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ORIGINAL CONTRIBUTION

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Highly monodisperse crosslinked polymethylmethacrylate microparticles by dispersion polymerization

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Abstract Highly monodisperse polymethylmethacrylate (PMMA) microparticles crosslinked with carboxylic group-containing urethane acrylates (CUA) were produced by simple dispersion polymerization in methanol solution. In contrast to conventional crosslinkers, the CUA employed as a crosslinker was excellent for maintaining the monodispersity of PMMA microparticles even at moderate crosslinker concentrations (to about 5 wt%). It was believed that the CUA helped form the monomer-swellable surface of primary particles, because of the structurally long tetramethylene oxide groups in the molecule. Carboxylic groups in the molecular backbone resulted in larger primary particles by increasing the solubility of the monomer mixture in the medium. Owing to these larger primary particles, the crosslinked PMMA particles showed lower polymerization rates than the linear ones during particle growth. However, at high CUA concentrations (about 10 wt%), bimodal distributions were observed. This was attributed to the high crosslinking density of the primary particle surfaces. Therefore, monomer diffusion toward the polymer phase was restricted, resulting in more favorable secondary nucleation in the medium.

Key words Highly monodisperse polymethylmethacrylate microparticles – Carboxylic group-containing urethane acrylate – Monomer-swellable surface – Long tetramethylene oxide groups – Lower polymerization rate

Introduction

Recently, there has been considerable interest in the development of polymer particles by dispersion polymerization [1–6]. This is mainly due to their spherical shape and highly monodisperse size distribution, which are essential in medical diagnostics [7, 8], liquid chromatography [9, 10], enzyme immobilization [11, 12], and drug delivery [13]. However, common results of crosslinking of polymer particles by dispersion polymerization have been broad size distributions, oddly shaped particles, and coagula.

Much research has been performed on the production of crosslinked micron-sized polymer particles by dispersion polymerization [14–17]. In the dispersion polymerization mechanism for monodisperse crosslinked polymer particles, it is proposed that particle growth occurs through precipitation of nucleated oligomers or particles onto the surface of primary particles, because of the nonswellability of the highly crosslinked primary particles. Therefore, the importance of preparing monomer-swellable primary particles has been stressed. Based on this concept we successfully produced highly monodisperse crosslinked polystyrene microparticles [18]. As a useful monomer-swellable crosslinker, a urethane acrylate was designed with flexible tetramethylene oxide in the middle and two vinyl groups at both ends. From our study, it was found that when primary particles formed this urethane acrylate helped the swelling of the primary

particles by styrene monomers due to its flexible molecular characteristics.

In this study, we prepared highly monodisperse crosslinked polymethylmethacrylate (PMMA) microparticles by incorporating a carboxylic group-containing urethane acrylate (CUA) as a monomer-swellable crosslinker. The effect of concentration and molecular weight of the CUA on particle size, size distribution, and morphology was examined.

Experimental

Materials

Isophorone diisocyanate (IPDI, Tokyo Chemical Industry Co.) was vacuum distilled before use. Polytetramethylene glycol (PTMG, $M_w = 1.0 \times 10^3$, 1.4×10^3, and 2.0×10^3 g mol^{-1}, Hyosung BASF), polyvinylpyrrolidone (PVP K-30, $M_w = 4.0 \times 10^4$ g mol^{-1}, Aldrich) di-2 ethylhexyl ester of sodium sulfosuccinic acid (Aerosol-OT, American Cyanamid), and dimethylolpropionic acid (DMPA, Aldrich) were used as received. The inhibitors in 2-hydroxyethyl methacrylate (HEMA, Aldrich) and in methylemethacrylate (MMA) monomer (Junsei) were removed through a removing column (Aldrich). 2,2-Azobis(isobutyronitrile) (AIBN, Junsei) was recrystallized from methanol.

Synthesis of carboxylic group-containing urethane acrylates (CUA) [19–22]

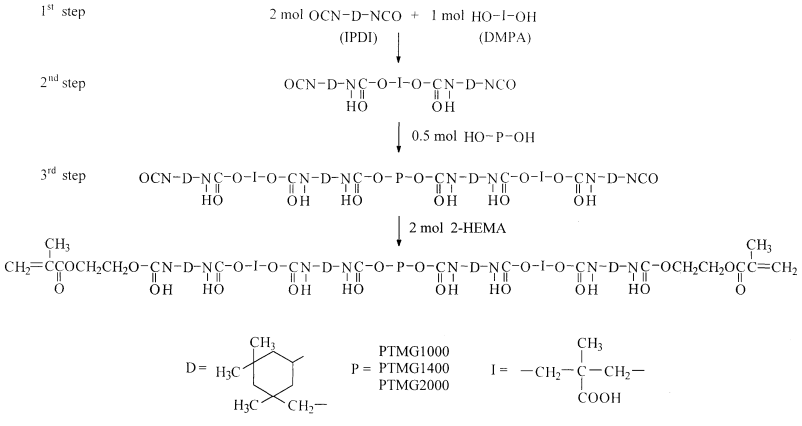
CUAs were synthesized by a stepwise reaction procedure. The schematic molecular structure is represented in Scheme 1. In the first step, 2 mol IPDI was poured into the glass reactor and nitrogen gas was circulated for 10 min to eliminate residual moisture. After dissolving 1 wt% of dibutyltindilaurate (DBTDL), 1 mol DMPA dissolved in dimethylacetamide (DMAc) was dropped into the reactor slowly at room temperature. The reaction temperature was raised to 80 °C so that 2 mol IPDI reacted with 1 mol DMPA, resulting in the molecular structure having a carboxylic group in the middle and isocyanates at the ends. The change in NCO value during the reaction was determined using the dibutylamine back titration method to find out the end point of the reaction [23].

In the second step, 0.5 mol PTMG was added slowly into the reactor to incorporate the soft segment into the molecular backbone using the same method as in the first step. In the last step, after dissolving 1 wt% of DBTDL into the reactor, 2 mol of HEMA was allowed to react with the residual NCO groups at 45 °C for 12 h; this introduces reactive vinyl groups at the ends of the molecules. The reaction end point was determined by the disappearance of the NCO stretching peak (2270 cm^{-1}) through IR spectroscopy. To purify DMAc, unreacted 2-HEMA, and DMPA, the reaction mixture was precipitated from water and filtered several times to give a crude product. The crude product was dried in vacuo.

We synthesized the urethane acrylates named CUA1, 2 and 3. The numbers 1, 2, and 3 correspond to the molecular weights of PTMG, 1.0×10^3, 1.4×10^3, and 2.0×10^3 g mol^{-1}, respectively.

Dispersion polymerization of MMA and CUA

The general dispersion polymerization procedure was followed [14, 16]; AIBN, PVP, Aerosol-OT, MMA, CUA, and methanol were weighed into 20 ml glass vials. After sealing in a nitrogen atmosphere, the vials were submerged in a thermostated water bath and tumbled with a rotation speed of 40 rpm. The polymerization was carried out for 24 h at 55 °C. The spheres obtained were centrifuged for 10 min at 8000 rpm. The supernatant was then decanted and the remaining precipitate was repeatedly washed by six centrifugations, and dried under vacuum at ambient temperature overnight. The standard recipe is summarized in Table 1.



Scheme 1 The reaction procedure and schematic molecular structure of the carboxylic group-containing urethane acrylates (CUA)

Table 1 The standard recipe for dispersion polymerization[a]

Ingredient	Weight (g)
MMA	0.950
CUA[b]	0.050
PVP K-30[c]	0.400
Aerosol-OT	0.045
AIBN[d]	0.010
Ethanol	8.545

[a] 55 °C; 24 h; 10 wt% of monomer concentration based on total weight
[b] The weight percent of CUA was varied against MMA (5 wt% in this example)
[c] Four wt% of PVP K-30 ($M_w = 4.0 \times 10^4$ g mol^{-1}) based on total weight was added
[d] One wt% of 2,2′-azobis (isobutyronitrile), AIBN, based on monomer weight was added

Measurements

Molecular weight distributions were measured at 25 °C using a model 410 gel permeation chromatograph equipped with Styragel HR 1–4 columns from Waters Associates. The flow rate of the tetrahydrofuran carrier solvent was 0.5 ml mol^{-1}. The average molecular weights of the CUAs calculated on the basis of the molecular weight versus the retention volume curve of monodisperse polystyrene standards are listed in Table 2.

The particle diameter was measured with a field-emission scanning electron microscope (FE-SEM, JSM-6340F, JEOL). Specimens were prepared by diluting the particles recovered with distilled water and placing a drop on a cover glass. The drop was dried at room temperature and then coated under vacuum with a thin layer of gold. At least 200 individual particle diameters were measured from SEM photographs and the average was taken. The polydispersity index (PDI) was obtained as follows:

$$D_n = \frac{\sum_{i=1}^{n} d_i}{N} \quad , \tag{1}$$

$$D_w = \frac{\sum_{i=1}^{n} d_i^4}{\sum_{i=1}^{n} d_i^3} \quad , \tag{2}$$

Table 2 Molecular weights of the carboxylic group-containing urethane acrylates (CUA)

Symbol	M_w (g · mol^{-1})	M_n (g · mol^{-1})	PI[a]
CUA1	8.3×10^3	6.3×10^3	1.32
CUA2	1.1×10^4	6.1×10^3	1.73
CUA3	1.4×10^4	7.1×10^3	1.91

[a] PI = M_w/M_n

$$\mathrm{PDI} = \frac{D_w}{D_n} \quad , \tag{3}$$

where D_n is number-average diameter, D_w is the weight-average diameter, N is the total number counted, and d_i is the diameter of particle i.

Conversion-time curves for the set of polymerizations were determined by a conventional gravimetric method. By fitting the first-order derivatives of the conversion-time curves, the polymerization rates were obtained and plotted against the fractional conversion.

Results and discussion

Effect of the CUA concentration

Crosslinked PMMA particles were prepared by varying the CUA concentration from 3 to 10 wt% in methanol at 55 °C for 24 h. Figure 1 shows SEM photographs at each CUA concentration based on the MMA monomer weight. Stable particles could be obtained over the size range 3–4 μm without coagulation at all CUA concentrations. In these SEM photographs, it was notable that not only were the particle sizes highly monodisperse but the particles were also spherical and very clear, even in the crosslinked state.

It is known that conventional crosslinkers form a hard, glassy surface on the primary particles, which eventually makes it difficult to swell the primary particles using vinyl monomers [16, 17]. Because of above effect, the polymer particles displayed broad size distributions and rough surfaces upon adding a small amount of crosslinker, such as divinylbenzene (more than 0.5 wt%). However, differing from general observations, in the case of adding CUA as a crosslinker, highly monodisperse crosslinked PMMA particles were obtained at moderate concentrations. This can be elucidated by considering the surface characteristics of primary particles crosslinked by CUA [18]. The primary particles crosslinked by CUA can be readily swollen by MMA monomers in the media during particle growth because of the peculiar molecular structure of CUA; long tetramethylene oxide groups in the backbone of the molecules. However, at high CUA concentrations (more than 10 wt%), other small particles were observed, as shown in Fig. 1d. It was believed that the high CUA concentration produced primary particles of high crosslinking density, which led to the precipitation of new primary particles onto the initial particles and to the favorable formation of secondary particles [16, 17].

The average particle sizes, size distributions, and conversions obtained with CUA are listed in Table 3. The final size of the crosslinked PMMA particles increased with an increase in the CUA concentration.

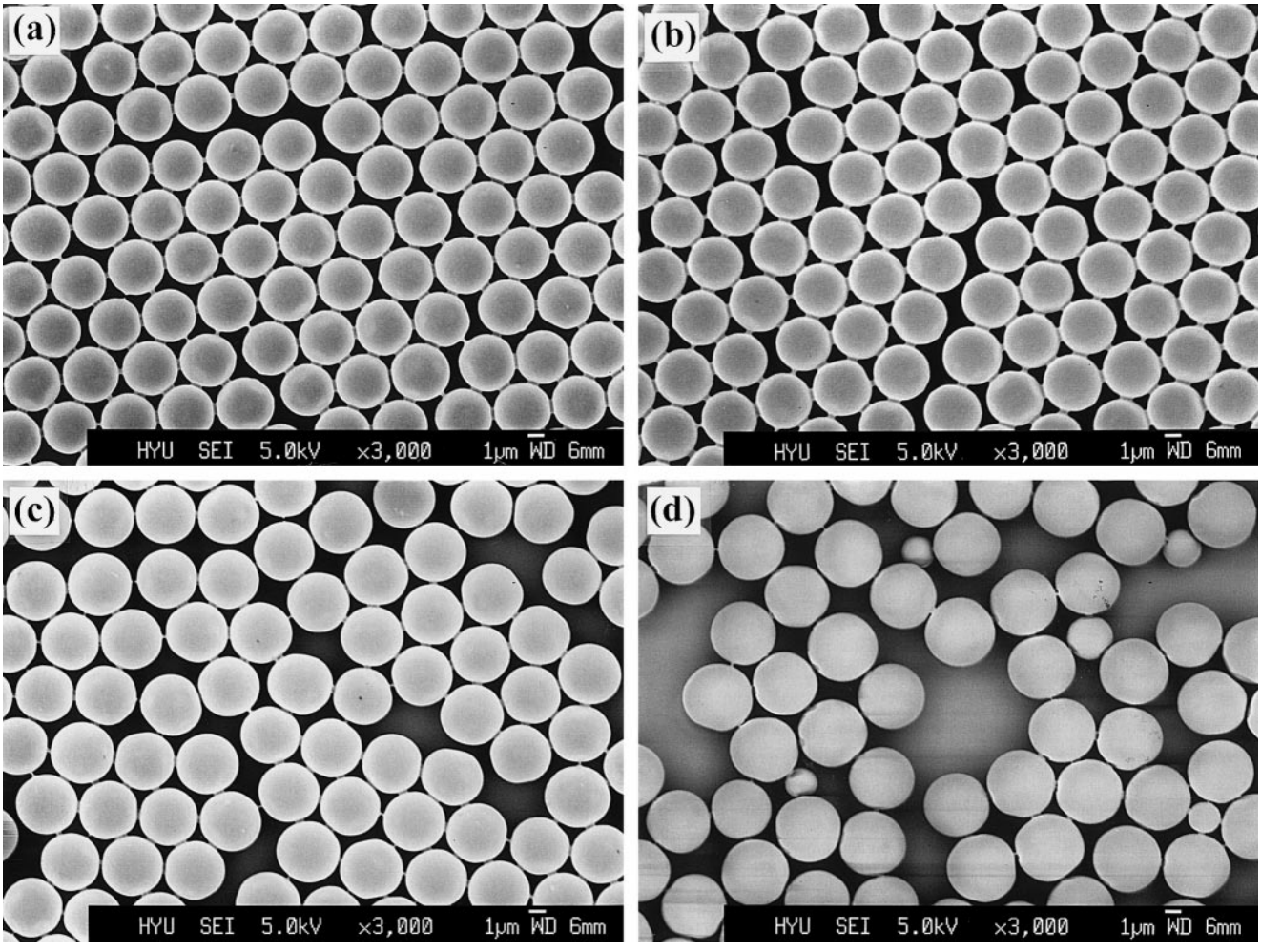


Fig. 1a–d SEM photographs of polymethylmethacrylate (PMMA) microparticles prepared by dispersion polymerization with different CUA concentrations (CUA3) at 55 °C for 24 h. **a** 0 wt%, **b** 3 wt%, **c** 5 wt%, and **d** 10 wt%

Table 3 The effect of CUA concentration on the crosslinked PMMA microparticles[a]

Symbol[b]	Particle size (μm)		PDI	Conversion	Remarks
	D_n	D_w	(D_w/D_n)	(%)	
CUA3-0[c]	3.42	3.59	1.05	93.2	mono disperse
CUA3-3	3.54	3.75	1.06	94.4	mono disperse
CUA3-5	3.74	3.96	1.06	92.3	mono disperse
CUA3-10	4.15	4.61	1.11	92.0	bimodal
CUA1-5	1.86	2.51	1.35	95.3	bimodal
CUA2-5	3.05	3.69	1.21	95.1	bimodal

[a] 55 °C; 24 h; 10 wt% of monomer concentration based on total weight
[b] CUA-α; α corresponds to the concentration of CUA based on total monomer weight
[c] Pure PMMA microparticles

This was attributed to the fact that the carboxylic groups in the molecular backbone of CUA not only enhanced the solubility of the monomer mixture but also stabilized the primary particles together with PVP [14]. Therefore, larger primary particles could be generated.

Effect of the molecular weight of CUA

In order to examine the effect of the molecular weight of CUA, crosslinked PMMA microparticles were produced by changing the molecular weight of PTMG.

Figure 2 shows SEM photographs of PMMA particles crosslinked with 5 wt% of CUA. In all figures, bimodal size distributions were observed instead of monodispersity together with a decrease in average particle sizes. The main reason for this result was likely to be the reduced molecular weight of CUA, as listed in Table 2. The lowered molecular weight of CUA caused the crosslinking density of the primary particles to increase. Therefore, in the particle growth stage, sec-

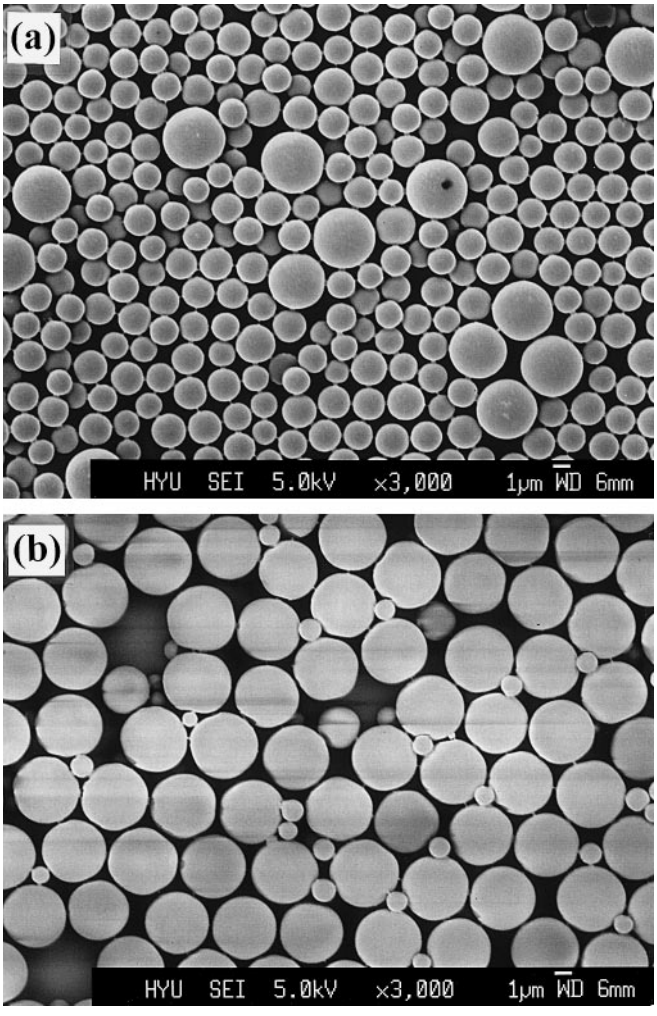


Fig. 2a,b SEM photographs of PMMA microparticles prepared by dispersion polymerization at 5 wt% of CUA (**a** CUA1 and **b** CUA2) at 55 °C for 24 h

ondary particles were readily generated, just as with a high concentration of crosslinker.

Polymerization kinetics for the crosslinked PMMA microparticles

Figure 3 shows the conversion for PMMA particles crosslinked by varying the CUA concentration as a function of polymerization time at 55 °C in methanol. In the conversion history, it was of interest to note that as the CUA concentration increased, the polymerization rate became slower. For a more precise explanation, the polymerization rate was obtained from the time-conversion curves of Fig. 3 at each conversion and replotted against the fractional conversion. The polymerization rate-fractional conversion curves obtained are shown in Fig. 4. Below a fractional conversion of 0.06, the

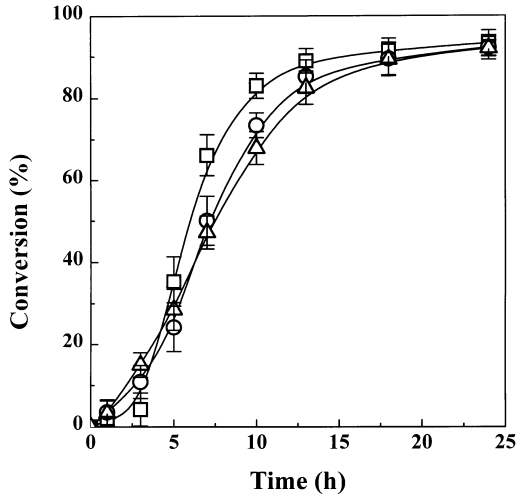


Fig. 3 Percentage conversion versus polymerization time for PMMA microparticles crosslinked by changing the CUA (CUA3) concentration; 0 wt% (-□-), 5 wt% (-○-), 10 wt% (-△-), at 55 °C in methanol

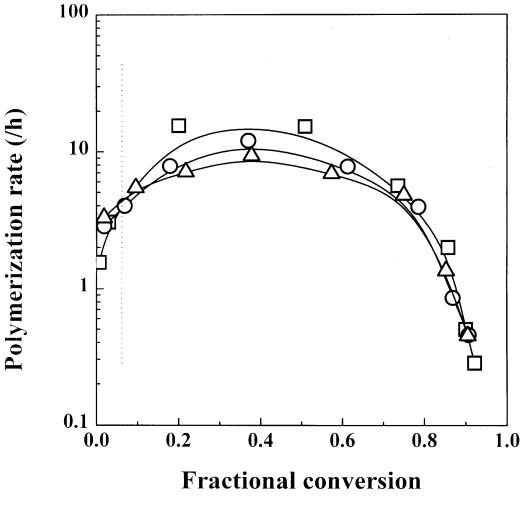


Fig. 4 Polymerization rate versus fractional conversion for PMMA microparticles crosslinked by changing the CUA (CUA3) concentration; 0 wt% (-□-), 5 wt% (-○-), 10 wt% (-△-), at 55 °C in methanol

polymerization rate of the crosslinked PMMA particles was higher than that of linear ones, which was because of the formation of a crosslinked oligomer radical network. Above a fractional conversion of 0.06 the opposite occurred. This result seemed to be attributed to the increased solubility of the monomer mixture by means of carboxylic groups in the urethane acrylate molecules finally generating large primary particles [4, 14]. This indicated that the total surface area decreased. Therefore, the equilibrium distribution of the monomer toward the particle phase was more unfavorable, which eventually resulted in a slower polymerization rate.

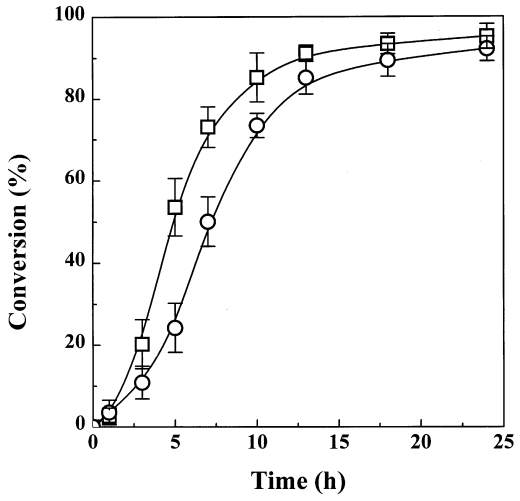


Fig. 5 Percentage conversion versus polymerization time for PMMA microparticles crosslinked by changing the molecular weight of the CUA; CUA1 (-□-) and CUA3 (-○-), at 55 °C in methanol. 5 wt% CUA was added

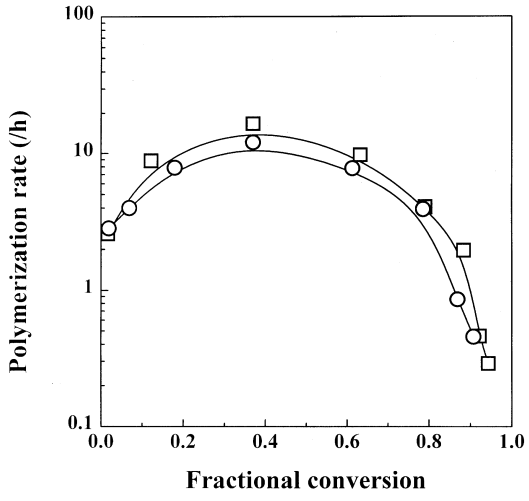


Fig. 6 Polymerization rate versus fractional conversion for PMMA microparticles crosslinked by changing the molecular weight of the CUA; CUA1 (-□-) and CUA3 (-○-), at 55 °C in methanol. 5 wt% CUA was added

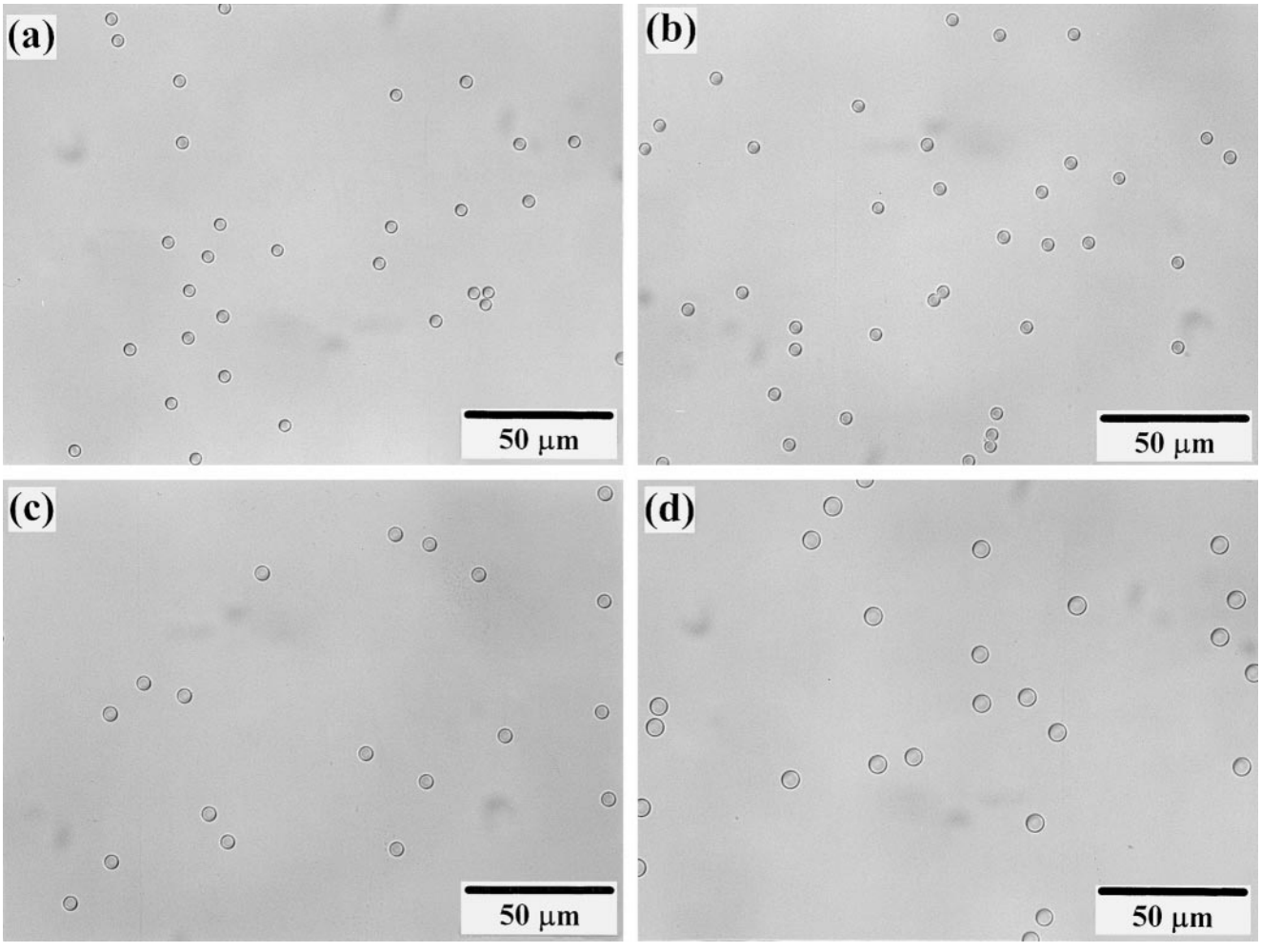


Fig. 7a–d Optical microscope photographs of PMMA microparticles crosslinked with 5 wt% of CUA (CUA3) in an ethanol/water mixture (65/35, w/w) at a temperature of **a** 25 °C, **b** 40 °C, **c** 50 °C, and **d** 65 °C

Figure 5 shows the conversion for PMMA particles crosslinked by changing the molecular weight of CUA (5 wt%) as a function of polymerization time at 55 °C in methanol. From the time-conversion curves shown in Fig. 5, the polymerization rates were replotted against the fractional conversion and are shown in Fig. 6. Over the range of fractional conversion, the PMMA particles crosslinked with CUA1 displayed a faster polymerization rate than those with CUA3. This faster polymerization rate of the particles crosslinked with CUA1 could be explained by considering the large number of small secondary particles in Fig. 2. These small particles explained the favorable equilibrium distribution of monomer toward particle phase, resulting in a faster polymerization rate.

Swelling of the crosslinked PMMA particles

In order to confirm the swelling of the crosslinked PMMA particles, the particle size was examined in an ethanol/water mixture (65/35, w/w) by changing the temperature. Figure 7 shows optical microscope (Nikon Microphot Fax) photographs of PMMA microparticles crosslinked with 5 wt% of CUA3 at different temperatures. At low temperatures, the particles remained unchanged; however, above 50 °C the particles started to swell. At 65 °C the particles swelled to about twice their normal size. This swelling ability of the crosslinked PMMA particles suggests the possibility of producing monodisperse composite particles by means of simple swelling procedure.

Conclusion

Highly monodisperse crosslinked PMMA microparticles were produced directly by simple dispersion polymerization of MMA and CUA. Highly monodisperse size distribution of the crosslinked particles was considered to be attributed to the monomer-swellable surface of the primary particles because of the long tetramethylene oxide groups in the backbone of the CUA. Carboxylic groups in the urethane acrylate molecules led to larger primary particles. This resulted in a lower polymerization rate compared with that of the linear polymer particle. The swelling of the PMMA particles obtained was confirmed in a heated ethanol/water mixture.

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