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Acetylation of poly(2-hydroxyethyl acrylate) gel beads obtained from sedimentation polymerization

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Abstract

Sedimentation polymerization of an aqueous 2-hydroxyethyl acrylate solution with some crosslinkers was carried out using a simple sedimentation polymerization apparatus to give millimeter-size and very narrow size distributed poly(2-hydroxyethyl acrylate) (PHEA) gel beads. Also, heterogeneous acetylation of the resulting PHEA gel beads with acylating agents such as acetic anhydride, a mixture of acetic anhydride and pyridine, and chloroacetic anhydride was performed under various conditions. The selective esterification of PHEA gel beads proceeded smoothly in toluene from surface to give a novel core-shell type gel consisting of an unreacted core and acetylated shell, and finally afforded almost quantitatively acetylated PHEA gel. The unreacted core became small while maintaining a spherical shape during reaction. The reaction resembled to that of the corresponding cylindrical PHEA gel, and was strongly affected by the network structure of the obtained PHEA gel beads and the reactivity of acylating agents.

Keywords: Poly(2-hydroxyethyl acrylate) gel bead; Sedimentation polymerization; Heterogeneous esterification

1. Introduction

Crosslinking polymer particles from nano-size to millimeter-size have been prepared and used in many fields [1]. The application area depends on the particle size since the performance is different by the size. For example, millimeter-size particles attract attention as a carrier of catalyst, chemicals, and microorganism because they have some advantages as follows; their handling such as separation is easy, the packed column and the fixed bed reactor, which filled up these particles, show little pressure drop, and the surface area per a volume is small. These size particles are generally synthesized by suspension polymerization [2]; however, the particle size distribution is very wide. The desired size of monodisperse particles is obtained from classification of the particles prepared by this method. Accordingly, the yield is very low. Instead of these size particles, pellet type gels have been used, but unfortunately, it may not always be practical to use pellet type gels.

Ruckenstein and coworkers [3] reported a suitable preparation method of millimeter-size monodisperse particles by sedimentation polymerization of an aqueous monomer solution. Furthermore, they investigated the synthesis of hybrid polymer gel beads from polymerization of water-soluble monomers and condensation of poly(vinyl alcohol) with glutaraldehyde [4] or hydrolysis of tetraethyl orthosilicate [5] at the same time, and the application of the obtained beads to adsorbents [4]. Cooper studied novel oil-in-water-in-oil sedimentation polymerization [6] and compressed fluid sedimentation polymerization [7]. The sedimentation polymerization mechanism has been described [3]; the surface gelation of droplets descending a heat medium takes place to give a stable skin which prevents coalescence at the base of the reactor, and the polymerization was completed at the base. Accordingly, the polymerization could give a bead with non-uniform internal structure, and it needs enough time of sedimentation to form the stable skin using a long cylindrical reactor with fine temperature control. The sedimentation time can be adjusted by viscosity of the heating medium easily because the particles settling velocity obeys Stokes' law. We

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proposed a simple and easy sedimentation polymerization apparatus using high viscous silicon oil as heating medium (Fig. 1) and the synthesis of porous beads with rapidly swelling–deswelling property by the sedimentation polymerization of *N*-isopropylacrylamide [8]. Although the sedimentation polymerization is useful method for synthesis of monodisperse functional particles, the beads provided by the sedimentation polymerization are interested as starting materials. However, their chemical modification, except for pyrolysis of the precursor hybrid beads obtained from polymerization of water-soluble monomers and hydrolysis of tetraethyl orthosilicate [5], has not been reported.

We have investigated the heterogeneous esterification of poly(acrylic acid) gel–1,8-diazabicyclo[5,4,0]undec-7-ene salt (DAA) pellet with alkyl halide [9]. The reaction proceeded from the outside to give a core-shell type gel (gel capsule) consisting of a hydrophilic unreacted core part and esterified shell layer. Also, a novel gel capsule consisting of a hydrophilic unreacted core and thermosensitive poly(*N*-alkylacrylamide) shell was obtained from selective amidation of DAA with alkylamine [10,11]. This synthetic method is suitable for synthesis of millimeter-size and core-shell type gels, which are composed of an uninterrupted network between a hydrophilic core and functional shell part. Their application to reserve type drug carriers has been tried. However, the gel capsule obtained from the reaction of DAA with alkyl halide burst in a few hours when it was dipped in water [9,12]. It may be attributed to a geometric weak point of pellet type gels, that is, they are weaker for stress as causes of destruction than the corresponding beads.

In the previous paper [13], we reported the esterification of poly(2-hydroxyethyl acrylate) (PHEA) gel with acetic anhydride and synthesis of core-shell type gel (gel capsule) containing esterified shell and unreacted core. This synthesis of gel capsules is simpler and easier than the preparation from reaction of DAA with alkyl halide. This study reports the synthesis of PHEA gel beads from the sedimentation polymerization using the simple sedimentation polymerization apparatus and the heterogeneous esterification of the resulting beads with acetic anhydride, a mixture of acetic anhydride and pyridine, and chloroacetic anhydride in toluene (Fig. 2). The reaction would not proceed through a fine spherical core-shell type gels if the bead with non-uniform internal structure were obtained from the polymerization.

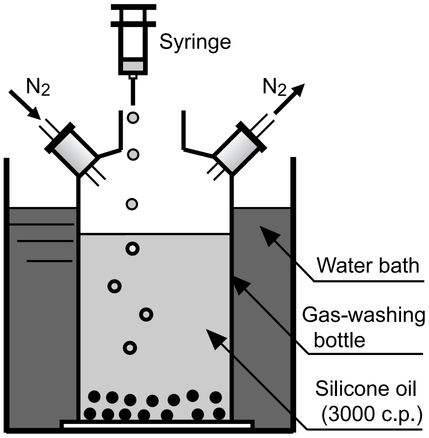


Fig. 1. Sedimentation polymerization apparatus.

2. Experimental

2.1. Materials

HEA, acetic anhydride, and solvents were distilled prior to use. Commercial *N*,*N*′-methylenebisacrylamide (MBAA), ethylene glycol dimethacrylate (EGDM), triethylene glycol dimethacrylate (TGDM), and chloroacetic anhydride were used without further purification. Cylindrical PHEA gels (length the same as diameter) prepared previously were used [13].

2.2. Apparatus

IR spectra were obtained on a Perkin–Elmer model IR-700 spectrophotometer.

2.3. Synthesis of PHEA gel beads by sedimentation polymerization [8]

A typical sedimentation polymerization of HEA is as follows. HEA (11.6 g, 0.1 mol), TEGDM (0.286 g, 1.0 mmol), and potassium persulfate (135 mg, 0.5 mmol) were dissolved in water (11.9 g) at 20 °C under nitrogen atmosphere. Silicone oil (GE Toshiba Silicones Co., 3000 cP) was charged into a washing bottle in a water bath at 70 °C and nitrogen gas was bubbled into the silicone oil over 3 h (Fig. 1). The monomer solution was injected dropwise into the silicone oil using a syringe with a needle (external diameter 1.5 mm, 90° tip). It was allowed to stand for 12 h at 70 °C under nitrogen stream. The resulting beads were immersed into a large amount of water and washed with methanol by a Soxhlet extractor to wash away unreacted substances. The gel was dried carefully and slowly, and finally dried in vacuo at 60 °C until constant weight. The average diameter ($2\bar{R}_0$) and average weight ($\bar{w}$) of a bead (G-2) is 2.25 mm (the relative standard deviation is 5.06%) and 7.13 mg, respectively. The other prepared PHEA gels are listed in Table 1.

2.4. Esterification of PHEA gel bead and its measurement [9–13]

A solution (50 ml) of acetic anhydride (0.50 mol l^{-1}) in toluene was charged into a 50 ml cylindrical cell in a water

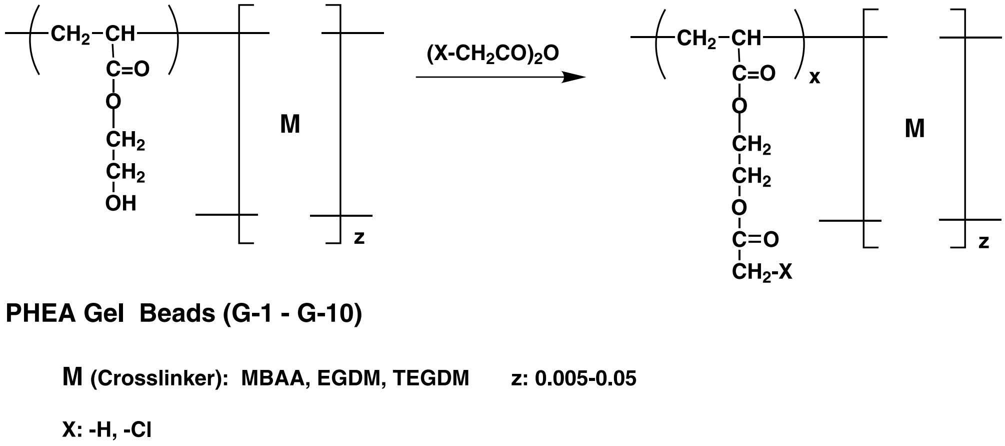


Fig. 2. Esterification of PHEA gel with acid anhydride.

bath at 80 °C. To the solution was added a PHEA gel bead. R_t and r_t of the sample, the external radii of shell and core after t min, respectively, were periodically observed by a digital video camera (Sonny, DCR-VX1000 and DCR-TRV950). After the disappearance of core part, the gel was washed with acetone by a Soxhlet extractor and dried in vacuo at 60 °C until constant weight. The other typical conditions and reaction results are listed in Table 2.

2.5. Measurement of swelling rate [9–13]

A sample was placed in water in a 50 ml cylindrical cell at a desired temperature. The change of external radius (R'_t/R'_0), where R'_0 and R'_t are external radii of the original gel and the gel swelled after $t=t$ min, respectively, was recorded using the digital video camera system described above.

3. Results and discussion

3.1. Synthesis of PHEA gel beads by sedimentation polymerization

Sedimentation polymerization of an aqueous HEA solution was carried out using a simple sedimentation polymerization apparatus (Fig. 1) consisting a 500 ml gas-washing bottle with 15 cm height of high viscous silicone oil (3000 cP) in a water bath proposed by the previous paper [13]. The sedimentation time of 3 mm diameter droplet of an aqueous monomer solution in this apparatus is about 15 min. It needs enough time of sedimentation and fine temperature control of heat medium to form a stable skin on droplets of a monomer solution. When the aqueous HEA solution was added dropwise to the silicone oil, a droplet of the monomer solution spreads over the surface of silicone

Table 1
Synthesis of PHEA gel beads by sedimentation polymerization

Gel	Needle (mm)	Conc. of HEA (wt%)	Crosslinker (mol%)	$2\bar{R}_0$[a] (mm)	$\bar{w}$[b] (mg)	σ[c] (%)
G-1	3.0[d]	50	TEGDM (1.0)	3.01	16.92	–
G-2	1.5	50	TEGDM (1.0)	2.25	7.13	5.06
G-3	1.0	50	TEGDM (1.0)	1.98	4.84	–
G-4	1.5	50	TEGDM (5.0)	2.22	6.83	5.22
G-5	1.5	50	TEGDM (2.0)	2.24	7.11	5.34
G-6	1.5	50	TEGDM (0.5)	2.19	6.75	6.52
G-7	1.5	25	TEGDM (1.0)	1.75	3.25	5.40
G-8	1.5	25	TEGDM (0.5)	1.73	3.20	4.27
G-9	1.5	25	EGDM (1.0)	1.64	2.67	8.94
G-10	1.5	25	MBAA (1.0)	1.83	3.59	5.37
G-11	1.5	25	MBAA (1.0)	1.80[e]		

Sedimentation polymerization of the NIPA solution (10 g) was carried out with MBAA (1.0 mol%) and potassium persulfate (0.02 g) at 80 °C.

[a] Average diameter of a polymer bead.

[b] Average weight of a polymer bead.

[c] The relative standard deviation.

[d] Teflon pipe 3.0 diameter was used.

[e] Cylindrical PHEA gel.

Table 2
Reaction of PHEA gel bead with acetic anhydride in toluene

Run no.	PHEA gel	$2R_0$ (mm)	Temp (°C)	τ (min)
1	G-2	2.32	60	2340
2	G-2	2.22	70	1280
3	G-2	2.28	80	680
4	G-2	2.26	90	400
5	G-4	2.21	80	1000
6	G-5	2.32	80	660
7	G-6	2.25	80	540
8	G-7	1.62	80	260
9	G-9	1.57	80	300
10	G-10	1.71	80	410
11	G-11	1.82	80	340
12	G-2	2.34	80	330[a,b]
13	G-2	2.26	80	150[c]

Reaction of PHEA gel with acetic anhydride was carried out in toluene.

[a] Chloroacetic anhydride was used instead of acetic anhydride.

[b] Content of chloroacetylated HEA unit is 98.2 mol% determined from the chlorine analysis.

[c] A mixture of acetic anhydride and pyridine was used instead of acetic anhydride.

oil and floats temporarily on the surface because the silicone oil is so viscous, and then the droplet sediments into the silicone oil. Since, droplets have a tendency to coalesce on the surface, they cannot be dropped successively onto the same spot. The polymerization of 25 and 50 wt% of aqueous HEA solutions containing 0.5–5.0 mol% crosslinker such as TEGDM, EGDM, and MBAA was carried out using this apparatus in the presence of 0.5 mol% potassium persulfate to HEA as a radical initiator. Typical conditions and results are summarized in Table 1. Although the polymerization did not occur at 30 °C, fine and transparent polymer beads were obtained from the polymerization of aqueous HEA solution droplets at 70 °C. The sedimentation polymerization could occur in surface gelation of droplets at the first stage [3]. The previous paper [8] reported that the sedimentation polymerization of *N*-isopropylacrylamide gave beads with a big void resulting in the surface gelation. However, void beads were not obtained, when the droplets of aqueous HEA solution were picked up as soon as they just reached the bottom. To polymerize perfectly, the droplets stood in the bottom for an overnight. When needles 1.0, 1.5, and 3.0 mm in diameter were used, average diameters ($\overline{2R_0}$) and average weights ($\bar{w}$) of the obtained beads were 1.98 mm and 4.84 mg, 2.26 mm and 7.13 mg, and 3.01 mm and 16.92 mg, respectively. However, the beads were not prepared from polymerization of 2-hydroxylethyl methacrylate, which shows less polymerizable than HEA, under the conditions. When 50 and 25 wt% of aqueous HEA solutions were added dropwise using a needle 1.5 mm in a diameter, average diameters of the obtained beads were about 2.2 and 1.8–1.7 mm, respectively. The particle size depended on the monomer concentration and the pipe size of needle for syringe, and was hardly affected by kinds and concentrations of crosslinkers. The typical particle size distribution of the obtained polymer beads is shown in Fig. 3. There are a few beads with about two-fold weight ($2R_0=$ 2.9–3.0 mm) derived from the coalescence of the monomer droplets on the surface of silicon oil. However, the relative standard deviation is about 4–7% which is almost the same as that using a syringe reported by Ruckenstein et al. [3] and is inferior to that using the automatic dropping system with a HPLC pump [7]. These results suggested that a very narrow size distribution was achieved in all the case.

3.2. Esterification of PHEA gel beads

The previous paper [13] reported that the heterogeneous esterification of cylindrical PHEA gel with some acylation agents proceed from the surface into interior in toluene. The reaction gave a core-shell type gel consisting of an unreacted core part and almost quantitatively reacted shell. A similar reaction of suspension-polymerized poly(vinyl alcohol) beads with glutaraldehyde to give a core-shell type gel was reported [14]. In the synthesis of a core-shell type gel, it is important to select a suitable solvent, which is

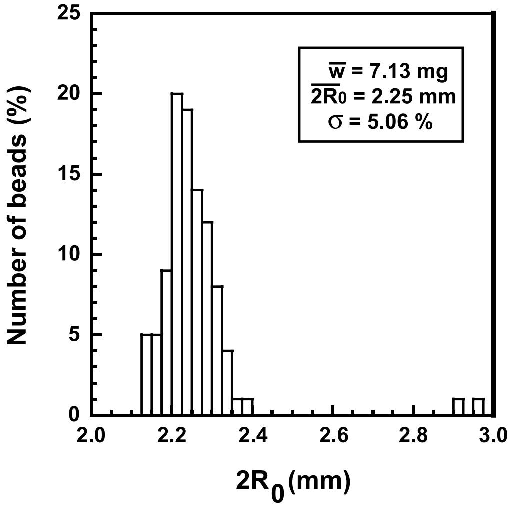


Fig. 3. Typical particle size distribution of G-2.

poor solvent for the starting gel and good solvent for the highly reacted gel. When the bead was dipped into the acetic anhydride solution in toluene, the swelling occurred and the gel was divided into a swollen shell and unswollen spherical core. Typical photographs in the reaction are shown in Fig. 4. The external diameter of gel increased with decreasing the core part while maintaining a spherical shape during reaction. The reaction was completed when the core disappeared. The reaction behavior resembled that of cylindrical uniform PHEA gel with acetic anhydride reported previously [13]. This suggested that the structure on the concentric sphere of the bead was uniform at least although the bead was obtained from the rapid polymerization. Esterification of G-2 bead containing 1.0 mol% TEGDM ($2R_0 = 2.2$–2.4 mm) with acetic anhydride (1.0 mol l^{-1}) was carried out in toluene at various temperatures (Fig. 5). The unreacted core part decreased almost linearly with increasing the reaction time. The time (τ) for the complete disappearance of unswollen core part was about 40 h at 60 °C, whereas the core part disappeared in 7 h at 90 °C.

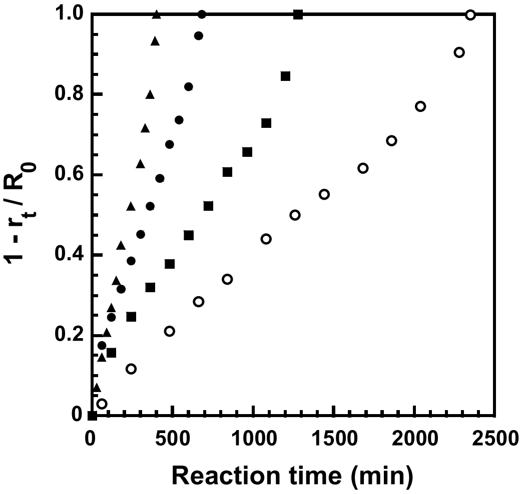
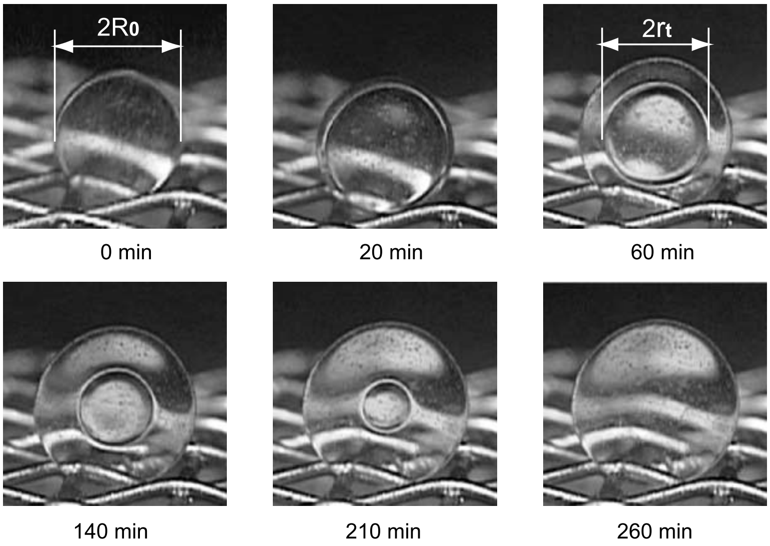


Fig. 5. Esterification of PHEA beads of acetic anhydride (1.0 mol l^{-1}) at various temperatures in toluene; ▲: 90 °C; ●: 80 °C; ■: 70 °C; ○: 60 °C (Table 2, Run No.1–4).

3.2.1. Esterification of various PHEA gel beads

The reaction of various PHEA gel beads (G-2–G-10) prepared by sedimentation polymerization of HEA with acetic anhydride was performed in toluene at 80 °C. The results and conditions are summarized in Table 2. The τ increased with increasing crosslinker content in the gel (Fig. 6). The disappearance of core part of G-6 containing 0.5 mol% TEGDM took 520 min, which is a half time of that of G-4 containing 5.0 mol% of TEGDM. The previous paper [13] reported that the esterification proceeded under conditions between the reaction control and the diffusion control of the unreacted-core model. Under reaction control and diffusion control conditions, the τ is proportional to R_0 and R_0^2, respectively [15]. G-2 prepared from polymerization of 50 wt% aqueous HEA solution is bigger compared with G-7 obtained from polymerization of 25 wt% aqueous HEA solution. Even if this factor was taken into consideration, the τ (Run No. 8) was mach smaller than that (Run No. 3). It seemed that the self-crosslinking reaction occurred to produce gel with higher degree of crosslinking than crosslinker content in the polymerization of 50 wt% aqueous HEA solution since the monomer concentration is too high. The τ decreased with decreasing the content and kind of crosslinkers in following order; MBAA (G-10) > EGDM (G-9) > TEGDM (G-7) (Fig. 7). It seemed that the acetylation of PHEA gel beads could depend on the network structure. The network structure affected the swelling behavior directly. When the obtained PHEA gel beads were dipped in water at 50 °C, the beads became bigger while maintaining a spherical shape during swelling



0 min
20 min
60 min
140 min
210 min
260 min

Fig. 4. Typical photographs in reaction of PHEA bead of acetic anhydride (Table 2, Run No.8).

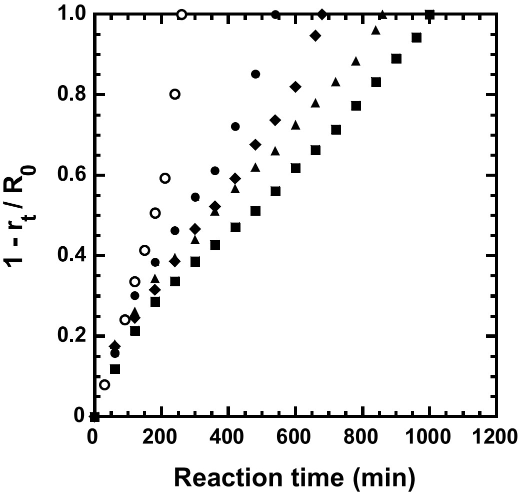


Fig. 6. Effect of TEGDM content on esterification of PHEA beads of acetic anhydride at 80 °C in toluene; ◆: G-2 (Run No. 3); ■: G-4 (Run No.5); ▲: G-5 (Run No. 6); ●: G-6 (Run No. 7); ○: G-7 (Run No. 8).

(Fig. 8). However, the swelling proceeded homogeneously and is different from the heterogeneous swelling in the acetylation of PHEA gel bead, which was resulted in a swollen part and unswollen part. The swelling was evaluated by R'_t/R'_0, where $2R'_t$ is external radius of the gel swelled in water for *t* min. The equilibrium swelling ratio decreased with decreasing the content and kind of crosslinker in following order; MBAA (G-10) > EGDM (G-9) > TEGDM (G-7) (Fig. 9). Especially, G-7 and G-8 crosslinked by TEGDM swelled slowly and showed higher equilibrium swelling ratio than the other beads. In addition, the gel obtained from polymerization of 25 wt% aqueous HEA solution is much higher equilibrium swelling ratio than that of 50 wt% aqueous HEA solution. The order agreed with that of τ. PHEA gel with the more flexible network structure showed the higher reactivity. The esterification of a G-10 and a cylindrical PHEA gel (G-11) containing 1.0 mol% MBAA ($2R_0 = 1.8$ mm) with acetic anhydride (1.0 mol l^{-1}) was carried out in toluene at 80 °C. The τ of the bead and the cylinder are 410 and 330 min, respectively. The bead showed lower disappearing rate than the corresponding cylinder. A small difference of the reaction pattern between bead and cylinder was observed. Theses differences may be attributed to that of the shape and the non-uniformity of the internal structure. These suggested that the acetylation of PHEA gel beads with acetic anhydride was strongly affected by the reaction temperature and the content of crosslinker.

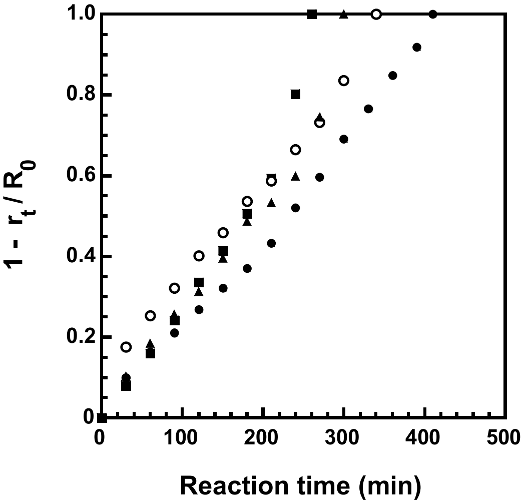


Fig. 7. Effect of kinds of crosslinkers on esterification of PHEA beads of acetic anhydride at 80 °C in toluene; ■: G-7 (Run No. 8); ▲: G-9 (Run No. 9); ●: G-10 (Run No. 10); ○: G-11 (Run No. 11).

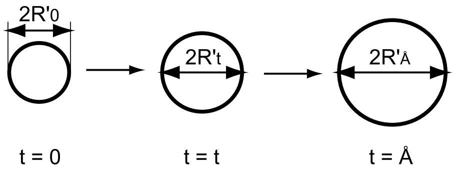


Fig. 8. Swelling behavior of PHEA gel bead in water at 50 °C.

3.2.2. Characterizations of the acetylated gel beads

The reaction of G-2 containing 1.0 mol% TEGDM ($2R_0$; 2.3 mm) of acetic anhydride (1.0 mol l^{-1}), a mixture of acetic anhydride (1.0 mol l^{-1}) and pyridine (1.0 mol l^{-1}), and chloroacetic anhydride (1.0 mol l^{-1}) was carried out in toluene (Fig. 10). The complete reaction with acetic anhydride, a mixture of acetic anhydride and pyridine, and chloroacetic anhydride gave EG-1 (Run No. 3), EG-2 (Run No. 13), and EG-3 (Run No. 12), respectively. The addition of pyridine caused the esterification to accelerate. Chloroacetic anhydride is more reactive than acetic anhydride and is less reactive than the mixture of acetic anhydride and pyridine. Therefore, the acetylation of PHEA gel beads was affected by the reactivity of acylating agents. These results indicated that the acetylation proceeded under conditions

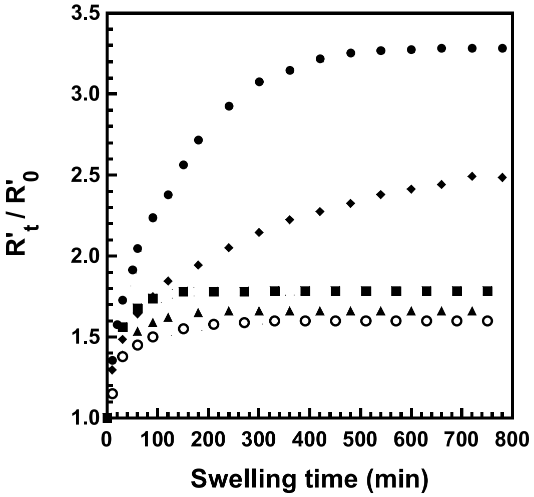


Fig. 9. Swelling of PHEA beads in water at 50 °C; ○: G-2 ($2R_0$= 2.25 mm); ◆: G-7 ($2R_0$=1.77 mm); ●: G-8 ($2R_0$=1.78 mm); ■: G-9 ($2R_0$=1.75 mm); ▲: G-10 ($2R_0$=1.86 mm).

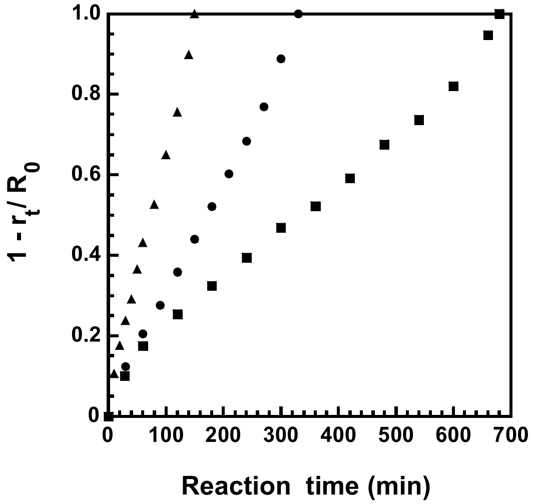


Fig. 10. Esterification of G-2 of some acetylating agents at 80 °C in toluene; ■: acetic anhydride (Run No. 3); ▲: a mixture of acetic anhydride and pyridine (Run No. 13); ●: chloroacetic anhydride (Run No. 12).

between the reaction control and the diffusion control of the unreacted-core model [13,15].

The IR spectrum of the PHEA gel showed a broad absorption around 3400 cm^{-1} (O–H stretching) and a strong absorption at 1740 cm^{-1} (C=O). EG-1, EG-2, and EG-3 showed no absorption around 3400 cm^{-1}. Previous paper [13] reported that the acetylated PHEA gel from esterification of cylindrical PHEA with acetic anhydride, a mixture of acetic anhydride and pyridine, and chloroacetic anhydride under similar conditions show 96.8, 100, and 98.7 mol% of esterification, respectively. These IR spectra agreed with those of the corresponding acetylated cylindrical PHEA. In addition, the contents of chloroacetylated HEA unit and unreacted HEA unit in EG-3 containing 1.0 mol% TEGDM unit are 98.2 and 0.8 mol%, respectively, calculated from the chlorine content (found: 18.04%, calc.: 18.13%). We estimated that the degree of esterification is the same as that of acetylated cylindrical PEHA. Since, the reaction proceeded through core-shell type gel consisting of an esterified shell layer and unreacted PHEA, and finally gave full acetylated PHEA gel bead, we expected that the reaction was suitable method for the synthesis of millimeter-size core-shell type gel beads.

4. Conclusion

(1) The millimeter-size PHEA gel beads with very narrow size distribution were obtained from the sedimentation polymerization.
(2) The acetylation of PHEA gel beads with acetic anhydride proceeded smoothly to give almost quantitatively esterified PHEA.
(3) The acetylation of PHEA gel bead proceeded through a fine spherical core-shell type gel. The obtained PHEA gel beads were also swollen in water while maintaining a spherical shape. These results indicate that the internal structure in the bead is relatively uniform.

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