Preparation of Composite-Crosslinked Poly(*N*isopropylacrylamide) Gel Layer and Characteristics of Reverse Hydrophilic–Hydrophobic Surface

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ABSTRACT: The composite-crosslinked poly(*N*-isopropylacrylamide) (PNIPAAm) gels were prepared by grafting *N*-isopropylacrylamide on the surface of glass plates modified by organosilanes. The glass plates as the substrate increase the mechanical strength of composite PNIPAAm gel layers. We investigated the effects of a series of organosilanes and the reaction time of organosilanes on surface characteristics, such as the static contact angle and the layer thickness. We discuss the equilibrium swelling ratio and the water release behavior of the gel layers in terms of the crosslinking density of the composite gels. The composite gels exhibit not only the characteristics of remarkable water release but also the reversed hydrophilic-hydrophobic surface properties. The gel layers are hydrophilic under 25°C and change to hydrophobic above 40°C. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 72: 1–11, 1999

Key words: polymer gel; poly(*N*-isopropylacrylamide); dynamic contact angle; organosilane; surface; temperature-sensitive polymers

INTRODUCTION

Hydrogels are water-swollen polymer gels. They are attracting a large amount of attention in both theoretical study and real application.^{1–3} The polymer gels can be divided into the following 2 kinds: (1) those with no significant sensitivity to environmental changes, and (2) those sensitive to the change of environmental conditions, such as pH,^{4,5} temperature,^{6,7} photo,^{8,9} pressure,¹⁰ and electric field.¹¹ Among the hydrogels, the temperature-sensitive polymer gel, poly(*N*-isopropylacrylamide) (PNIPAAm), has been of great interest^{12,13} because PNIPAAm demonstrates a lower critical solution temperature (LCST) and temperature-dependent characteristics.¹⁴ It swells with an extended chain conformation in aqueous solution below 32°C and deswells with a compact chain conformation in aqueous solution above 32°C. The phenomenon is caused by reverse formation and cleavage of the hydrogen bond between water molecules and the hydrophobic molecular groups of PNIPAAm. We believed that the pentagonal water structure is generated among water molecules adjacent to the hydrophobic molecular groups of PNIPAAm.¹⁵ Since the pentagonal structure is stable at low temperatures and unstable at high temperatures, the reversed swelling-deswelling process can be observed with the variation of temperature.

As the volume phase transition brings about dramatic changes in the physical properties of the PNIPAAm gels, PNIPAAm and its copolymer gels are expected to be applied as new types

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of materials to serve as an (1) actuator,¹⁶ (2) a temperature-modulated bioconjugator to control enzyme activity,¹⁷ and (3) a separation module to extract water from the solution of macromolecules.¹⁸ Stimuli-responsive PNIPAAm gels have promising potential for designing an intelligent drug delivery system because they can be used as a molecular device for self-regulating drug delivery.^{19–22} One disadvantage of PNIPAAm gel is its poor mechanical properties. When the gel is fully swollen absorbing a large amount of water, it becomes unstable and is easily damaged by the effects of small stresses.

The surfaces modified by PNIPAAm to achieve the characteristics of hydrophobic-hydrophilic reverse have received a large amount of attention.²³⁻²⁵ Most research work concerns the formation of thin PNIPAAm layers on substrates by chemical grafting,²⁶ plasma,²⁷ and ultraviolet (UV) light.²⁸ Such surfaces modified by a PNIPAAm layer exhibit reversed hydrophobic-hydrophilic properties and can be used in the incubation process of cells.²⁹ However, the thin layer of PNIPAAm limits its application both because of its reversed surface properties and the amount of water or chemicals that can be delivered during environmental changes.

The main purpose of the present study at Pacific Northwest National Laboratory is to develop a technique to generate the compositecrosslinked PNIPAAm gel layers with covalent linkages to the surface of ceramic plates, such as glass plates. The composite-crosslinked PNIPAAm gels were prepared by first introducing vinyl groups on the glass surface then grafting NIPAAm with vinyl groups by radical polymerization in the presence of a crosslinking agent. The glass plate as a substrate increases not only the strength of composite gels, especially with a lower crosslinking density, but also keeps the size of the composite gels unchanged in the horizontal direction. Meanwhile, the thick layer of PNIPAAm gel makes it possible to deswell or swell a large volume of water as the result of reversing surface properties. It might be possible to use this strategy to develop a temperature-sensitive controlled-release system, which consists of porous ceramic materials as the interior reservoir of chemicals and the thick coating layer with the temperature-sensitive polymer gels as the delivering media.³⁰

EXPERIMENTAL

Materials

N-isopropylacrylamide (NIPAAm, 97%, Aldrich) and potassium persulfate (K₂S₂O₈, 99%, Aldrich) were purified by recrystallization from hexane and ethanol, respectively. N,N-methylbisacrylamide (BisAAm, 95%, Aldrich), N,N,N',N'-tetramethylethylenediamine (TMEDA, 99%, Aldrich), vinyldimethylchlorosilane (VDCS, Gelest), vinyltrimethoxysilane (VTMS, Gelest), decyltrichlorosilane (DTCS, Gelest), and methylacryloxypropyltrimethoxysilane (MAPTS, Gelest) were used without purification. Methanol (99.8%, Aldrich), ethanol (99.8%, Aldrich), and anhydrous toluene (99.8%, Aldrich) were distilled before use. Ultrapure water with a conductivity of 18 S cm^{-1} was used in all experiments. Clay Adams provided glass plate that was 1 mm thick, and Wafer Net, Inc. provided silicon wafers that were 0.5 mm thick.

Surface Modification

Silicone wafers and glass plate used as substrates were cut to be 20×10 mm wide and were washed with ethanol and ultrapure water, respectively. They were immersed into the precleaning agent, 1N HNO₃ aqueous solution containing 1% HF, for overnight at room temperature, then rinsed by ultrapure water thoroughly. During this process, hydroxyl groups were generated on the surface of substrates as shown by contact-angle measurements. To couple the organosilane on the surface of a silicone wafer or glass plate, the dried silicone wafer or glass plate was dipped in 5% (v/v) solution of organosilane in anhydrous toluene for a different duration. The reactions were performed at room temperature in a plate-bottom flask with one neck (250 mL), under a nitrogen atmosphere. An orbit shaker (Lab Line Instrument Inc.) was used to stir the solution in the flask. The samples were taken out at different times and rinsed three times for 1 min each in toluene. Finally, the samples were cured in an oven at 100°C for 5 min and stored in a vacuum oven at room temperature before measurements.

Preparation of Composite Crosslinked PNIPAAm Gels

The preparation method of composite crosslinked PNIPAAm gels can be schematically demonstrated as in Figure 1. Two methods can be employed to introduce the vinyl groups on the sur-



Figure 1 Schematic illustration of the preparation of composite crosslinked PNIPAAm gels: (a) vinyl groups grafted on the oxide surface by VTMS; (b) vinyl groups grafted on the oxide surface by VDCS; (c) NIPAAm and BisAAm grafted on the organosilane modified surface.

face of substrates: the condensation reaction of an alkoxysilane, such as the VTMS and OH groups, and the condensation reaction of a chlorosilane, such as the VDCS and OH groups. We set up the reaction in a round-bottom flask with one neck (100 mL). We used the following typical reaction procedure: 1.0 g of NIPAAm, 0.03 g of BisAAm, and 0.01 g of $K_2S_2O_8$ were dissolved in 20 mL of water, in which the glass piece was immersed. The flask was first vacuumed and subsequently filled with nitrogen. This process was repeated three times. To initiate the polymerization, 0.2mL of TMEDA was added to the solution by syringe. The temperature of the polymerization was kept at 6°C by immersing the flask into the bath with a mixture of water and ice. During the polymerization, the gel was gradually generated on the surface of the glass plate and in the solution. The composite crosslinked PNIPAAm gels with glass plate as substrate and the crosslinked PNIPAAm gels ($\sim 2 \text{ mm}$) as the top layer were made by carefully separating the glass plate from the gel and washing with a large volume of water. The composite gels with smooth plate were stable in water and did not show any sign of peeling after more than 6 months of storage in water.

Static Contact Angle

The static contact angle of water on the surface of substrates was measured by a contact angle goniometer (100-00, rame-hart, inc.). One water drop (10 μ L) was deposited on the dry surface of a silicone wafer or glass plate. The angle was measured as soon as possible after a sessile drop of water formed on the surface of the substrates. The static contact angle can be read directly from the goniometer. All measurements were done at room temperature and about 40% humidity. The five points on the surface were chosen at random for the measurement. The mean data were taken as final data as seen in the Discussion and Results section and they have standard deviations less than 5%.

Dynamic Contact Angle and Surface Tension

The dynamic contact angle and surface tension of glass plates with and without the grafted PNIPAAm gel were measured using a dynamic Wilhelmy plate technique³¹ (DCA-312, Cahn Instrument Inc.). The temperature of the test chamber (100 mL) was controlled by a thermostated circulator to ± 0.2 °C. The advancing contact an-

Organosilane	Abbreviation	Structure	MW	bp (°C)
Vinyldimethylchlorosilane	VDCS	H ₂ C=HCClSi (CH ₃) ₂	120.65	82
Vinyltrimethoxylsilane	VTMS	H ₂ C=CHSi(OCH ₃) ₃	148.23	123
Decyltrichlorosilane	DTCS	$CH_3(CH_2)_9Si(Cl)_3$	275.72	133
Methylacryloxypropyltrimeth-oxysilane	MAPTS	$HC = C(CH_3)COO(CH_2)_3Si(OCH_3)_3$	248.35	78

Table I Basic Properties of Organosilanes Used to Modify the Ceramic Substrates

gles and surface tension were measured at an immersion speed of 6 mm/min with a 15-mm immersion depth. A computer automatically recorded the hysteresis curve for the surface tension-immersion depth in water. Each measurement took five consecutive strokes. The data of the last three strokes were employed to calculate the contact angle and surface tension using the standard calculation procedure (DCA4A, Cahn Instrument Inc.). The mean data with a standard deviation less than 5% are shown in the Discussion and Results section.

Ellipsometery

Spectroscopic ellipsometry (with a Gaertner Ellipsometer) was used to determine the thickness of the oxide layer and the immobilized organosilane layer on the surface of silicone wafers. All samples were dried in the vacuum oven at 30°C overnight before measurement. The measurements were done immediately after the samples were taken out of the oven. At least five points on the sample surface were measured, and the thickness of the oxide and organosilane layers was calculated by one standard procedure (Auto, Gaertner Ellipsometer). The refractive index of the monolayer and underlying oxide was taken as 1.46.³² The thickness of the organosilane layer was calculated by subtracting the thickness of the oxide layer from the total thickness.

Swelling of Composite Crosslinked PNIPAAm Gels

We investigated the equilibrium swelling of the crosslinked PNIPAAm gels by immersing samples in water at a fixed temperature for 48 h to ensure reaching equilibrium (see Fig. 4 for the water uptake rate). After the samples were taken out from water and carefully wiped with tissue paper to remove the adherent water from gel surface, they were weighed. The swelling ratio of samples, S, was expressed as $S = (W_s - W_d)/W_d$, where W_s and W_d are the weight of the swollen and dried samples, respectively.

Rate of Water Release

Rate of water release by composite crosslinked PNIPAAm gels from the equilibrium swollen state to an equilibrium shrinking condition was measured by immersing samples in water at 15°C for 48 h, then transferring them to the water at a higher temperature. The samples were removed from the water at a specific time and weighed after being wiped with tissue paper to remove excess water on the gel surface. The rate of water release was expressed as the ratio of M_t to M_m , where M_t and M_m are the total amount of diffusion water at time t and after infinite time.

RESULTS AND DISCUSSION

Surface Modification

Organosilane is a useful chemical for modifying the surface of ceramic material.³³ Two kinds of organosilanes, alkoxysilane and chlorosilane, are widely employed for this purpose. In this study, we used four organosilanes as coupling agents to introduce functional groups on the surface of substrates. Their basic properties are listed in Table I. Among them, VDCS, VTMS, and MAPTS have vinyl groups that can be further employed to react with NIPAAm after coupling on the surface of substrates. Compared with other organosilanes, DTCS, without a vinyl group, but with a longer carbon-carbon chain, is used to study the thickness of the coupling layer. Figure 2 shows the change of the static contact angle of the glass plate modified by different organosilanes with the coupling time. The glass plate without the modification of organosilane has the lower contact angle ($\sim 18^\circ$) compared with the glass plates modified by organosilanes. This is because the hydroxyl groups cover the original glass plate surface, and the hydroxyl groups form the hydrogen bond with water molecules; that is, the surface exhibits typically hydrophilic characteristics. The static contact angle of all glass plates in-



Figure 2 Relationship between the coupling time and static contact angle of glass plate. The concentration of organosilane is 5% (v/v) in anhydrous toluene, the coupling temperature is 22°C, and the substrate is glass plate.

creases after the modification by organosilanes because of the hydrophobic characteristics of organosilane. The highly active chloride atoms in VDCS and DTCS react with hydrogen on the hydroxyl groups of the glass plates to form HCl, resulting in attachment of the activated organosilane, which adheres to the glass plates, as shown in Figure 1. The contact angle of the resulting glass plates rapidly increases and arrives at the equilibrium value, as shown in Figure 2, after 10 h. While MAPTS and VTMS were used as the coupling agent, the contact angle increases gradually with the coupling time and arrives at the equilibrium value only after 50 h because of the slow reaction process of MAPTS and VTMS with the hydroxyl group of the glass plate. Normally, this kind of reaction includes four steps.³⁴ At the beginning, the Si(OCH₃)₃ group is hydrolyzed, and the condensation to oligomer follows. The oligomers form the hydrogen bond with the hydroxyl groups of the substrate. Finally, a covalent linkage is formed with the substrate by the concomitant loss of water during the drying or curing process.

Figure 3 shows the thickness of the organosilane layer generated on the surface of the silicone wafer with the change of coupling time. The theoretical thicknesses of a monolayer of organosilane molecules, calculated by the length of the chemical bond,³⁵ are also shown in Figure 3 for comparison. When VTMS is used as the coupling agent, the experimental data match with the theoretical data very well, indicating that it is possible to generate a monolayer of VTMS molecules on the substrate. The deviation of the experimental predication from theoretical data was found when DTCS was used as the coupling agent at the longer coupling time. It might be attributed to the generation of multimolecular layers with the loose network structure.³⁴ Especially, the probability of the generation of multi molecular layers increases for the organosilane with a long chain at a longer coupling time.

Preparation of Composite Crosslinked PNIPAAm Gels

Three composite crosslinked PNIPAAm gels were prepared. The polymerization recipes are listed in Table II. The glass plate as the substrate for a crosslinked PNIPAAm gel improves the mechanical properties of the PNIPAAm gel, especially with lower crosslinking density. In this way, the requirement for the crosslinking density of the PNIPAAm gels can be greatly reduced for property measurements and for application. The composite gel can be picked up by tweezers from the solution without much damage. However, when the molar ratio of NIPAAm to BisAAm is 85, the mechanical property of the gel is so poor that it is impossible to perform any further measurements, although the gel can be generated on the surface of a glass plate.



Figure 3 Effect of the coupling time on the thickness of the organosilane layer. The concentration of organosilane is 5% (v/v) in anhydrous toluene, the coupling temperature is 22° C, and the silicone wafer is used as a substrate.

Swelling of Composite Crosslinked PNIPAAm Gels The swelling of composite crosslinked PNIPAAm gels as a function of temperature is shown in Figure 4. It is clear that each of composite gels can deliver about 14 and 20 g of water when the temperature changes from 20 to 40°C, depending on the crosslinking density of the gels. The larger amount of water is delivered by the gels with



Composition of gel, NIPAAm/BisAAM = 45 (molar ratio)

Figure 4 Equilibrium swelling ratios of the composite crosslinked PNIPAAm gels in pure water. The thickness of the gel is about 2 mm, and the glass plate is used as the substrate.

NIPAAm to BisAAm (Molar Ratio)	NIPAA (g)	BisAAm (g)	$\underset{(g)}{\overset{K_2S_2O_8}{\overset{(g)}{aaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa$	TMEDA (mL)	Water (mL)	T_0 /°Cª
10	1.0	0.136	0.01	0.2	20	31
45	1.0	0.030	0.01	0.2	20	33
85	1.0	0.017	0.01	0.2	20	—

Table IICompositions of Polymerization Solutions Used to Prepare the
Composite Crosslinked PNIPAAm Gels

Polymerization temperature: 6°C.

^a Obtained from the measurement of equilibrium swelling ratio.

higher molar ratio of NIPAAm to BisAAm, corresponding to lower crosslinking density. In a PNIPAAm solution, the phase transition behavior can be clearly observed at the phase transition temperature, which indicates the remarkable change of the polymer solution's physical properties.³⁶ Such a transition is still quite sharp in the swelling process of composite crosslinked PNIPAAm gels when the temperature changes, as shown in Figure 4. The phase transition temperature of polymer gels, T_0 , lies in the vicinity of 31 and 33°C, respectively, as shown in Table II. All composite gels exhibit a negative thermosensitive response, swelling below T_0 and deswelling above T_0 . It is clear that the amount of cross-linked agent corresponding to the crosslinking density of the composite gels can control the swelling ratio. The increase of crosslinking density in a polymer gel moves the phase transition temperature to a low temperature. This is because the crosslinking agent, BisAAm, is more hydrophobic compared to the monomer, NIPAAm,



Figure 5 Cumulative amount of released water and released time. The thickness of the gel is about 2 mm, and the glass plate is used as the substrate. The composition of PNIPAAm gel is as follows: NIPAAm to BisAAm = 45 (molar ratio).



Composition of gel: NIPAAm/BisAAM = 45 (molar ratio)

Figure 6 Cumulative amount of released water and released time. The thickness of the gel is about 2 mm, and the glass plate is used as the substrate. The composition of PNIPAAm gel is as follows: PNIPAAm to BisAAm = 10 (molar ratio).

and, consequently, the increase of the crosslinking agent increases the hydrophobic properties of the gel. The increased crosslinking density of a polymer gel also limits the absorption of water by the gel. Therefore, the phase transition temperature decreases as a result of the increase of the hydrophobic properties of a polymer gel.³⁶

Rate of Water Release

The rate of water release by composite gels was measured by equilibrated gels at different temperatures. Figures 5 and 6 show the rate of water release from composite crosslinked PNIPAAm gels as a function of release time. The rate of water release increases rapidly in the course of gel shrinkage when the temperature approaches T_0 . The gel is transparent when the temperature is below T_0 and becomes opaque with some small bubbles when the temperature is above T_0 . This is probably because the outer surface of the gel is the first region affected by temperature, and the collapsed skin layers are denser than the bulk matrix. The heterogeneous structure makes the gel appear opaque. This denser layer limits the diffusion of water from the gel during the initial period of shrinkage, which causes interior pressure to accumulate within the gel and small bubbles to form on the surface.³⁷ As interior pressure increases further, water finally overcomes the resistance of the denser layer and can release from the bubbles. The shrinkage force is relative to the elastic constant of polymer, which increases with the temperature and the crosslinking density of polymers.³⁸ Therefore, the rate of water release increases with temperature. By comparing the water release rate of two kinds of gels shown in Figures 5 and 6, it can be seen that the rate of water release increases with the increase of crosslinking density of gels. At the same temperature, the interior pressure of the gel with a higher crosslinking density is higher than that with a lower crosslinking density. Therefore, the interior water is more rapidly expelled by higher interior accumulation pressure in the higher crosslinking gels.

Hydrophilic-Hydrophobic Surface Properties Versus Temperature

Temperature-dependent surface properties were evaluated by the dynamic contact angle at a temperature range from 10 to 50°C. Figure 7 shows the effect of temperature on the advancing contact angle of glass plates with OH and SiCH= CH_2 groups, which were introduced by



Figure 7 Effect of temperature on dynamic contact angle. The thickness of the gel is about 2 mm, and the glass plate is used as the substrate.

treating with a preclean solution and VTMS. The surface behavior of the crosslinked PNIPAAm gel is also given in the figure as a comparison. The contact angles did not change on the surfaces with OH and SiCH=CH₂ groups. This is because neither the OH nor the SiCH=CH₂ groups have a temperature response. The lower contact angle of a glass plate with OH groups and the higher contact angle of a glass plate with SiCH=CH₂ are attributed to the hydrophilic and hydrophobic properties of OH and SiCH=CH₂ groups, respectively.

Figure 8 shows the effect of temperature on the surface tension of glass plates with and without a PNIPAAm gel layer. The surface tension of glass plates with OH and SiCH—CH₂ groups does not change in the whole range of temperature measurement. The glass plate with SiCH—CH₂ groups exhibits the lower surface tension (~ 12 dyn/cm), compared to the higher surface tension of the glass plate with OH groups (~ 65 dyn/cm).

This is because the water molecules can wet the surface of the OH groups very well, and the energy to move the glass plate in water increases. The repellency between hydrophobic vinyl groups and hydrophilic water molecules decreases the energy to move the glass plate. Consequently, the surface tension increases or decreases with the increase or decrease of the moving energy.³⁹ The glass plate grafted by a crosslinked PNIPAAm gel layer shows the reversed surface tension. The surface tension increases at the low temperature but decreases at the high temperature. This change is the result of the reversed characteristics of the hydrophilic/hydrophobic surface.

CONCLUSION

Both alkoxysilane and chlorosilane can be employed as the coupling agent to introduce the vinyl groups on the surface of ceramic substrates



Figure 8 Effect of temperature on surface tension. The thickness of the gel is about 2 mm, and the glass plate is used as the substrate.

with OH groups. Compared with the surface modified by a slow condensation reaction between the alkoxysilane and hydroxyl groups of the substrate surface, the contact angle of the surface rapidly arrives at its equilibrium value because of the faster reaction of chlorosilane with the hydroxyl groups. When the temperature is above the LCST of PNIPAAm, the denser layer is generated on the outer surface of the gel, which causes hydrostatic interior pressure to accumulate within the gel. The interior pressure increases as both the hydrophobic properties and the crosslinking density of the gel increase. Consequently, the rate of water release increases. The surface of composite crosslinked PNIPAAm gels not only demonstrates the characteristics of water release, but also the temperature response, that is, the completely hydrophilic properties below 20°C and the hydrophobic properties above 40°C. As the temperature increases, the contact angle increases, and the extents of increase depend on both the crosslinking density and the hydrophobic properties of the polymer gel. As a result of the faster release of water from the gel with a higher crosslinking density, the gel surface shows more hydrophobic characteristics.

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REFERENCES

- DeRossi, D.; Kajiwara, K.; Osada, Y.; Yamauchi, A. Eds., Polymer Gels; Plenum Press: New York, 1989.
- Russo, P. S., Ed., Reversible Polymeric Gels and Related Systems; ACS Symposium Series 350; American Chemical Society: Washington, DC, 1987.
- Peppas, N. A. Ed., Hydrogels in Medicine and Pharmacy; CRC Press: Boca Raton, FL, 1986; Vol. 1.
- Kataoka, K.; Koyo, H.; Tsuruta, T. Macromolecules 1995, 28, 3336.
- 5. Nishi, S.; Kotaka, T. Macromolecules 1986, 19, 978.
- Kaneko, Y.; Sakai, K.; Kikuchi, A.; Yoshida, R.; Sakurai, Y.; Okano, T. Macromolecules 1995, 28, 7717.
- Aoki, T.; Nagao, Y.; Sanui, K.; Ogata, N.; Kikuchi, A.; Sakurai, Y.; Kataoka, K.; Okano, T. Polym J 1996, 28, 371.
- 8. Suzuki, A.; Tanaka, T. Nature 1990, 346, 345.
- Fissi, A.; Pieroni, O.; Ruggeri, G.; Ciardelli, F. Macromolecules 1995, 28, 302.
- Urry, D. W.; Hayes, L. C.; Parker, T. M.; Harris, R. D. Chem Phys Lett 1993, 201, 336.

- Tanaka, T.; Nishio, I.; Sun, S. T.; Nishio, S. U. Science 1982, 29, 218.
- 12. Dagani, R. Chem Eng News 1997, June, 27.
- 13. Schild, H. G. Prog Polym Sci 1992, 17, 163.
- Heskins, M.; Guillet, J. E.; James, E. J Macromol Sci, Chem 1968, A2(8), 1441.
- 15. Urry, D. W. Sci Am 1995, Jan, 64.
- Snowden, M.; Murray, M.; Chowdry, B. Z. Chem Ind 1996, 15, 531.
- 17. Dong, L. C.; Hoffman, A. S. J Controlled Release 1986, 4, 223.
- Freitas, R. F. S.; Cussler, E. L. Chem Eng Sci 1987, 42, 97.
- 19. Riccka, J.; Tanaka, T. Macromolecules 1984, 17, 2916.
- Gutowska, A.; Bae, Y. H.; Jacobs, H.; Feijen, J.; Kim, S. W. Macromolecules 1994, 27, 4167.
- Shoemaker, S.; Hoffman, A. S.; Priest, J. H. Appl Biochem Biotechnol 1987, 15, 11.
- 22. Kurahashi, H.; Furusaki, S. J Chem Eng Jpn 1993, 26, 89.
- Iwata, H.; Odata, M.; Uyama, Y.; Amemiya, H.; Ikada, Y. J Membr Sci 1991, 55, 119.
- Lee, Y. M.; Ihm, S. Y.; Shim, J. K.; Kim, J. H.; Cho, C. S.; Sung, Y. K. Polymer 1995, 36, 81.
- Kubota, H.; Nagaoka, N.; Katakai, R.; Yoshida, M.; Omichi, H.; Hata, Y. J Appl Polym Sci 1994, 51, 925.
- Okano, T.; Yamada, N.; Sakai, H.; Sakurai, Y. J Biomed Mater Res 1993, 27, 1243.
- Takei, Y. G.; Aoki, T.; Sanui, K.; Ogata, N.; Sakuarai, Y.; Okano, T. Macromolecules 1994, 27, 6163.

- 28. Liang, L.; Feng, D. X.; Liu, J.; Rieke, P. C.; Fryxell, G. E. Process Miniaturization: 2nd International Conference of Microreaction Technology, p. 290, New Orleans, Mar 1998, The American Institute of Chemical Engineers, New York.
- Okano, T.; Kikuch, A.; Sakurai, Y.; Takei, Y.; Ogata, N. J Contr Rel 1995, 36, 125.
- 30. Hoffman, A. S. J Contr Rel 1987, 6, 297.
- Smith, L.; Doyle, C.; Gregonis, D. E.; Andrade, J. D. J Appl Polym Sci 1982, 26, 1269.
- Fryxell, G. E.; Rieke, P. C.; Wood, L. L.; Engelhard, M. H.; Wiliford, R. E.; Graff, G. L.; Campbell, A. A.; Wiacek, R. J.; Lee, L.; Halverson, A. Langmuir 1996, 12, 5064.
- Plueddemann, E. P. Silane Coupling Agents; Plenum Press: New York, 1982.
- 34. Arkels, B. CHEMTECH 1977, 7, 766.
- 35. Lide, D. R., Ed. CRC Handbook of Chemistry and Physics, CRC Press: New York, 1996; Chapter 9.
- Feil, H.; Bae, H. Y.; Kim, S. W. Macromolecules 1993, 26, 2496.
- Kaneko, Y.; Yoshida, R.; Sakai, K.; Sakurai, Y.; Okano, T. J Membr Sci 1995, 101, 13.
- Hall, C. Polymer Materials; John Wiley & Sons: New York, 1981; Chapter 3.
- Atkins, P. W. Physical Chemistry; W. H. Freeman and Company: New York, 1996; Part 28.