14.6 Preparation of Polymer Microspheres by Radiation-induced Polymerization

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Abstract Cross-liking monomer, diethylene glycol dimethacrylate gives microspheres from organic solution by radiation-induced polymerization. /One of the remarkable result is that the number of the microspheres is not changing during the polymerization. Ethyl methacrylate, maleic anhydride, styrene and acrylamide are used as comonomers. These comonomers give the microspheres in the range of 0 to 0.4 as mol fractions.

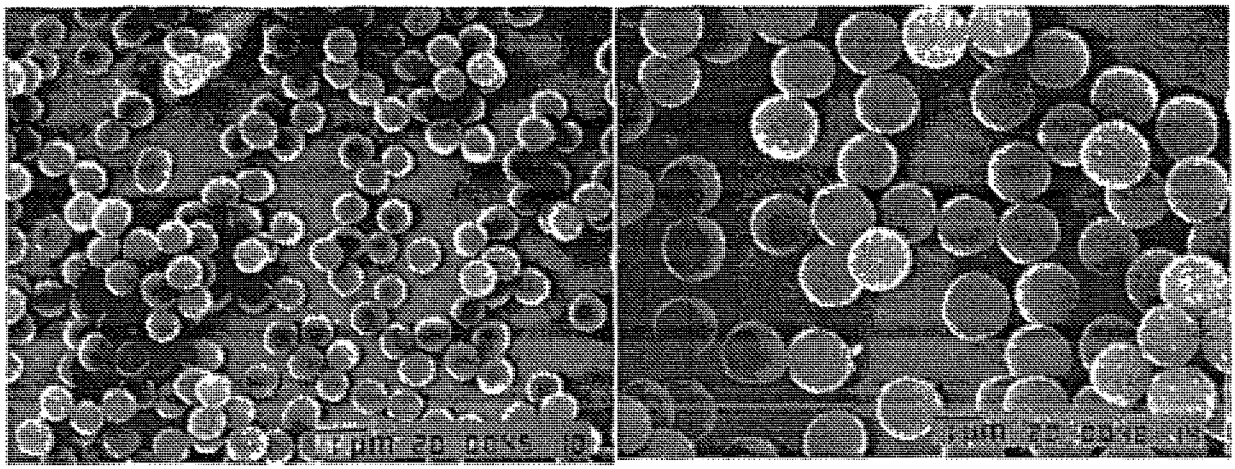
INTRODUCTION

Recently, microspheres (fine particles with spherical shape) are getting new interests as functional materials. Applications of the microspheres have been expanding in many fields. Remarkable applications of the microspheres are in the biological and medical fields as immuno-assays, cell labeling, and drug carriers. Emulsion- and dispersion-polymerizations are well-known as the methods for the preparation of polymer particles. A unique method has been reported which gives monodisperse microspheres by the radiation-induced polymerization.[1] It is characteristic that a mixture of a monomer and a solvent gives monodisperse microspheres in the absence of any kind of additives. The mechanism is considered to be different from those of the conventional methods, but the details of the formation mechanism have not yet been known. This report deals with the development of the monodisperse microspheres by the radiation-induced polymerization and the possiblity of thier applications. [2-5]

EXPERIMENTAL

Diethylene glycol dimethacrylate (2EGDM), supplied from Shin Nakamura Kagaku, was purified by passing through active alumina. Ethyl methacrylate (EMA), styrene, maleic anhydride, and acrylamide, were purchased from Wako Pure Chemical. Ethyl methacrylate and styrene were purified by distillation. Maleic anhydride and acrylamide were purified by recrystallization from benzene. Organic solvents, purchased from Wako Pure Chemical, were used without further purification otherwise noted.

In a typical experiment, solutions of 2EGDM (10 vol %) in organic solvents were degassed



(a) (b)

SEM photographs of poly-2EGDM microspheres. (a) 15 min, (b) 120 min. 4 kGy h^{-1}. 10 vol % of 2EGDM in ethyl acetate.

and sealed in 20 ml glass vessels. The degassing was carried out by five-times freeze-melt repeatings. The samples were irradiated with ^{60}Co γ rays without stirring. The dose rate was 4 kGy h^{-1} and the irradiation time was 2 h otherwise noted.

Teflon filters of a 0.2 μm pore size (Advantest) were used for the separation of the microspheres from the irradiated solutions. The microspheres were washed with the solvents and dried under vacuum. The microspheres were photographed by using a scanning electron micrograph (SEM) (JELO, JST-300).

RESULTS AND DISCUSSION

Figures 1(a) and 1(b) show the SEM photographs of the microspheres prepared in ethyl acetate. The microspheres both obtained at 15 min as Fig. 1(a) and 2 h as Fig. 1(b) have a complete spherical shape. The diameter increases with irradiation time. The microspheres grow with narrow size distribution. This means that the microspheres grow independently during the polymerization.

Figure 2 shows the time-conversion curve for the microspheres. The monodisperse microspheres are obtained with the yields more than 80 % by 2h polymerization. The size of the microspheres can be controlled by irradiation time. The easiness of the termination of the polymerization must be one of the advantages of the radiation-induced polymerization.

The number of the microspheres was calculated by assuming that the specific gravity of the microspheres is the same as that of the polymer obtained by the radiation- induced bulk polymerization of 2EGDM. The specific gravity of the 2EGDM polymer block was determined to be 1.24. Figure 3 shows the number of the microspheres plotted against irradiation time. The number of the microspheres is constant through the irradiation period. This agrees with the expectation from the monodispersity of the microspheres. The number of the microspheres

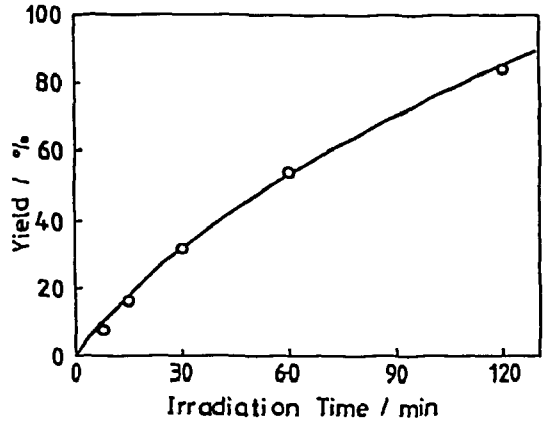


Figure 2. Time-conversion curve of the microsphere. Concentration of 2EGDM was 10 vol %, in ethyl acetate. Dose rate was 4 kGy h^{-1}.

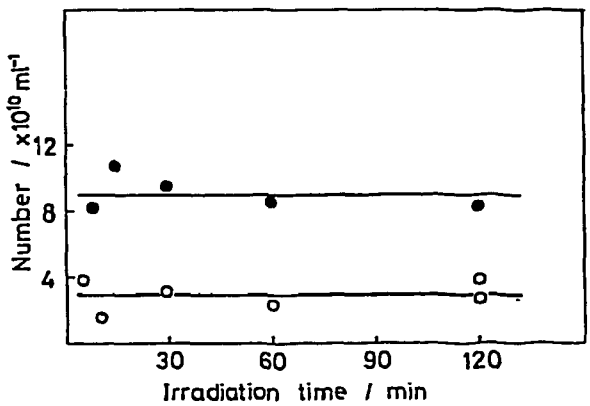


Figure 3. Relationship between irradiation time and number of microspheres. (●) 10 vol %, at room temperature, (○) 5 vol % at 40 °C, with ethyl acetate. 4 kGy h^{-1}.

becomes constant at the conversion below 10 % within the irradiation time of 5 min. The radicals produced after the irradiation time of 5 min do not contribute to the formation of the nuclei of the microspheres. That is to say, the formation of the nuclei is inhibited by the presence of the microspheres.

The results of the radiation-induced polymerization of 2EGDM monomer in various solvents are presented in Table 1 together with the viscosities and the solubility parameters of the solvents. The solubility of the monomer in the solvents increases with decreasing difference in their solubility parameters between 2EGDM and the solvents. The solubility parameter of the 2EGDM monomer was calculated to be 8.9. The solvent of which solubility parameter is close to 8.9 is considered to be a good solvent for 2EGDM monomer. Monodisperse microspheres and polymeric gel are produced depending on the solvents. It seems that the solubility parameters of the solvents giving separate microspheres are relatively close to that of 2EGDM. It is suggested that good solvents for the monomer are suitable for the formation of the microspheres. Thus, it is considered that the good solvent makes growing microspheres stable in the solution to avoid the aggregation of the microspheres.

Table 1. Solvent Effect on the Formation of Microspheres[a]

Solvents	Result	Yield %	Size μm	δ[b] %	Viscosity cp (25°C)
Methyl formate	Microspheres	50.4	4.80	10.2	0.33
2-Butanone	Microspheres	64.1	4.01	9.4	0.38
THF	Microspheres	72.6	2.81	9.9	0.46
Ethyl acetate	Microspheres	82.3	1.30	9.1	0.43
Ethyl caprylate	Microspheres	94.7	1.01	7.3	
Ethyl propionate	Microspheres	85.2	0.98	8.4	0.56[c]
Benzene	Gel			9.2	0.87
Ethanol	Gel			12.8	1.08
1,4-Dioxane	Gel			10.1	1.08[c]
Acetic anhydride[d]	Gel			10.3	0.78[c]

a Concentration of 2EGDM was 5 vol %. (4 kGy h^{-1} and 4 h)
b Solubility parameter ($cal^{-1/2} cm^{-3/2}$)
c 30 °C
d Irradiation time were 2h.

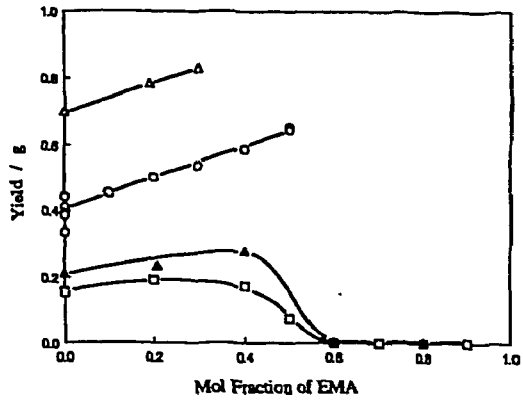


Figure 4 Effect of EMA on the yield of 2EGDM based copolymer microspheres. Each feed solution contains (□) 5 vol %, (▲) 7 vol %, (○) 10 vol %, and (△) 15 vol % 2EGDM.

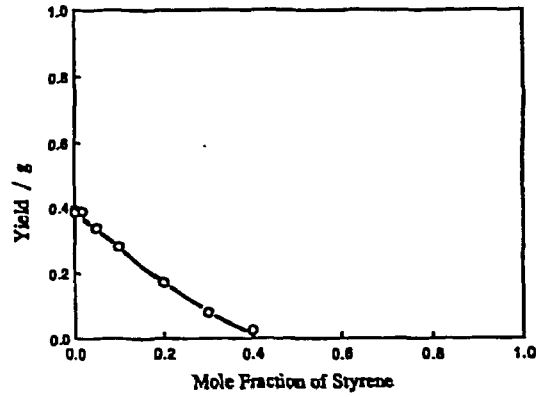


Figure 5 Effect of styrene on the weight yield of copolymer microspheres. Feed solution contains 10 vol % 2EGDM.

The formation of the microspheres is also affected by the viscosities of the solvents. The microspheres are obtained in the solvents with relatively low viscosities. This is probably due to the large mobility of the monomer and oligomer molecules and the propagating radicals in the solvents. The size of the microspheres varies with the solvents. It seems that the size increases with decreasing viscosity.

Figure 4 shows the copolymerization effect of EMA on the formation of 2EGDM based microspheres, i.e., the relationship between monomer composition in the feed solution and the weight yield of the microspheres. The mole fraction was changed under keeping the 2EGDM concentration constant. Thus each feed solution in a series of runs contains the same concentration of 2EGDM monomer. (This is because the decrease of 2EGDM concentration also causes the decrease of the microsphere yield)

The yield curves show two different manners due to the concentration of 2EGDM monomer. The weight yield of microspheres increases with increasing mole fraction of EMA in the feed solution until 0.4 for the solutions containing the low concentrations of 2EGDM (5 and 7 vol %). The weight yield decreases rapidly when the mole fraction of EMA exceeds 0.4 and then no microspheres are obtained when the mole fraction exceeds 0.6. The formation of copolymer microspheres is not favorable for the solution containing low 2EGDM (5 and 7 vol %). On the other hand, instead of the decrease of the weight yield, the gelation occurred at the high mole fractions of EMA in the feed solution containing high concentration of 2EGDM (10 and 15 vol %). The yield of the microspheres increased simply with increasing amount of EMA. But the gelation occurred when the mole fraction of EMA exceeded 0.6 for the 10% 2EGDM solution and 0.4 for the 15 vol % 2EGDM solution. The allowed region for the mole fraction of the solutions containing 10 vol % 2EGDM monomer is wider than the solutions containing 15 vol % 2EGDM. Therefore the suitable basic concentartion of 2EGDM for copolymerization is considered to be arround 10 vol %.

In the case of copolymerization effect for 2EGDM and maleic anhydride, yield of microspheres was not affected by the addition of maleic anhydride. The yield of microspheres is

not zero even the mole fraction of maleic anhydride exceeds 0.5 in the case of both the solutions containing 5 and 10 vol % 2EGDM monomer. No gelation was observed in the whole range of mole fraction of maleic anhydride. These results were different from those for the other comonomers.

In the case of copolymerization with acrylamide, yield increases slightly with increasing mole fraction of acrylamide. The decrease of yield was not observed, but gelation was observed when the mole fraction of acrylamide exceeded about 0.5. The size of the microspheres decreases with increasing amount of acrylamide. The addition of acrylamide causes the reduction in size.

Figure 5 shows the effect of copolymerization with styrene on the formation of the 2EGDM based microspheres. The weight yield of microspheres decreases rapidly with increasing mole fraction of styrene in the feed solution. This rapid change was not observed for the other comonomers mentioned in this paper. The effect of the addition of styrene is different from that of the copolymerization with EMA as the standard case and styrene seems to disturb the polymerization.

The copolymerization of 2EGDM and styrene seems to be a poor combination from the productive point of view. However, it can be a possible procedure for the preparation of large size microspheres, because there remains unreacted monomers in solutions under the 2 h irradiations. The low yield can be supplemented by enlonging the irradiation time. The size of copolymer microspheres, obtained from the feed solution of 10 vol % 2EGDM containing 0.2 mole fraction of styrene by 4 h irradiation, is 2.6 μm and the weight yield is 60 %.

Conclusion

The combination of closs-linking monomer such as 2EGDM, good solvent and radiation-induced polymerization is effective to obtain monodisperse microsphere. Copolymer microspheres of 2EGDM with EMA, acrylamide, maleic anhydride and styrene are obtained successively. Although the ratio of comonomer to 2EGDM is limited, the copolymerization make it possible not only to give functional group onto the microspheres, but also to controll the size of the microspheres.

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(2) Y. Naka, et. al , *J. Polym. Sci., Part A, Polym. Chem.*, **29**, 1197-1202 (1991).
(3) Y. Naka and Y. Yamamoto, *J. Polym. Sci., Part A, Polym. Chem.*, **30**, 1287-98 (1992).
(4) Y. Naka and Y. Yamamoto, *J. Polym. Sci., Part A, Polym. Chem.*, **30**, 2149-58 (1992)
(5) Y. Naka, et.al., in preparation.