-*b*-DXL) is also influenced by the constituent of networks. With the increase of content of AA, the swelling degree decreases in CH₂Cl₂ and water, and increases in CH₃OH.

Figure 4 shows that the swelling behavior of both poly(NIPAM-*b*-DXL) and poly(AM-*b*-DXL) is thermosensitive. With the increase of temperature, the poly(NIPAM-*b*-DXL) showed a peak point at 40°C, after which the swelling degree of the networks decreased. Evidently above this low critical solution temperature (LCST) (40°C), phase separation occurs as it does in the case of PNIPAM. There is an elevation of LCST (compared to the earliest report of 31°C)¹⁴ resulting from the copolymerization with PDXL.

The swelling of the networks in both water and organic solvents can be explained by a

**Figure 4** Swelling behavior of networks at different temperatures: 1, poly(AM-*b*-DXL); 2, poly(NIPAM-*b*-DXL). M_n (PDXL) = 2950.**Figure 5** DSC analysis of poly(AA-*b*-DXL) networks and macromonomer. M_n (PDXL) = 2950; [PDXL] : [AA] = 1 : 3 mol/mol.

microphase-separated bicontinuous structure.¹⁵ DSC analysis gives further support for the hypothesis of a microphase-separated structure. Figure 5 shows a DSC analysis of the PDXL and polymer networks of poly(AA-*b*-DXL) under the same heating process. It clearly shows an endotherm at 50°C, which is attributed to the melting of the crystalline PDXL in the PDXL curve, whereas in the polymer networks curve, another endotherm at 27°C appeared as a result of the copolymerization with PAA. Because the PDXL segments act as crosslinking agent in the networks and the two chain segments of PDXL and PAA possess different degrees of flexibility, the polymer networks show a microphase-separated interconnecting structure.

Degradation of Polymer Networks

All polymer networks prepared can degrade completely in acid solution. Degradation of poly(AA-*b*-DXL) is shown in Figure 3. In a water solution of pH 1.5, the networks can become soluble in 24 h. The solvents used had a significant influence on degradation, of which the degradation of poly(AA-*b*-DXL) is as example. Table II shows that the solvents with high polarity can cause the networks to degrade faster under the same acid condition.

With the addition of isopropyl alcohol, the degradation was delayed because the hydroxy functions, attributed to the higher basicity, reduce the protonation of the acetal groups and hence the rate of degradation.

After the complete degradation of poly(AA-*b*-DXL) networks (with [CF₃SO₃H] = 0.01 mol/L) in CH₂Cl₂, there is some residue left in the bottle, most of which solved in CH₂Cl₂. Figure 6 shows

Table II Degradation of Poly(AA-*b*-DXL) Networks in Different Acid Solutions at 25°C

Solvent	[H ⁺] ^a (mol/L)	[OH] ^b (mol/L)	Degradation Time (h)
CH ₂ Cl ₂	0.01	0.0	2
CH ₂ Cl ₂	0.005	0.0	2.5
CH ₂ Cl ₂ + isopropyl alcohol	0.01	0.01	2.5
CH ₂ Cl ₂ + isopropyl alcohol	0.01	0.1	12
THF	0.01	0.0	4
H ₂ O	0.01	0.0	25

^a CF₃SO₃H content.^b Isopropyl alcohol content.

the FTIR spectra of the original networks and the degraded residues. Only peaks of PAA were found in the latter, and no absorbance in 1024–1120 cm⁻¹, which belonged to the C—O—C functions of PDXL. It proved that the networks had been de-crosslinked.

CONCLUSIONS

The polymer networks containing polyacetal segments with pH sensitivity, temperature sensitivity, or other special physical properties can be prepared by copolymerization of polyDXL with different monomers that determine the properties of networks. As a combination of these two segments, the networks possess two important physical properties: swelling and degradation. The swelling behavior of polymer networks prepared in this investigation is both solvent dependent and composition dependent. Degradation is also

influenced by solvents, acid concentration, and so forth. Based on this study, more attention should be paid to this kind of new materials.

This work was supported by the National Nature Sciences Foundation of China (59773019).

REFERENCES

- Goethals, E. J.; DeClercq, R. R.; Walraedt, S. R. *J Macromol Sci Pure Appl Chem* 1993, A30, 679.
- Goethals, E. J.; DeClercq, R. R.; DeClerq, H. C.; Hartmann, P. J. *Makromol Chem Macromol Symp* 1991, 47, 151.
- Goethals, E. J.; Trossaert, G.; DeVos, R.; DeClercq, R. R. *Makromol Chem Macromol Symp* 1991, 48/49, 427.
- Van Meirvenne, D.; Goethals, E. J. *Makromol Chem Suppl* 1989, 15, 61.
- De Clercq, R. R.; Goethals, E. J. *Macromolecules* 1992, 25, 1109.
- Franta, E.; Kubisa, P.; Onld Kada, S.; Reibel, L. *Makromol Chem Macromol Symp* 1992, 60, 145.
- Benhira, A.; Franta, E.; Francois, J. *Macromolecules* 1992, 25, 5697.
- DeClercq, R. R.; Trossacert, G. G.; Hartmann, P. J.; Walraedt, S.; Goethals, E. J. *Macromol Symp* 1994, 77, 395.
- Tanaka, T. *Sci Am* 1981, m244, 124.
- Hoffman, A. S. *J Controlled Release* 1987, 6, 297.
- Ohmine, I.; Tanaka, T. *J Chem Phys* 1982, 77, 5725.
- Hoffman, A. S.; Afrassiabi, A.; Dong, L. C. *J Controlled Release* 1986, 4, 213.
- Franta, E.; Gerard, E.; Gnanou, Y.; Reibel, L.; Rempp, P. *Makromol Chem* 1990, 191, 1689.
- Schild, H. G. *Prog Polym Sci* 1992, 17, 163.
- Chen, D.; Kennedy, J. P.; Allen, A. J. *J Macromol Sci Chem* 1998, 25, 389.

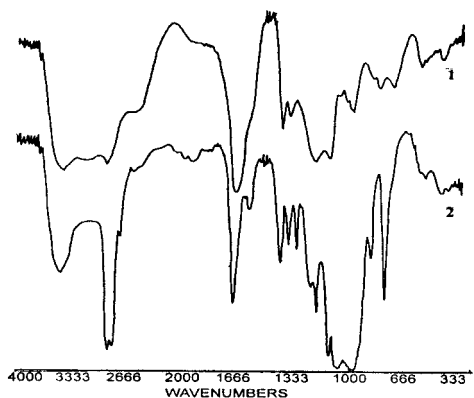


Figure 6 FTIR spectrum of (1) degraded residues and (2) poly(AA-*b*-DXL) networks. M_n (PDXL) = 2950; [PDXL] : [AA] = 1 : 3 mol/mol.