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Polymerization, Self-Bridging, and Degradation of Acryloyl- and Methacryloyl-L-proline Methyl Esters Induced by Radiation and Characteristics of Gel Swelling

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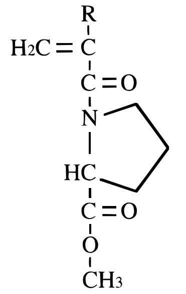
In recent years, thermoresponsive gels have received much interest, and their applications to sensors, drug delivery systems, intelligent materials, and actuators have been proposed.[1−7] We have studied the syntheses and phase transitions of gels based on acryloyl- and methacryloyl polymers with pendant amino acids such as alanine and proline.[8−12] These gels have a potential applicability as drug delivery systems because they contain a naturally occurring amino acid constituent.

Here we describe the syntheses and swelling behavior of gels consisting of polymers having acryloyl- and methacryloylproline methyl ester (A- and MA-ProOMe) residues, which have a lower critical solution temperature (LCST) of 14 °C in water. A-ProOMe can form a linear polymer by radiation-induced polymerization in alcohol. In this alcoholic solution, formation of a gel consisting of A-Pro-OMe needs incorporation of another multifunctional monomer acting as a cross-linker in the polymerization. Recently, we found that the gel consisting of A-ProOMe could be formed without the cross-linker in an aqueous solution as well as in the bulk system, although the latter needed very high doses of irradiation. In this study, we found that MA-ProOMe can polymerize to give a self-bridged gel only in an aqueous system; it failed to polymerize in the alcoholic solution and also in the bulk system with and without cross-linker. Thus, we compared the polymerization and gel formation of A-ProOMe and MA-ProOMe in the aqueous solution and also the swelling behavior of the resulting gels. The gels were obtained by irradiation a 20 wt % aqueous solution of these monomers with ^{60}Co γ-radiation[13] at 25 °C at a dose rate of 1 kGy/h, then extracted with ethanol in a Soxhlet apparatus, and dried in vacuo. The degree of gelation (yield) was estimated from the weight ratio of the ethanol-insoluble fraction to the feed monomer.



R = H: A-ProOMe
R = CH_3: MA-ProOMe

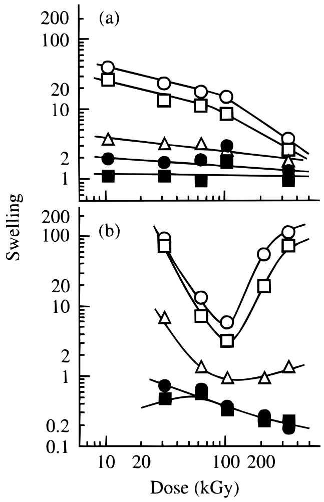


Figure 1. Effect of dose on the equilibrium swelling of two gels, (a) A-ProOMe and (b) MA-ProOMe, treated at temperatures of (○) 0, (□) 10, (△) 20, (●) 40, and (■) 60 °C after the equilibrium swelling with water at 0 °C (ice-water temperature).

The irradiation doses required for onset of gel formation, which is determined by extrapolation to 100% sol fraction of logarithmic plots between sol fraction and irradiation dose, are 1.7 and 20 kGy for A-ProOMe and MA-ProOMe, respectively. Such a large difference in the irradiation dose for gel formation between the two monomers is due to the difference in their chemical structures and in the reactivity of the monomeric radicals formed by the irradiation. When the aqueous solution containing these monomers is irradiated, monomeric radicals are formed by an indirect process involving first formation of products by radiolysis of water molecules (e^-_{aq}, $H^\bullet$, and $OH^\bullet$),[14] followed by the reaction of these products with monomer molecules to give polymerization of the monomers. With further irradiation, the resulting polymer molecules could be radiolyzed because the $H^\bullet$ and $OH^\bullet$ radicals tend to strongly abstract hydrogens from the polymer molecules. The resulting polymeric radicals contribute to initiate the chain reactions to form cross-linkings. The radicals on the polymer molecules consisting of A-ProOMe, similar to other polymers having a CH_2CHR structure, can react easily with radicals on the other polymer molecules to give a cross-linked gel. On the other hand, the radicals on the polymer of MA-ProOMe, having a $CH_2CR_1R_2$ structure, could have some difficulty in accessing the radicals on the other polymers because of the presence of substituted methyl groups at the α-position. Then formation of the cross-linkings could occur suddenly at a high concentration of radicals. In fact, the onset of the gel formation for poly(MA-ProOMe) needs the higher irradiation dose of 20 kGy compared to 1.7 kGy for poly(A-ProOMe). With further irradiation, the radicals formed at a high density on the MA-ProOMe polymer molecules could fail to recombine with radicals on other polymers to result in the scission of their polymer molecules.

Figure 1 shows the equilibrium swelling[15] of two gels obtained at various irradiation doses. These two gels

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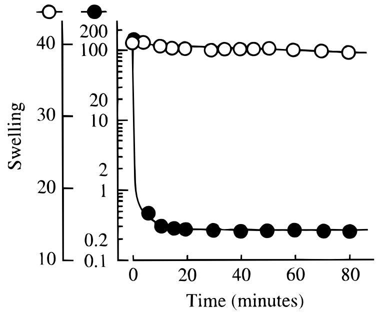

Figure 2. Shrinking profiles of two gels, (○) A-ProOMe and (□) MA-ProOMe, which were obtained in 60% yield with irradiation doses of 10 and 320 kGy, respectively, when the specimens were treated at 30 °C after the equilibrium swelling with water at 0 °C.

have the same characteristic of forming a swollen phase at a low temperature and a collapsed one at a higher temperature. The swelling behavior of these gels, however, is quite different: the swelling of the gel consisting of A-ProOMe at higher temperatures decreases with increasing irradiation dose but that of MA-ProOMe decreases rapidly at a moderate irradiation dose and increases rapidly at higher irradiation doses. It should be noted that the gel having A-ProOMe residues obtained in 60% yield by an irradiation dose of 10 kGy showed a volume change defined as the ratio $V_{\text{swollen at }0°\text{C}}/V_{\text{collapsed at }60°\text{C}}$ (V_0/V_{60}) of 40. The volume change decreased gradually with increasing irradiation dose to reach 3.5 at 350 kGy. Contrary to this, the gels consisting of poly(MA-ProOMe) obtained in 60% yield with an irradiation dose of 320 kGy showed a V_0/V_{60} value of 470.

The two gels obtained in 60% yield showed quite different shrinking kinetics as shown in Figure 2. Poly(A-ProOMe) gel with an equilibrium swelling of 40 at 0 °C below LCST is hardly shrunken throughout an experimental period of 80 min after a temperature jump to 30 °C over the LCST. On the contrary, an extremely rapid shrinking to its equilibrium state was observed for poly(MA-ProOMe) gel: 140 for a swollen state at 0 °C to 0.3 for a collapsed one at 30 °C within 10 min after the temperature jump. This difference in the shrinking behavior of these gels should be caused by the structures of the gels. To clarify this, we observed these gels by microscopy, as shown in Figure 3. The gel of poly(A-ProOMe) obtained in 60% yield showed the presence of a rigid surface barrier which lacks pores and a number of pores in the interior of the gel. The existence of this barrier markedly retards the rate of permeation of water from the interior of the gel, maintaining water in the matrix for a long time.[4,11] On the other hand, poly(MA-ProOMe) gel obtained in the same 60% yield at 320 kGy as poly(A-ProOMe) has a surface with a number of micropores until the shrunken state has been established, despite the remarkable shrinking of the gel and decrease of the pore size. The shrinking was accelerated by the release of water from the inside the gel through the porous structure in the short period of time. The formation of the barrier at the surface of the gel observed for poly(A-ProOMe) obtained in 60% yield was also observed for the gel of poly(MA-ProOMe) obtained in 31% yield at 100 kGy. The barrier of the gel of poly(MA-ProOMe), however, disappears at irradiation doses over 100 kGy. The microscopic observation and shrinking behavior of the gels suggest that a microscopically observed organized structure of the gels could result from a specific cross-linking structure of the polymer networks even if they have different chemical structures of A-ProOMe and MA-ProOMe.

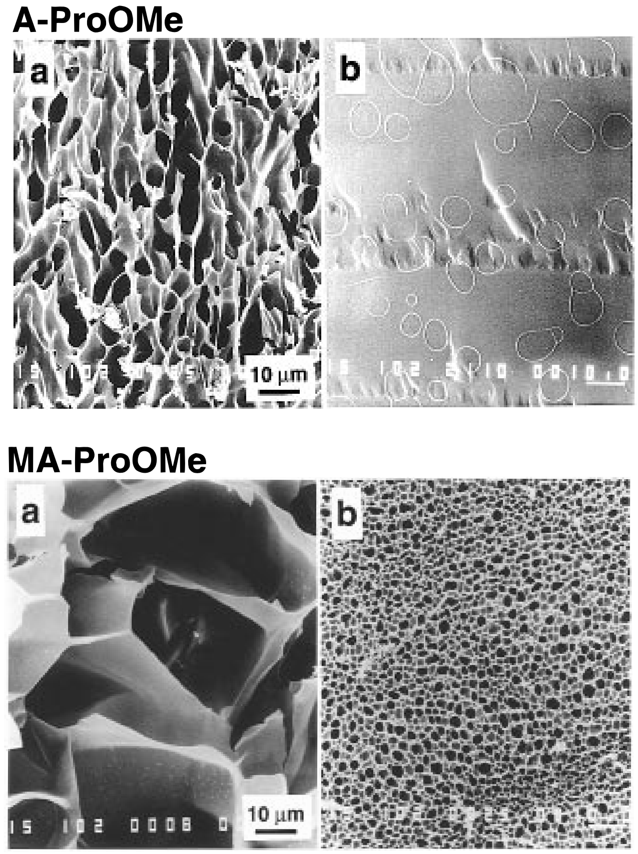

Figure 3. Scanning electron microphotographs of surface structures of two gels, treated for 40 min at 30 °C (a) and for 1 day at 0 °C (b). The swollen and deswollen gels were immediately immersed in liquid nitrogen, then lyophilized, and observed microscopically. A poly(A-ProOMe) gel showed the formation of a rigid surface barrier immediately after the specimen preswollen with water at 0 °C was immersed in water kept at 30 °C and, as a result, it was found that the thickness of this barrier increases with the passage of time to reach approximately 95 μm after 40 min of temperature jump.

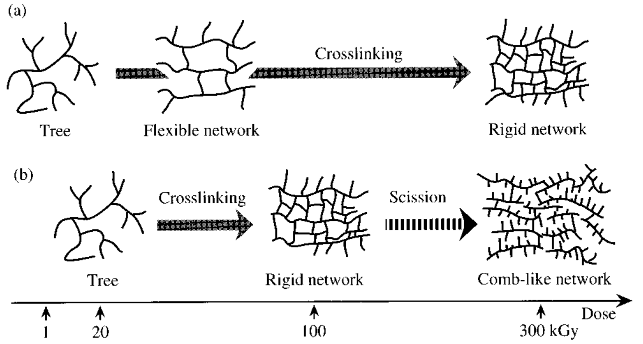

Figure 4. Proposed scheme for illustrating the changes in the microstructure of two gels, (a) A-ProOMe and (b) MA-ProOMe, with increasing dose.

Based on the evidence mentioned above, we propose a scheme for illustrating the changes in the microstructure of two polymers with increasing irradiation dose shown in Figure 4. During the early phase of polymerization, the network consists of polymer chains united through multifunctional junctions that result in giant molecules with branches and entanglement. We call it a tree structure.[16,17] In this open structure, the chains have high flexibility and mobility and tend to go as far as possible from each other when the gel swells below the LCST. This means a high volume change. With further irradiation, the branches and also main chains will be chemically bound to each other to give a structure that we call a closed flexible network. The higher the fraction of the closed over the open structure, the less flexible the gel. At that point, most of the monomers were converted to polymers; further cross-linking is due to the polymeric radicals. These polymer radicals will form further cross-links, and the gel structure will change from a flexible to a rigid network. The rigid networks, which are obtained at the irradiation doses of 320 and 100 kGy for A-ProOMe and MA-ProOMe, respectively, caused the formation of a highly organized water layer (icelike structures) around the hydrophobic polymer chains below the LCST contributing to the enthalpy of mixing that outweighs the unfavorable free energy related to the exposure of the hydrophobic ProOMe side chains to water molecules.[18-21] When the temperature is raised, the hydrophobic interactions become dominant over the polymer−solvent interaction, leading to the formation of a rigid surface barrier. The further irradiation, however, induced partial degradation of the previously formed network for MA-ProOMe owing to the failure for the formation of further cross-linkings with the polymer radicals, which results in the formation of a comblike network with relatively short branched chains. This structure is again more flexible, accompanied by an increased volume change: $V_0/V_{60} = 700$ for the gel of poly(MA-ProOMe) obtained at 320 kGy.

In conclusion, we synthesized the gels by a simultaneously occurring process of radiation-induced polymerization and cross-linking of A-ProOMe and MA-ProOMe in aqueous solution without any cross-linker. We call these gels self-bridged gels. Their different swelling behavior originates in the different microstructures, which is a result of the different mechanisms of polymerization and cross-linking for these two monomers.

References and Notes

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