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ORIGINAL CONTRIBUTION

Convenient synthesis of microspheres by self-assembly of random copolymers in supercritical carbon dioxide

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Abstract A novel and convenient synthesis of microspheres was attained by molecular self-assembly of random copolymers in supercritical carbon dioxide. Poly{2-(perfluorooctyl)ethyl acrylate-*ran*-2-(dimethylamino)ethyl acrylate} random copolymers (P[POA-*r*-DAA]), with 7:3, 8:2, and 9:1 as the molar ratios of 2-(perfluorooctyl)ethyl acrylate (POA)/2-(dimethylamino)ethyl acrylate (DAA), were soluble in supercritical CO_2 and had their cloud points at about 75 bar higher than the critical pressure of CO_2. The CO_2 density at the cloud points decreased with an increase in temperature. Although the copolymers made a slight difference in the cloud point in the absence of perfluoroazelaic acid (PA), they made a marked difference in the presence of PA. The copolymer with a lower DAA content had a cloud point at lower CO_2 density. The scanning electron microscopy observation demonstrated that the copolymers produced microspheres in the presence of PA at 0.5 as PA/DAA in the heterogeneous state below the cloud points. The microspheres were unstable to pressure and changed to unspecific forms as a result of increasing the CO_2 pressure, although the microspheres were stable to temperature. The POA/DAA ratio in the copolymer had effect not only on the cloud point but also on the size of the microspheres. The copolymer with a lower DAA content formed smaller microspheres.

Keywords Poly{2-(perfluorooctyl)ethyl acrylate-*ran*-2-(dimethylamino)ethyl acrylate} · Perfluoroazelaic acid · Supercritical carbon dioxide · Cloud point · Microspheres

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Introduction

Micro and nano-sized polymer particles have many industrial applications such as coating [1–3], painting [4, 5], cosmetics [6, 7], adhesives [8, 9], and drug carriers [10, 11]. These microspheres are ordinarily prepared by heterogeneous polymerizations in water. Suspension polymerization produces microspheres with a 10- to 800-μm diameter [12, 13], whereas dispersion polymerization provides 1- to 30-μm-sized particles [14–16]. Emulsion polymerization gives much smaller microspheres of 70–250 nm [17–19]. In recent years, the heterogeneous polymerizations in supercritical carbon dioxide have attracted considerable attention from the viewpoint of the environmental preservation.

Carbon dioxide has many benign natures for the environment, that is, it is spontaneous, nontoxic, odorless, and recyclable. Carbon dioxide also has the mild critical point (31 °C, 74 bar) [20] and requires no process of dryness when used as a solvent in industry. Consequently, liquid and supercritical carbon dioxide is important as a solvent to take the place of organic solvents. The heterogeneous polymerizations in supercritical carbon dioxide were found by DeSimone et al. They succeeded in preparing microspheres of poly(methyl methacrylate) [21, 22], polystyrene [23], poly(vinyl acetate) [24], polyacrylonitrile [25], poly(*N*-vinylpyrroridone) [26], and poly (glycidyl phenylether) [27] through the suspension or dispersion polymerization using surfactants consisting of CO_2-philic and CO_2-phobic moieties. In the polymerizations, the combination of the surfactant and the monomer is significant to produce mono-dispersed microspheres in good yield.

We found a novel and convenient method to prepare microspheres in supercritical carbon dioxide through molecular self-assembly of random copolymers in the presence of a bifunctional carboxylic acid. We already released a publication on the synthesis of microspheres by the micelle formation of a diblock copolymer containing amino groups through noncovalent bond cross-linking with dicarboxylic acids in an organic solvent [28]. This micellization provided thermally stable micelles with the cores cross-linked. This paper describes the synthesis of microspheres of polymers through the micellization of a poly{2-(perfluorooctyl)ethyl acrylate-*ran*-2-(dimethylamino)ethyl acrylate}, P(POA-*r*-DAA) by a dicarboxylic acid in supercritical carbon dioxide.

Experimental

Instrumentation

The proton nuclear magnetic resonance (^{1}H NMR) measurement was conducted using a Varian 300 FT NMR spectrometer. The size exclusion chromatography (SEC) was performed using a Tosoh GPC-8020 instrument equipped with a DP-8020 dual pump, a CO-8020 column oven, and a RI-8020 refractometer. Two polystyrene gel columns, Tosoh TSKgel GMH$_{HR}$-M, were used with hexafluoroisopropanol as the eluent at 40 °C. The scanning electron microscopy (SEM) measurements were made using a JEOL JSM-6300 electron microscope. The cloud point measurement was performed with a Nekken variable volume view cell (with a window made of tempered glass) equipped with an Eyela CCA-1110 cooler and a Nihon Seimitsu Kagaku NP-D-321 personal pump.

Materials

2-(Perfluorooctyl)ethyl acrylate (POA) was washed with aqueous alkaline solution and saturated sodium chloride solution and dried in vacuo for several hours. 2-(Dimethylamino)ethyl acrylate (DAA) was distilled under reduced pressure over calcium hydride. Azobisisobutyronitrile (AIBN) was recrystallized in chloroform. Hexafluorobenzene to be used as a solvent for ^{1}H NMR measurement was distilled over calcium hydride. Extrapure perfluoroazelaic acid (PA) was used without further purification.

Synthesis of P(POA-*r*-DAA): general procedure

POA (1.64 g, 3.16 mmol), DAA (0.198 g, 1.38 mmol), and AIBN (7.4 mg, 0.0451 mmol) were placed in ampule. After the contents were degassed, the ampule was sealed in vacuo. The polymerization was carried out at 60 °C for 10 min and was terminated by cooling with liquid nitrogen. The reaction mixture was dissolved in hexafluorobenzene and poured into hexane to precipitate a polymer. The precipitate was dried in vacuo for several hours to obtain P(POA-*r*-DAA) (0.994 g).

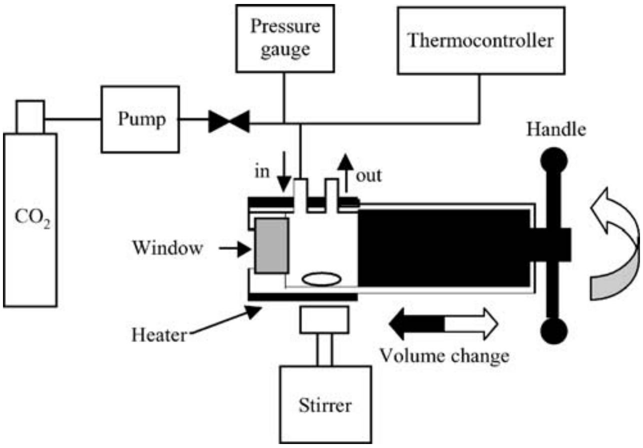

Fig. 1 A schematic of the experimental variable volume view cell

Cloud point measurement

A schematic of the experimental variable volume view cell used for the cloud point measurement is shown in Fig. 1. P(POA-*r*-DAA) (30 mg) was placed in the cell, and CO$_2$, liquefied with a cooler, was added to it. The cloud point was defined as the point at which the contents of the cell turned slightly opaque, indicating precipitation of the polymer from solution.

Synthesis of microspheres of P(POA-*r*-DAA) with PA

P(POA-*r*-DAA) (POA/DAA = 7:3, 30 mg) and PA (5.5 mg) were placed in the variable volume view cell, and then liquid CO$_2$ was added. The solution was stirred at 184 bar at 35 °C for 10 min. After the pressure of the homogeneous solution was reduced to 129 bar by the volume compressed, the heterogeneous solution was sprayed into a plastic bag made of polyethylene to collect the polymer particles. Polymer particles (35 mg) were obtained.

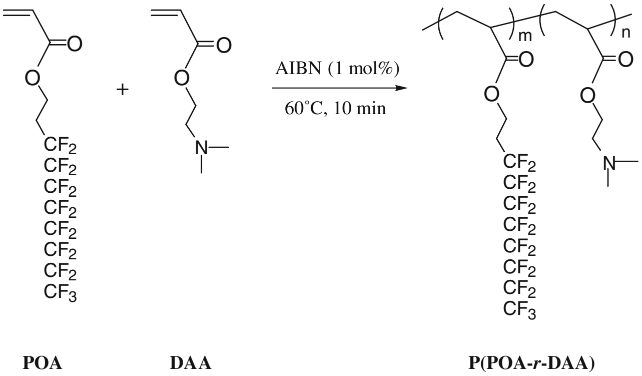

Fig. 2 Synthesis of the P(POA-*r*-DAA) random copolymers

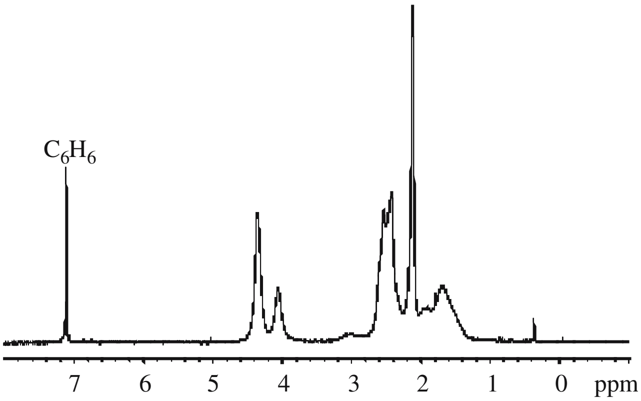

Fig. 3 A ^{1}H NMR spectrum of P(POA-*r*-DAA) with POA/DAA of 7:3. Solvent, C_6F_6 including C_6D_6

SEM measurement of P(POA-*r*-DAA) microspheres with PA

The polymer particles were put on a carbon adhesive tape and was subjected to SEM measurement after coated with Pt.

Results and discussion

P(POA-*r*-DAA) random copolymers were prepared by radical copolymerization of POA and DAA. The polymerization was carried out in bulk by AIBN at 60 °C (Fig. 2). The polymerization proceeded rapidly to produce a viscous solid within 10 min. A ^{1}H NMR spectrum of the copolymer is shown in Fig. 3. The broad signals at 0.9–3.4 ppm were based on the main chain. Signals of the DAA units were observed at 2.08, 2.38, and 4.07 ppm. The sharp signal at 2.08 ppm originated from the methyl groups attached to the amino group, whereas the signal at 2.38 ppm was based on the methylene bonded to it. The signal at 4.07 ppm was assigned to the other methylene bonded to the carboxyl group. Signals of the POA units were also observed at 2.52 and 4.36 ppm. The former was attributed to the methylene attached to the perfluoroalkyl group, and the later was to the other methylene bonded to the carboxyl group. The POA/DAA ratio in the copolymer was estimated on the basis of the signal intensity at 4.36 and 4.07 ppm. We thus obtained three different random copolymers with POA/DAA ratios of 7:3, 8:2, and 9:1. The molecular weight (Mn) and molecular weight distribution (Mw/Mn) of the copolymers were Mn (Mw/Mn) = 50,400 (7.35), 55,300 (8.37), and 58,400 (10.95) for 7:3, 8:2, and 9:1 of the POA/DAA ratios on the basis of SEC with poly(methyl methacrylate) standards.

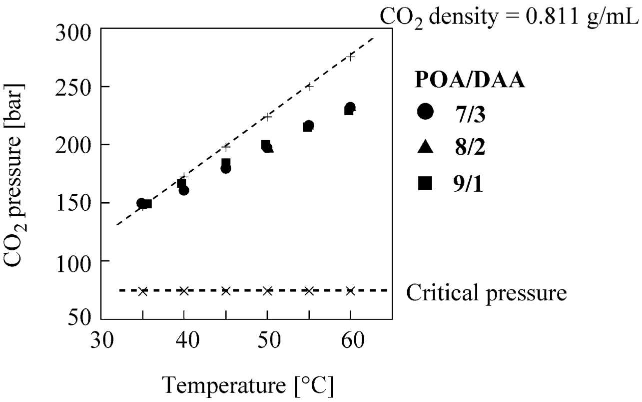

Fig. 4 Plots of the experimental cloud points of the copolymers at each temperature vs the CO_2 pressure

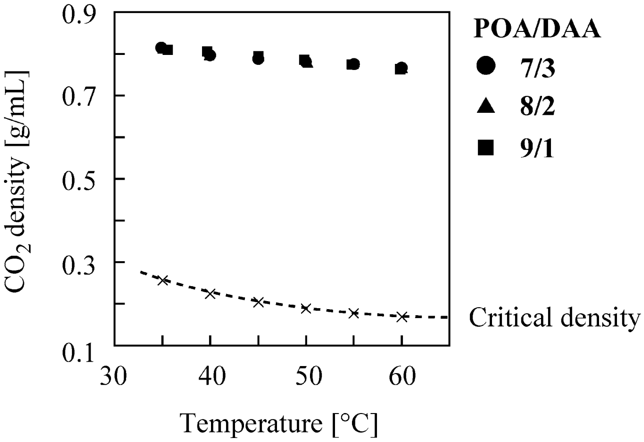

Fig. 5 Plots of the experimental cloud points of the copolymers at each temperature vs the CO_2 density

The P(POA-*r*-DAA) copolymers dissolved in supercritical CO_2 and had their cloud points at about 75 bar higher than the critical pressure of CO_2. At the pressure lower than the cloud point, the copolymers were not completely dissolved in CO_2 even in the supercritical state, so that two phases of the liquid of the CO_2 and the solid of the copolymer were observed. Figure 4 shows the plots of the

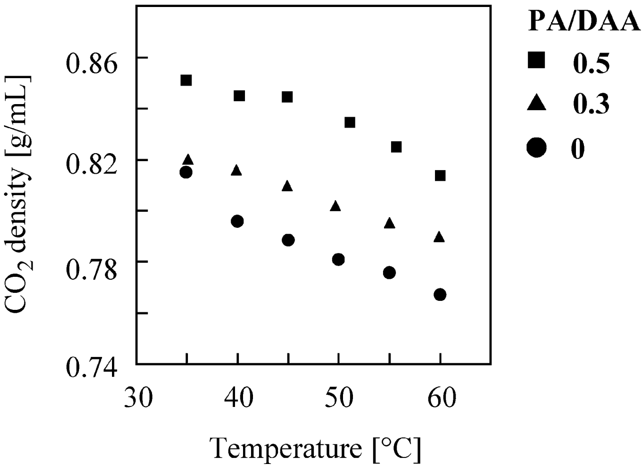

Fig. 6 Plots of the cloud points of the copolymer with 7:3 of POA/DAA in the presence of PA at 0.3 and 0.5 of PA/DAA

experimental cloud points of the copolymers at each temperature vs the CO_2 pressure. The pressure at the cloud points increased as a result of increasing the temperature. This phenomenon is natural because the density of CO_2 decreases with an increase in temperature at identical pressure. Accordingly, the cloud points were plotted vs the CO_2 density (Fig. 5). The CO_2 density at the cloud point decreased as a result of increasing the temperature, indicating that the solubility of the copolymers into CO_2 increased as the temperature increased. In addition, the copolymers made a slight difference in the cloud point.

The solubility of the copolymers in supercritical CO_2 decreased in the presence of PA. Figure 6 shows the cloud points of the copolymer with 7:3 of POA/DAA in the absence and presence of PA at 0.3 and 0.5 as a molar ratio of PA to the DAA unit. As a result of increasing the amount of PA, the cloud points were shifted to a higher side of the CO_2 density. The copolymer became less soluble in the presence of PA. The decrease in the solubility should be caused by a noncovalent bond cross-linking between the amino groups in the copolymer via the dicarboxylic acid of PA.

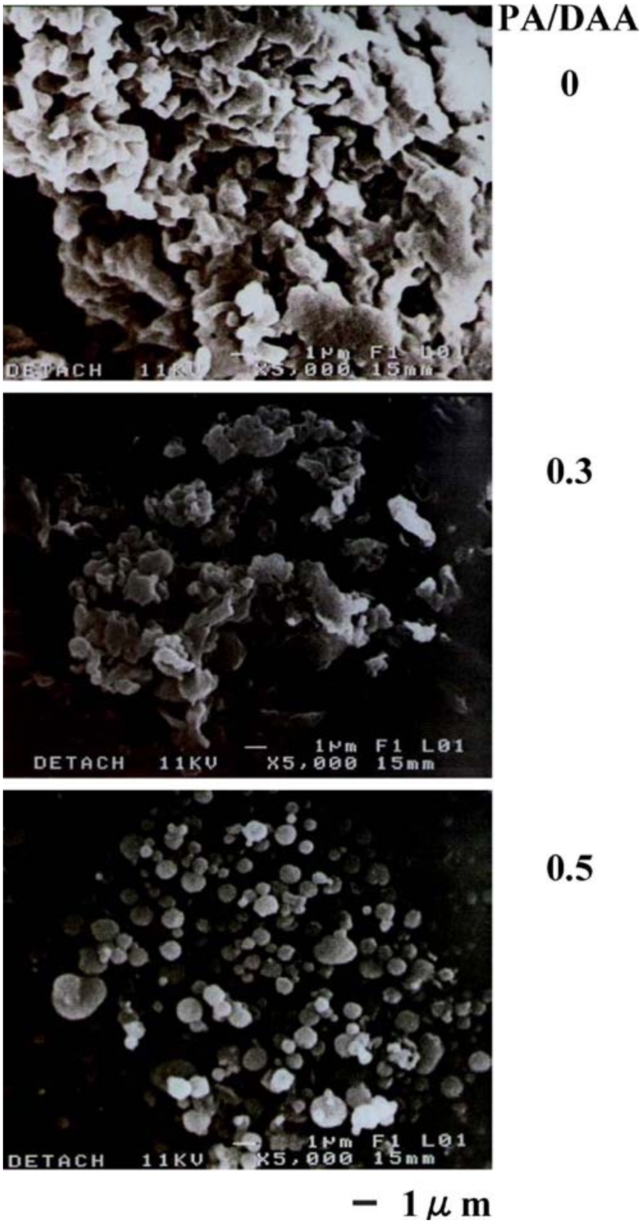

Fig. 7 SEM images of the copolymer in the absence and presence of PA. POA/DAA = 7:3, heterogeneous state

SEM observation demonstrated that the copolymer formed different shapes in the absence and presence of PA in supercritical CO_2. Figure 7 shows the SEM images of the copolymer with and without PA. The images were obtained for the polymer particles produced in the two-phase state. This two-phase state was obtained by decreasing the pressure of the homogeneous solution in which the copolymer and PA were completely dissolved in supercritical CO_2 at the pressure higher than the cloud point. The copolymer took unspecific forms in the absence of PA. There was a slight difference in the shape at 0.3 as the PA/DAA ratio. On the other hand, the copolymer had spherical

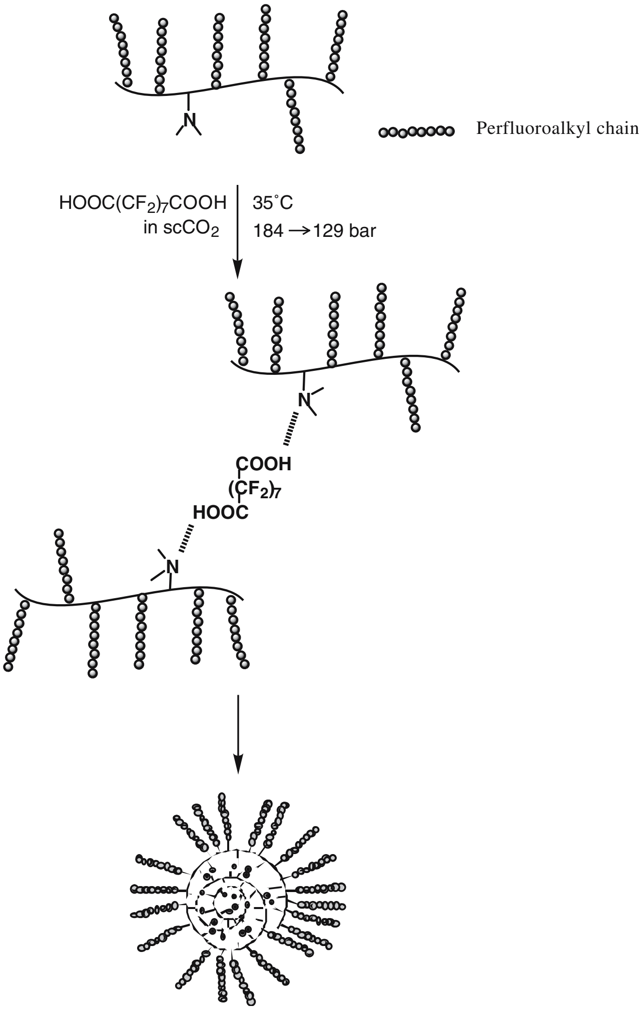

Fig. 8 A schematic of the formation of the microspheres

forms at the 0.5 ratio. The size of the particles was about 0.7 μm. At 0.5 of PA/DAA, all the amino groups interact with the carboxylic group of PA, so that no-free amino groups are expected to exist in the copolymer. Therefore, the microspheres should be formed by cross-linking between the amino groups in the copolymer through the electrostatic interaction with PA (Fig. 8).

We explored the stability of the microspheres vs pressure. Figure 9 shows the SEM images of polymer particles obtained from three different states: the heterogeneous state below the cloud point, the state at the exact cloud point, and the homogeneous state over it. The pressure at the heterogeneous state was 20.5 bar lower than the cloud point pressure, whereas that at the homogeneous state was 34.5 bar higher. The particles included PA at the 0.5 ratio. The spherical particles formed in the heterogeneous state partly changed to unspecific forms as a result of increasing the pressure to the cloud point pressure. The microspheres completely changed to unspecific forms over the cloud point. These changes were based on the cross-linking by the weak electrostatic interaction and on an increase in the solubility of the microspheres into supercritical CO_2 as a result of increasing the density of CO_2. Consequently, the shape of the polymer particles was dependent not only on the acid concentration but also on the pressure of CO_2.

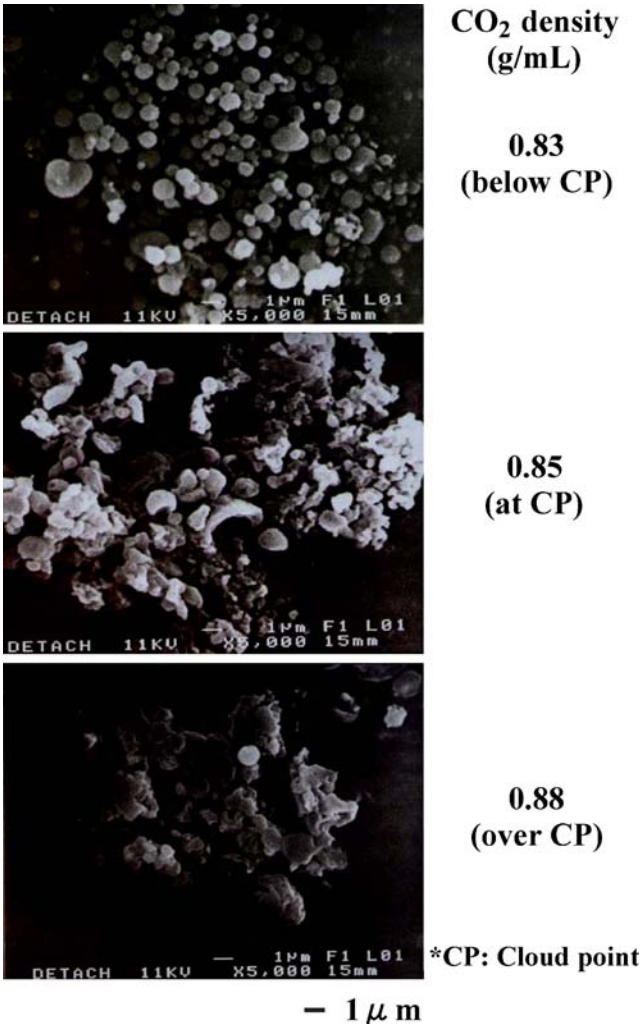

Fig. 9 SEM images of polymer particles obtained from the heterogeneous state below the cloud point, the state at the exact cloud point, and the homogeneous state over it. POA/DAA = 7/3, PA/DAA = 0.5

The spherical shapes of the polymer particles were independent of the temperature. Figure 10 shows the SEM images of the polymer particles obtained at 35, 45, and 60 °C at 0.5 of PA/DAA. The particles were prepared in the heterogeneous states at which the pressures were 20.5 bar lower than the cloud point pressure at each temperature. The polymer particles maintained their spherical shapes at 45 and 60 °C. In addition, the copolymer with PA took more completely spherical shape with an increase in the temperature. It may be accounted for by the fact that the perfluoroalkyl chains extend much more at higher tempera-

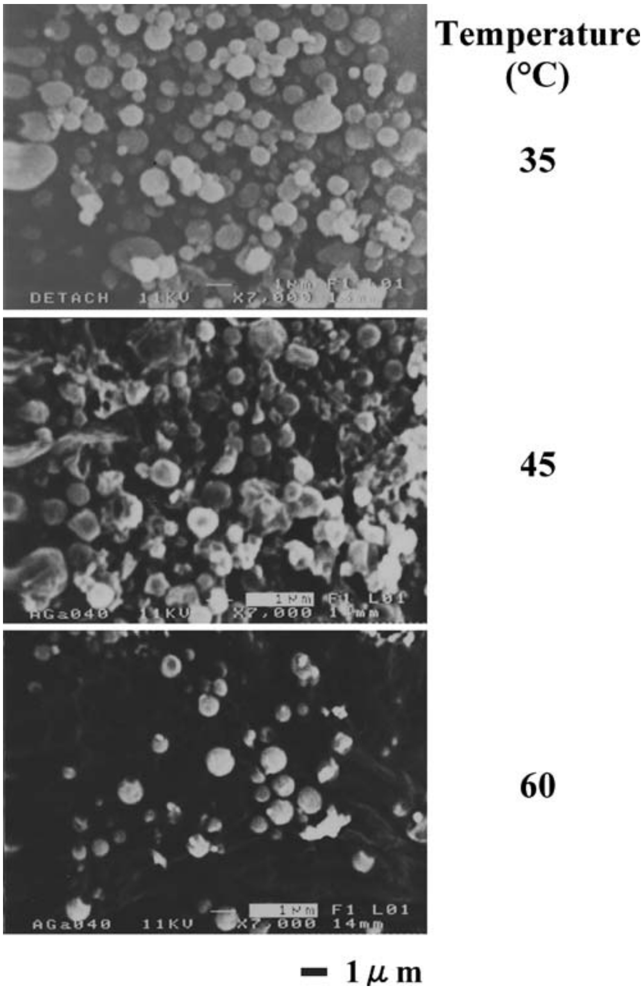

Fig. 10 SEM images of the polymer particles obtained at 35, 45, and 60 °C. PA/DAA = 0.5

ture, resulting in that the copolymer more easily form spherical particles at the higher temperature.

The POA/DAA ratio in the copolymer affected the cloud point and size of the microspheres. Figure 11 shows the cloud points of three different copolymers with POA/DAA of 7:3, 8:2, and 9:1 in the presence of PA at 0.3 and 0.5 of PA/DAA. Although there was a negligible difference in the cloud point among the copolymers in the absence of PA, the copolymers made a marked difference in the presence of it. This difference was much greater as the amount of PA increased. The copolymer having a lower DAA content showed lower cloud point in the presence of PA. The SEM observation revealed that the copolymer with a lower DAA content formed smaller microspheres. Figure 12 shows the SEM images of the microspheres obtained from the copolymers with PA at the 0.5 ratio. The size of the microspheres decreased as the DAA content decreased. The copolymer with the 8:2 ratio formed the microspheres with about 0.6 μm as the particle size, whereas the 9:1 copolymer produced microspheres with 0.4 μm. The decrease in the size of the microspheres with the decrease in the DAA content may be accounted for by the fact that the copolymer with lower DAA content forms a lower degree of cross-linking with the dicarboxylic acid, providing smaller aggregation numbers of the microspheres. The microspheres obtained from the copolymers with 8:2 and 9:1 of POA/DAA showed the same results about the amount of PA and the pressure of CO_2 as those from the copolymers with 7:3. It was deduced that the size of microspheres was manipulated by the POA/DAA ratio in the copolymer.

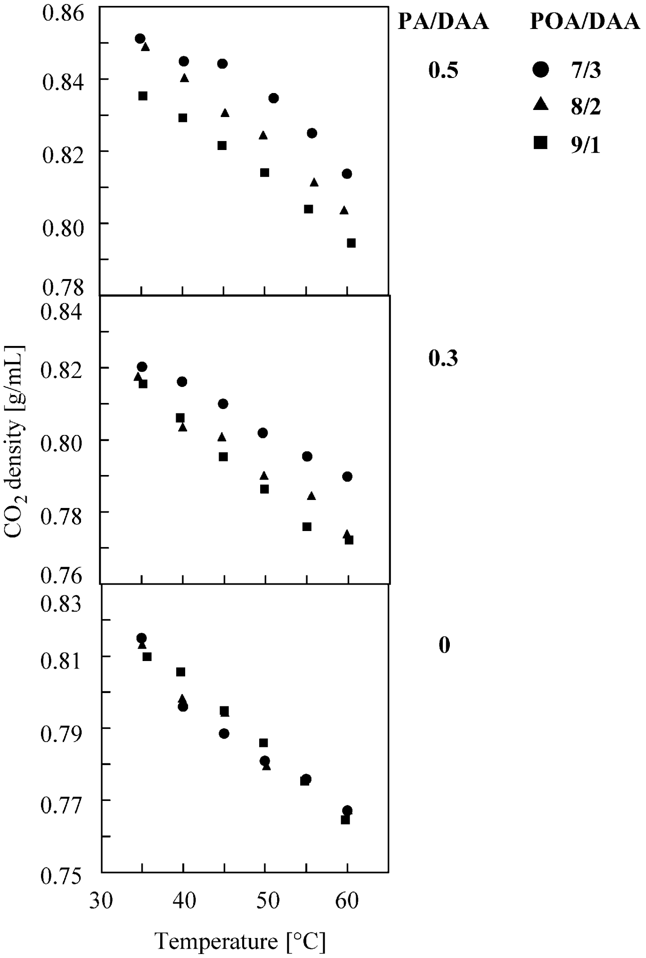

Fig. 11 Plots of the cloud points of the copolymers with POA/DAA of 7:3, 8:2, and 9:1 in the absence and presence of PA at 0.3 and 0.5 of PA/DAA

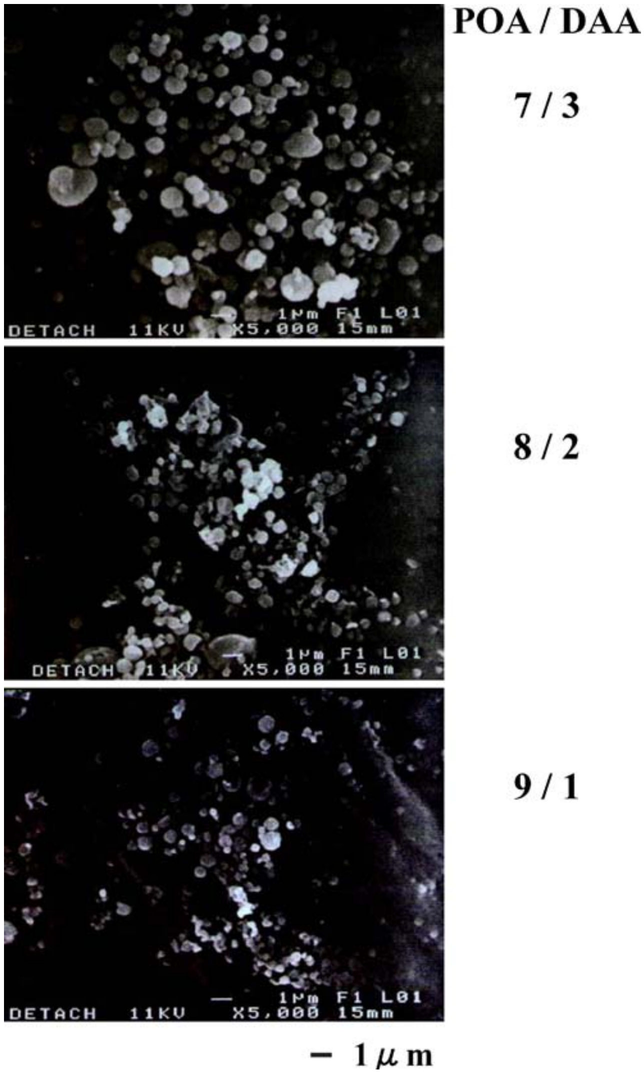

Fig. 12 SEM images of the microspheres obtained from the copolymers with POA/DAA of 7:3, 8:2, and 9:1. PA/DAA=0.5, heterogeneous state

Conclusion

We found the convenient synthesis of the microspheres by the self-assembly of the P(POA-*r*-DAA) random copolymers using the dicarboxylic acid of PA in supercritical carbon dioxide. The microspheres were formed through the noncovalent bond cross-linking of the electrostatic interaction between the amino group and the carboxylic acid. Based on the weak association, the microspheres changed to unspecific forms as a result of increasing the pressure. This implies that the polymer particles can be used as pressure-sensitive microspheres. On the other hand, the microspheres were stable in the increase in the temperature. The particle size was less than 1 μm and decreased with the DAA content decreasing. The DAA content also affected the solubility of the copolymers in the presence of PA. It was found that the solubility and the size of macrospheres were manipulated not only by the amount of PA but also by the DAA content in the copolymer.

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