Influences of Intramolecular Cyclization on Structure and Cross-Linking Reaction Processes of PVA Hydrogels

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ABSTRACT: Poly(vinyl alcohol) (PVA) hydrogels were prepared in aqueous solutions at different concentrations using glutaraldehyde (GA) as cross-linker. The gel fraction, increase rate of gels, critical gel point, and swelling ratio were measured. Furthermore, the influences of intramolecular cyclization on the cross-linking processes and the structure of formed hydrogels were studied. The results show that the degree of intramolecular cyclization and the ratio of [−CHO]/[−OH] at critical gel point (r_c) increase with the decrease of PVA concentration. The bulk gels do not form when PVA concentration is below 1.1×10^{-2} g/mL even at higher GA/PVA mixture ratio. In the concentration range of $(2.20-12.3) \times 10^{-2}$ g/mL, intramolecular cyclization fraction is basically not changed with gel fraction above the critical gel point. The way of gel growing is controlled by PVA concentration. In a certain range, the lower the PVA concentration is, the higher the increase rate of gels is. The equilibrium swelling ratio decreases with increasing PVA concentration. The structure of PVA hydrogels can be adjusted by changing the cross-linker or polymer concentrations.

Introduction

Polymer gels are important materials of both fundamental and technological interest. In recent years, hydrophilic gels called "hydrogels" have received considerable attention. PVA is one of the highly hydrophilic and water-soluble polymers with high chemical stability. Hydrogels can be prepared from aqueous PVA solutions through several techniques such as the photo-cross-linking method, irradiation methods using electron beams and γ-rays, the freezing-thawing method, and the chemical cross-linking method.[1] Since PVA hydrogels have good biocompatibility, low toxicity, good mechanical properties (high storage modulus and mechanical strength), and super water-absorbing capability, much attention has been paid to their applications in various biomedical fields such as artificial kidney membranes,[2] contact lenses,[3] wound bandages and dressings,[4] cell immobilization,[5] tissue engineering,[6] and drug delivery systems.[7] Understanding of the polymer network formation in the presence of a solvent, the resulting network structure and properties are essential to develop hydrogels with controlled swelling and properties for specific biomedical applications.[8]

During the past decades, the preparation, properties, and applications of PVA hydrogels have been extensively studied. Bao et al.[9] developed hydrogel beads with PVA to substitute for damaged or degenerated intervertebral disk nucleus. Wang et al.[1] prepared a bulk gel from aqueous oxygen-free solutions containing PVA by γ-ray irradiation at concentrations around 20 g/L. Anionic polyelectrolyte gels were prepared by An et al.[10] through the chemical cross-linking reaction of highly phosphorylated PVA (P-PVA) with glutaraldehyde. Their results showed that the water absorbability depends directly on the cross-linking density and degree of crystallinity in the hydrogel. The water absorbencies of these cross-linked P-PVA increase initially with an increase of the ratio of [GA]/[P-PVA] and then decrease after passing through a maximum. PVA gels with high absorbability and eminent mechanical strength were prepared through the cross-linking reaction of KOH aqueous solution of PVA with epoxy−chloropropane.[11] Hassan et al.[12] prepared PVA gels by repeated cycles of freezing at −20 °C for 8 h and thawing at +25 °C for 4 h. The stability of gels can be significantly enhanced by increased the number of freezing and thawing cycles.

There is an important assumption in the polymer gelation theory presented by Flory[13] and Stockmayer[14] that only intermolecular and intramolecular reactions can be neglected below the critical gel point. But in the real polymer solutions, the experimental results of critical gel point and sol−gel distribution were different from the theoretical calculation values. The deviations were caused just by the intramolecular cyclization. The other researchers developed further this theory and presented some theoretical models and updated formulas. Zheng[15] and Suematsu[16] developed the gelation theory of low molecular mass molecules with multifunctional units. They obtained the expression of the gel point as a function of the concentration, and their theory makes prediction of the existence of a critical dilution. Elliott[8] investigated the effect of solvent concentration, cross-linking agent size, and cross-linking agent concentration on the extent of cross-linking and primary cyclization during the photopolymerization of multifunctional monomers. Rankin[17] has simulated the gelation process of alkoxysilane polycondensation under acidic conditions with extensive cyclization by Monte Carlo simulation. Lin[18] has analyzed the effects of intramolecular cyclization to account for the significant deviations from the classical tree picture in rigid polycyanate networks.

In the past, the experiments on intramolecular cyclization of gels mainly focus on the polycondensation systems of multifunctional monomers, and there are few experimental results about intramolecular cyclization of hydrogels prepared directly using long chain polymer with linking agent. In this paper, the gelation of long chain polymer is studied. The influences of intramolecular cyclization on the cross-linking reaction processes and the structure of formed hydrogels in the PVA−GA system are studied in detail.

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Experimental Section

Materials. PVA sample with degree of polymerization of 1750 was commercially obtained from the Beijing Organic Chemical Plant. The degree of saponification was 88 mol %. 50% (w/w) glutaraldehyde (GA) solution was purchased from Tianjin Tiantai Fine Chemical Limited Co. Hydrochloric acid, analytical grade, was obtained from the Beijing Chemical Plant.

Gelation Process. The PVA solutions were prepared by adding a set amount of polymer to distilled water with stirring at room temperature for 15 min. Then the temperature was raised to 90 °C, and enough time was given to achieve complete dissolution. Afterward, the solution was filtered to remove the impurities. At last the solutions with concentrations of 2.20×10^{-2}, 5.12×10^{-2}, 8.03×10^{-2}, 8.50×10^{-2}, 12.3×10^{-2}, and 17.8×10^{-2} g/mL were prepared.

A series of PVA solutions were weighed, and 0.2 mL of aqueous solution of HCl (1.4 M) as catalyst was added to the solution with stirring. Then various amounts of GA aqueous solution (0.2822 M) as a cross-linker were added to the above solution with stirring. Afterward, the reaction mixtures were kept at 20 °C for 5 days, and the cross-linked PVA hydrogels were obtained The resulting gels were soaked with water for 24 h, filtered, and washed with distilled water. The procedure was repeated five times to remove the sol completely. The dry gels were dried to be constant weight. The gel fraction is labeled as *Gel* and sol fraction is labeled as *s* are calculated as

$$Gel = m_{gel}/m_{PVA}$$

$$s = 1 - Gel$$

where m_{gel} and m_{PVA} are the dry weight of the gel and the weight of PVA, respectively.

The intrinsic viscosity of PVA was measured at 25 °C with an Ubbelohde viscometer. The value is 65.76 mL/g. The molecular weight of PVA is 8.72×10^4 calculated using the Mark−Houvink equation with K and α being 45.3 and 0.64, respectively,[19] and the weight-average degree of polymerization is 1.78×10^3.

The swelling degree of the gel was calculated using the expression

$$W_c(\%) = (W_s - W_d)/W_d \times 100\%$$

where W_c is the water uptake in grams per gram of gel, and W_s and W_d are the weights of the gels after swelling and subsequent drying.

Results and Discussion

Gelation Processes. Figure 1 shows the variation of gel fractions with the content of cross-linker at various PVA concentrations. The bulk gel did not form at a certain range of lower cross-linker concentration. The gel fraction increased rapidly with the increase of cross-linker content above the critical gel point and then became smooth gradually after gel fractions up to 90%. The ratio of [−CHO]/[−OH] at critical gel point (r_c) can be obtained by extrapolating gel fraction to 0%. The variation of r_c with concentration of PVA is represented in Figure 2. The r_c increases with the decrease of PVA concentration, which is consistent with the results of polycondensation in the small molecules system.[16]

The curve in Figure 1 can be divided into three regions: the first one in which no gels formed, the second one in which gel fractions increased significantly in a narrow range of [−CHO]/[−OH] until up to about 90%, and the third one in which gel fractions increased gradually due to the increase of intramolecular cross-linking with the increase of intermolecular cross-linking.

Intramolecular Reactions at the Critical Gel Point. According to the molecule tree model,[20] any one of PVA chains can be taken as the first generation, and it assumes that there are no intramolecular reactions occurring in this system. The molecule chains that bond to the first generation through intermolecular reactions are taken as the second generation, and the rest may be deduced by analogy to the *n*th generation. If there are M −OH groups in the *n*th generation, denoted by $M^{(n)}$, the number of −OH groups that would react with cross-linker in the $(n + 1)$th generation can be calculated from

$$M^{(n+1)} = M^{(n)} q(\langle a \rangle - 1)$$

where q is the extent of reaction of the −OH groups and $\langle a \rangle$ is the weight-average degree of functionality of PVA.

If $M^{(n+1)} < M^{(n)}$, the molecule tree is constringent and forms sol, and if $M^{(n+1)} > M^{(n)}$, the molecule tree is radialized and forms gel. Therefore, if there is no intramolecular reaction in the system, the condition of critical gel is

$$M^{(n+1)} = M^{(n)}$$

So that the theoretical value of the critical extent of reaction q_c can be deduced from above two equations, obtaining

$$q_c = \frac{1}{\langle a \rangle - 1} \approx \frac{1}{\langle a \rangle} \tag{1}$$

In our system, the weight-average degree of functionality of PVA is $1.78 \times 0.88 \times 10^3$, so $q_c = 6.38 \times 10^{-4}$.

Because the functional groups (−OH) of PVA are much more than the functional groups (−CHO) of cross-linker, and the cross-linker must be consumed completely during the reaction process, Figure 1 can also be considered as the gel fraction variety with the real extent of reaction (q_{exp}) of −OH groups on PVA. The experimental value of extent of reaction, q_{exp}, can be calculated from [−CHO]/[−OH]. If there were no intramolecular reactions, the experiment value of critical extent of reaction (q_{exp_c}) should be equal to the theoretical value q_c. But in real polymer solution, especially in dilute solution, there are some intramolecular reactions besides intermolecular reactions.[15] So the experiment value of critical extent of reaction must be higher than the theoretical one (q_c). This fact means that the intramolecular cyclization in our system cannot be ignored. The degree of intramolecular cyclization can be defined as $(q_{exp} - q)$. The fraction of intramolecular cyclization, f, can be given as follows:

$$f = \frac{(q_{exp} - q)}{q_{exp}} \times 100\% \tag{2}$$

Figure 3 shows the variety of f at critical gel points with PVA concentration. The fraction of intramolecular cyclization is decreased linearly with the increase of PVA concentration within the measured range of concentration. Calculated from the line, the fraction of intramolecular cyclization will be up to 100% when PVA concentration decreased to 1.08×10^{-2} g/mL, which is consistent with the experiment result. The bulk gel indeed did not found in diluted PVA solutions ($<1.1 \times 10^{-2}$ g/mL) even at higher GA/PVA mixture ratio, but the solution became turbid.

Fraction of Intramolecular Cyclization above the Critical Gel Point. On the basis of Flory's ideal network assumptions, all −OH functional groups are equally reactive. The fraction of sol, s, can also be expressed as follows:

$$s = \frac{N'}{N}$$

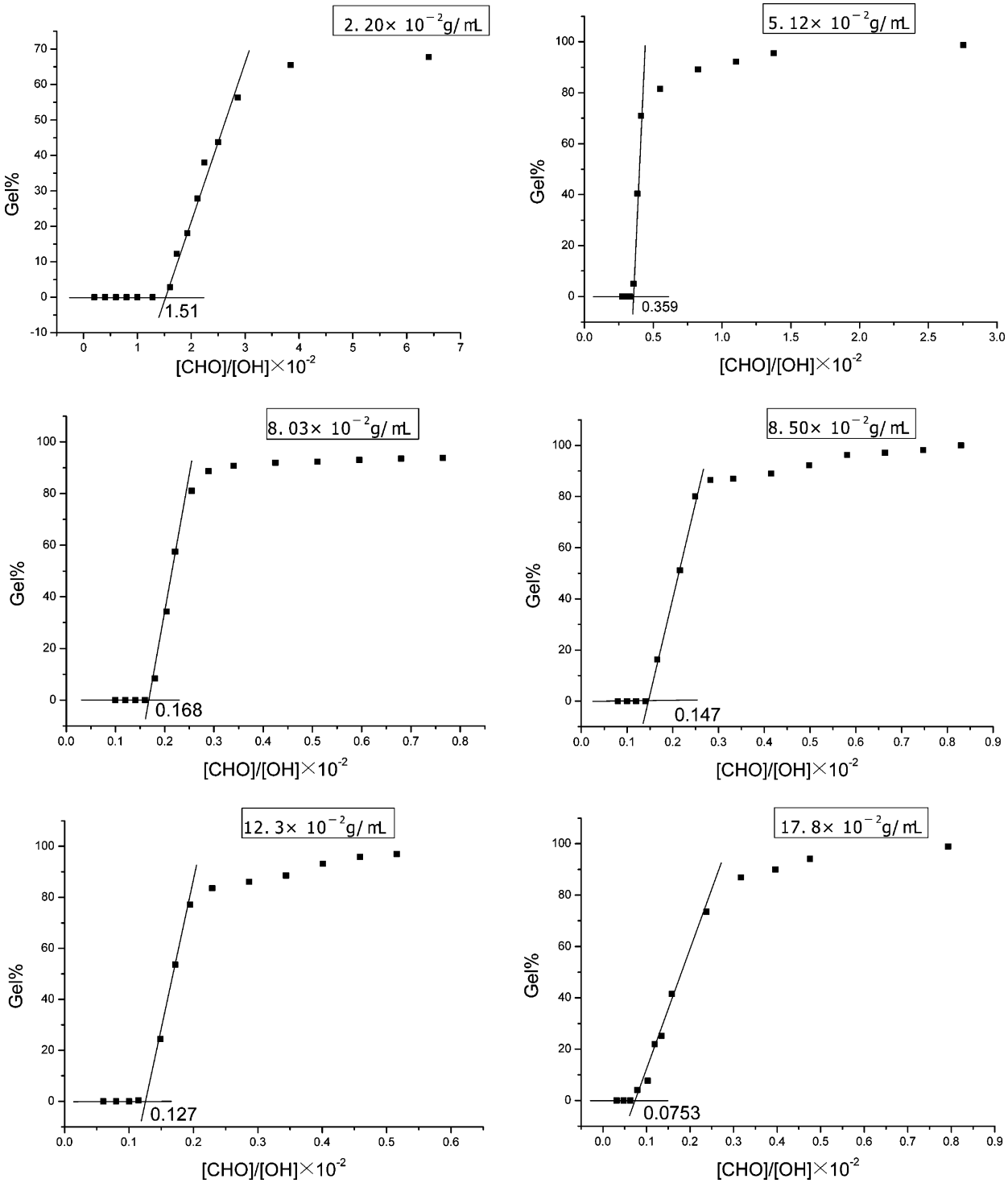

Figure 1. Variation of gel fractions with the content of cross-linker at various PVA concentrations.

Here N' and N are numbers of sol functional groups and total functional groups on the PVA chains, respectively.

The selections of a molecule chain in the system and a functional group on the molecule chain are random, and $\langle a \rangle$ is weight-average degree of functionality of −OH on a PVA molecule chain. The probability of this functional group links with sol is

$$q\frac{N'(1-q')}{N(1-q)} = qs\frac{1-q'}{1-q}$$

where q' and q are sol and total reaction extents, respectively.

As the number of residual functional groups is $\langle a \rangle - 1$, the probability of these groups link with sol is

$$q\left(1-q+qs\frac{1-q'}{1-q}\right)^{\langle a\rangle-1}$$

This molecule chain would become sol only when the two probabilities are equal, that is

$$qs\frac{1-q'}{1-q} = q\left(1-q+qs\frac{1-q'}{1-q}\right)^{\langle a\rangle-1}$$

or

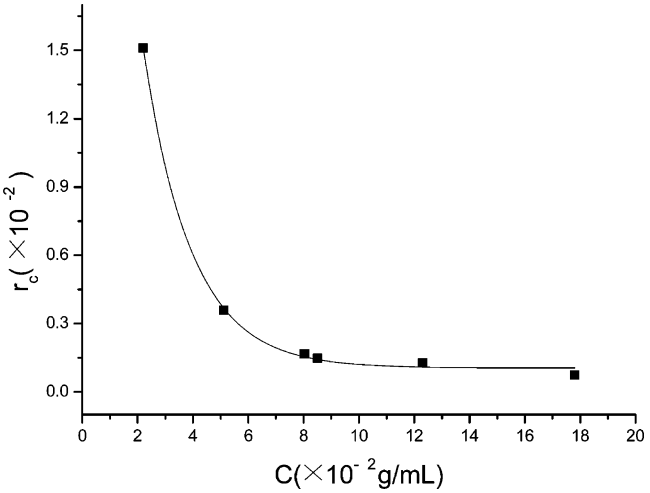

Figure 2. r_c as a function of PVA concentration.

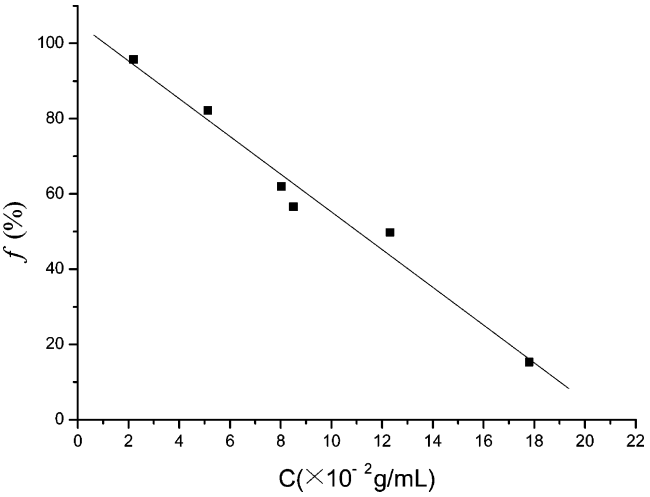

Figure 3. Variety of f at critical gel points with PVA concentration.

$$s\frac{1-q'}{1-q} = \left(1 - q + qs\frac{1-q'}{1-q}\right)^{\langle a\rangle - 1} \tag{3}$$

When the entire molecule chain is considered, the relation between the numbers of sol functional groups and total functional groups is

$$N' = N\left(1 - q + sq\frac{1-q'}{1-q}\right)^{\langle a\rangle >}$$

namely

$$s = \left(1 - q + sq\frac{1-q'}{1-q}\right)^{\langle a\rangle} \tag{4}$$

Combining eqs 3 and 4, we get[20]

$$q = \frac{1 - s^{1/\langle a\rangle}}{1 - s^{1-(1/\langle a\rangle)}} \tag{5}$$

As the $\langle a\rangle \gg 1$ in this system, q can be approximately expressed with Taylor progression as the following equation:

$$q = -\frac{\ln s}{1-s}\frac{1}{\langle a\rangle} \tag{6}$$

The total reaction extent above critical gel point can be calculated theoretically by using eq 6. The intramolecular cyclization fractions can be calculated using eq 2 from the real reaction extent q_{exp} which is equal to the ratio of [−CHO] to [−OH]. The results are presented in Figure 4. In the concentration range of (2.20−12.3) × 10^{-2} g/mL, intramolecular cyclization fractions were not changed almost with the increase of gel fraction above the critical gel point when keeping the PVA concentration constant and approximately the same as that at the critical gel points. But the intramolecular cyclization fraction increased with the increase of gel fraction at PVA concentration being 17.8 × 10^{-2} g/mL.

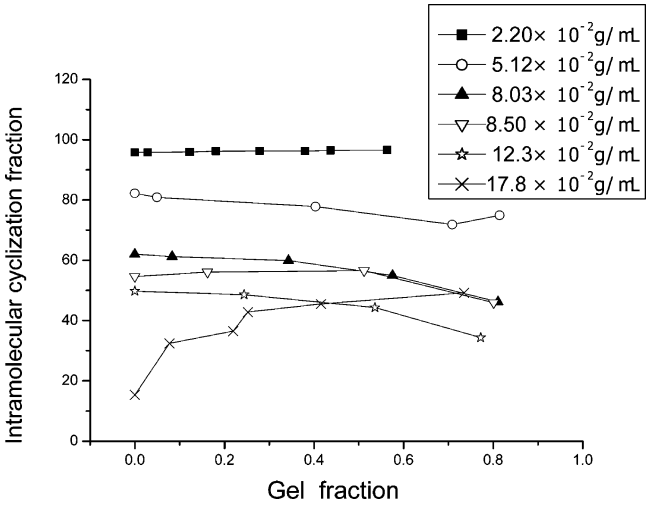

Figure 4. Intramolecular cyclization fraction as a function of gel fraction.

Table 1. Slope in the Second Region in Figure 1 at Various PVA Concentrations

concn ($\times 10^{-2}$ g/mL)	2.20	5.12	8.03	8.5	12.3	17.8
slope	0.449	15.7	10.6	7.46	11.8	4.79

Increase Rate of Gel. The slope in the second region in Figure 1 presents the increase rate of gel with the increase of linking degree. The increase rate of gel is extremely slow at the concentration of 2.20 × 10^{-2} g/mL, and the rate becomes very rapid when the concentration is above 5.12 × 10^{-2} g/mL. After that, the rate decreases gradually with increasing PVA concentration. The rate becomes slow again at 17.8 × 10^{-2} g/mL (see Table 1).

It is well-known that polymer molecule chains disperse as random coils in dilute solution. The distance of two molecule chains decreases with the increase of PVA concentration until those molecules overlap or interpenetrate. Only when the functional groups of polymer chain move to an effective distance can the intermolecular cross-linking reaction occur. The reaction speed is low in dilute solution, as intermolecular cross-linking reaction demands the motion of whole chains. In contrast, the local chain segment motion can lead to intermolecular reaction in semidilute and concentrated solution, so the reaction rate is higher.

On the basis of the equations of overlap threshold C^*[21−23]

$$C^* \approx 3M_r/4\pi N_A R_g^3 \tag{7}$$

and the following equation[24]

$$[\eta] \cong 6.2R_g^3 N_A/M_r \tag{8}$$

C^* can be represented by combining eqs 7 and 8 as follows:

$$C^* \cong 1.48/[\eta] \tag{9}$$

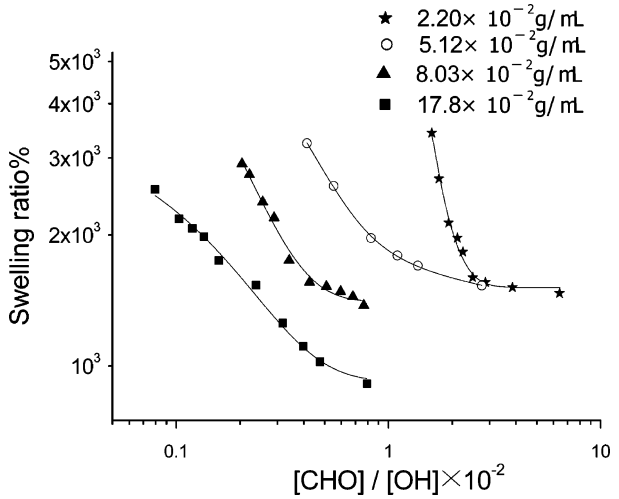

Figure 5. Weight swelling ratio of PVA hydrogels at various concentrations.

The overlap threshold C^* in this system can be calculated from eq 9 with a value of 2.25×10^{-2} g/mL. As the concentration of 2.20×10^{-2} g/mL is around the overlap threshold C^*, the intramolecular cyclization fractions are higher (about 96%) due to less chain overlapping and entangling. In the meantime, the intermolecular cross-linking reaction requests the motion of whole chains, and the process is rather slower than the diffusion process of the local chain segment motion, so the increase rate of gel fraction at this concentration was 10−30 times lower than those at other concentrations. For the concentration of 17.8×10^{-2} g/mL, intramolecular cyclization fractions increased with the increase of gel fractions, so the increase rate of gel fraction also became low.

Above the critical gel point, there are two ways of gel increasing: one is that cross-linking reactions occur among sol molecules, and the other is that cross-linking reactions occur between sol molecule and gel. Surely, the increase rate of gel fraction of the latter is higher than that of the former. The way of gels increasing is controlled by the topological structure of gels. In the concentration range of $(5.12-12.3) \times 10^{-2}$ g/mL, intramolecular cyclization fraction increased with the decrease of PVA concentration, and the increase rate of gel fraction increased with the decrease of PVA concentrations. It indicates that the way of gel increasing is inclined to the latter.

Swelling Behavior. Swelling ratio is one of the most important parameters to valuate cross-linked polymer. The relation between swelling ratio and the mean molecular weight of network chains is

$$\frac{\bar{M}_c}{\rho_p \overline{v_1}}\left(\frac{1}{2} - \chi_1\right) = W_c^{5/3}$$

where W_c is swelling degree of gels, M_c is the mean molecular weight of network chains, $\overline{v_1}$ is partial molar volume of solvent, ρ_p is density of polymer, and χ_1 is interaction parameter for PVA and water. The higher swelling ratio is, the lower $\bar{M}_c$ is.

The dependence of swelling ratio on cross-linker content is shown in Figure 5. It can be seen that swelling ratios are not identically at the same mixture ratio of ([−CHO]/[−OH]), and the swelling ratio decreases with increasing the concentration of PVA. Because it is a cross-linking system of long chains, there would be some permanent physical entanglement points due to the entanglement effect of polymer chains. Those permanent physical entanglement points can act as cross-linker and make apparent $\bar{M}_c$ small and swelling ratios decrease. These results reflect that the topological structure of the networks depends on the concentration of polymer;[25] that is, the higher PVA concentration is, the stronger entanglement effect is and the lower swelling ratio is. So we can control the structure of network by adjusting the concentration of PVA.

The swelling ratio of gels decreases with increasing the cross-linker content at same PVA concentration; i.e., $\bar{M}_c$ decreases with increasing the cross-linker content. Because the distribution of polymer chains in solution is homogeneous and the reactivity of all functional groups (−OH) is equal, $\bar{M}_c$ is dependent on the cross-linker content strongly. By this way, it is possible to adjust the network structure of gels via changing the content of cross-linker.

Conclusions

The intramolecular cyclization influences on sol−gel distribution, the increase rate of gels, and swelling ratio have been studied for the PVA−GA system. The influences of polymer concentration on intramolecular cyclization fraction have also been discussed. Both the fraction of intramolecular cyclization and critical gelation mixture ratio of [−CHO]/[−OH] will increase when PVA concentration decreases. The bulk gels do not form when PVA concentration is below 1.1×10^{-2} g/mL. In a certain range of PVA concentrations, intramolecular cyclization fraction is basically independent of the increase of gel fraction above the critical gel point. The ways of gel growing are controlled by PVA concentration. In a certain range, the lower PVA concentration is, the higher increase rate of gels is. The swelling ratio decreases with increasing PVA concentration and cross-linker content. The results show that intramolecular cyclization is a very important influence factor on the structure of network, especially in dilute solution.

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