Studies on Monodisperse Microsphere Formation by Radiation-Induced Polymerization

(放射線重合による単分散ミクロスフェアの生成に関する研究)

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Contents

General Introduction

Preparation of polymer particles has been an important subject in polymer chemistry.[1,2] Dispersed polymer particles, so called "latex", have been used as row materials or intermediates of industrial products.[3] Polymer particles in the latex lose spherical shapes during the industrial processes. Recently, fine particles with spherical shape are getting new interests as functional materials used as being spherical. Then, the term "microsphere" is introduced into the field of polymer chemistry to be used.[4] Microsphere is the name for the spherical polymer particle with sizes of micrometer range. Applications of the microspheres have been expanding in many fields such as packing materials of liquid chromatography, spacers of liquid crystal display, laser elements, calibration standards, catalyst supports, and toners for dry copies.[4-7] Remarkable applications of the microspheres are in the biological and medical fields as immuno-assays, cell labeling, and drug carriers.[8-12] In order to be used as functional materials, particles have to satisfy many requirements on shape, size, size distribution, and surface and inner functions.

The preparation methods for polymer particles have been investigated for many years.[13-26] Emulsion- and dispersion-polymerizations are well-known as the methods for the preparation of polymer particles. Basically, in the case of emulsion polymerization, the monomers form liquid particles in water with a help of surfactants and then turn to polymer particles.[1] In the case of dispersion-polymerization, the monomers are dissolved in organic solvents, and the resulting

polymer are separated from the solvent phase to form the polymer phase with a help of stabilizers.[27] Although the added surfactant and stabilizer have an important role in the particle formation, they sometime remain as contaminants to be undesirable for the practical use. Many investigations have been employed to reduce or not to use the additives in these methods. Much efforts have been made on these methods to improve the productibility and the characteristics of the products.[28-30] A use of cross-linking agents as co-monomers has been developed as another way for the preparation of microspheres.[13]

A unique method has been reported which gives monodisperse microspheres by the radiation-induced polymerization.[31,32] Cross linking reagents are used as monomers in this method. This method is classified into the dispersion polymerization from the stand point of the use of organic solvents. It is characteristic of this method 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 other methods mentioned above, but the details of the formation mechanism have not yet been known.

The present thesis deals with the development of the monodisperse microspheres by the radiation-induced polymerization and the clarification of the formation mechanism. Attention is focused on the selection of monomers and solvents and effective conditions for the preparation of monodisperse microspheres such as concentration, temperature, irradiation time, dose, and so on., to reveal the formation mechanisum. This thesis consists of the following five chapters.

In chapter 1, the mechanism of the monodisperse microspheres is described. The generation of the nuclei and the change in the number of the microspheres during the polymerization are investigated. The nuclei of the microspheres are produced in the early stage of the polymerization, and inhibit the formation of

additional nuclei during their propagation. The monodisperse microspheres are produced with the help of strong permeability of γ rays.

In chapter 2, the solvent effects on the microsphere preparation are described. The affinity between monomer and solvent and the forms of the monomer molecules in the solutions are the important factors for the microsphere formation.

In chapter 3, the growth mechanism of microspheres is described. The number of the microspheres during the polymerization is strongly affected by the monomer concentration. Two polymerization processes contributing to the microsphere formation are introduced on the basis of a consideration of the numbers of the microspheres. A mechanism including a cross linking reaction as an important process is proposed.

In chapter 4, the preparation of the copolymer microspheres is described. Copolymerization is expected to control the properties of the microspheres. Ethyl methacrylate, maleic anhydride, styrene and acrylamide are used as comonomers. The mechanism for the copolymerization giving microspheres is also discussed.

In chapter 5, the preparation of nonspherical polymer particles is described. Ultrasonic vibration is applied during the radiation-induced polymerization to affect the growth of the microspheres. Dependence of the shape of the particles on the conditions applying the ultrasonic vibration is discussed.

Chapter 1

Preparation of Monodisperse Poly(diethylene glycol dimethacrylate) Microspheres

1.1 Introduction

Much attention has been paid to the preparation of monodisperse microspheres.[13-26] Barrett has reported that a rapid nucleation in the early stage of polymerization is desired for the formation of monodisperse microspheres.[27] Thus, seed polymerization is used for the preparation of the monodisperse microspheres, where core particles are prepared in the first step and the microsphere grows without new nucleation in the second step.[31] Radiation-induced polymerization of diethylene glycol dimethacrylate has been reported to give monodisperse microspheres in a single step.[31,32] Inspite of the easiness as a preparation method, nothing is clear on the microsphere formation. The characteristics of the preparation of poly(diethylene glycol dimethacrylate) microspheres by the radiation-induced polymerization and the mechanism of the monodisperse microspheres are described in this chapter.

1.2 Experimental

Materials. Ethylene glycol dimethacrylate (1EGDM), diethylene glycol dimethacrylate (2EGDM), triethylene glycol dimethacrylate (3EGDM), tetraethylene glycol dimethacrylate (4EGDM) and 2-ethyl-2-(hydroxymethyl)-1,3-propanediol trimethacrylate (TMPT, trimethylolpropane trimethacrylate) ,

CH_3 CH_3

$H_2C=C$ $C=CH_2$

$O=C-O-(CH_2CH_2-O)_n-C=O$
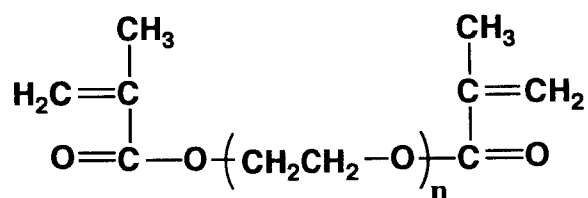
n = 1 : Ethylene glycol dimethacrylate   (1EGDM)

n = 2 : Diethylene glycol dimethacrylate   (2EGDM)

n = 3 : Triethylene glycol dimethacrylate   (3EGDM)

n = 4 : Tetraethylene glycol dimethacrylate   (4EGDM)

$H_2C=CH$ $HC=CH_2$

$O=C-\underset{H}{N}-CH_2-\underset{H}{N}-C=O$

N,N'- Methylenebisacrylamide

$H_2C=C-CH_3$

$O=C$

     CH_3 O CH_3

$H_2C=C$ CH_2 $C=CH_2$

$O=C-O-CH_2CCH_2-O-C=O$

CH_2CH_3
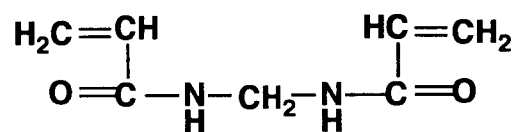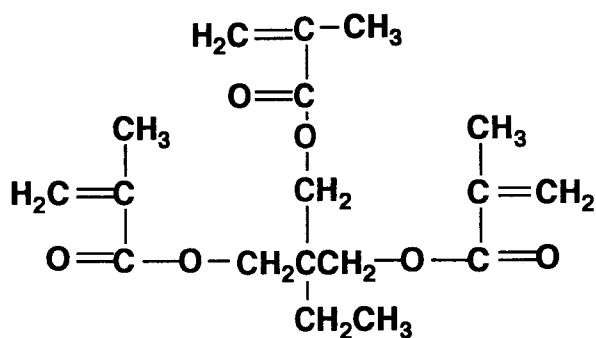
2-Ethyl-2-(hydroxymethyl)-1,3-propanediol trimethacrylate

Trimethylolpropane trimethacrylate (TMPT)

Figure 1.1. Structure of monomers.

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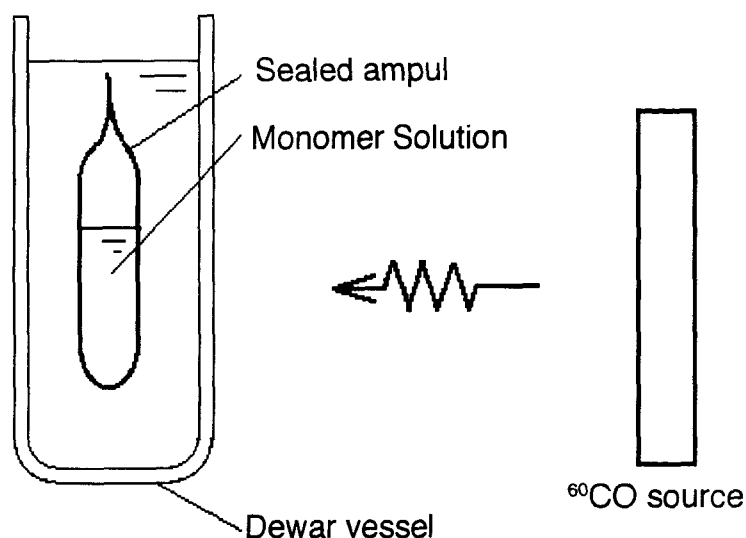
Figure 1.2.   Radiation -induced polymerization by the ^{60}Co source.

supplied from Shin Nakamura Kagaku, were purified by passing through active alumina. The structures of the monomers are shown in Fig. 1-1. *N,N'*-methylenebisacrylamide and organic solvents, purchased from Wako Pure Chemical, were used without further purification otherwise noted.

Polymerization. Screening tests were curried out with 2 cm^3 of 5 vol % solutions deoxygenated by nitrogen bubbling. The samples were irradiated with ^{60}Co γ rays at room temperature without stirring (ca. 25 °C). The total dose was around 2 kGy.

N,N'-methylenebisacrylamide (20 mg) dissolved in THF (2 cm^3) were degassed by nitrogen bubbling. The sample was irradiated with ^{60}Co γ rays at room temperature without stirring. The dose rate was 4 kGy h^{-1} and the irradiation time was 15 min . The particles were washed with THF, and then dried under vacuum.

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

were degassed 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 as shown in Fig. 1-2. The dose rate was 4 kG h^{-1}. 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.

Measurements. The microspheres were photographed by using a scanning electron micrograph (SEM) (JELO, JST-300) and transmitting electron micrograph (TEM) (Hitachi, 600). The sizes of the microspheres were measured from the SEM photographs by a degitizer (NEC MG-10) connected to a personal computer (NEC 9801-RA). The diameters were calculated from three points on the outer circles of the microspheres.

1.3　Results and Discussion

1.3.1　Screening Tests of 2EGDM Type Monomers

The radiation-induced polymerization of 2EGDM monomer gives microspheres from various solvents. Since closs linking is considered to be important for the microsphere formation of 2EGDM, the other 2EGDM type bi- and tri-functional methacrylates were exmanined. The results of the screening tests for the combination of various monomers and solvents are presented in Table 1.1. A tpical SEM photograph of poly-2EGDM microspheres is shown in Fig. 1.3. The irradiation resulted in the formation of particles, aggregated particles, gel, and soluble polymer depending on the conditions. The monomers except for 2EGDM did not give fine particles. The polymer obtained from 3EGDM seemed not to be fine particles but somewhat aggregated particles. The difference among 1EGDM, 2EGDM, 3EGDM, and 4EGDM is the number of ethylene oxide units (-C_2H_4O-)

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Table 1.1.   Screening Test for the Combinations of Monomers and Solvents.[a]

Solvents	Monomers				
	1EGDM	2EGDM	3EGDM	4EGDM	TMPT
Methanol	Gel	Gel	Gel	Gel	Gel
Ethanol	Gel	Gel	Gel	Gel	Gel
Propanol	Gel	Gel	Gel	Gel	Gel
2-Propanol	Gel	Gel	Gel	Gel	Gel
tert -Butyl alcohol	Gel	Particles	Gel	Agg.	Gel
Benzene	Liq.	Liq.+Gel	Liq.+Gel	Liq.	Liq.
Toluene	Liq.	Liq.	Liq.+Gel	Liq.+Gel	Liq.
Hexane	Gel	Gel	Gel	Gel	Gel
Methyl formate	Gel	Particles	Liq.	Liq.	Gel
Methyl acetate	Gel	Particles	Agg.	Liq.	Gel
Ethyl actate	Gel	Particles	Agg.	Agg.	Gel
Propyl actate	Gel	Particles	Agg.	Agg.	Gel
Methyl propionate	Gel	Particles	Agg.	Liq.	Gel
Methyl butylate	Gel	Particles	Agg.	Agg.	Gel
Methyl succinate	Gel	Particles	Liq.	Liq.	Gel
Ethyl succinate	Gel	Particles	Liq.	Liq.	Gel
Methyl malonate	Gel	Liq.	Liq.	Liq.	Gel
Ethyl malonate	Gel	Liq.	Liq.	Liq.	Gel

[a]   Monomer concentration was 5 vol%. Solutions were deoxygenated by nitrogen bubbling. Total dose was 2 kGy. : Liq. and Agg. mean the soluble polymer and aggregated particles, respectively.
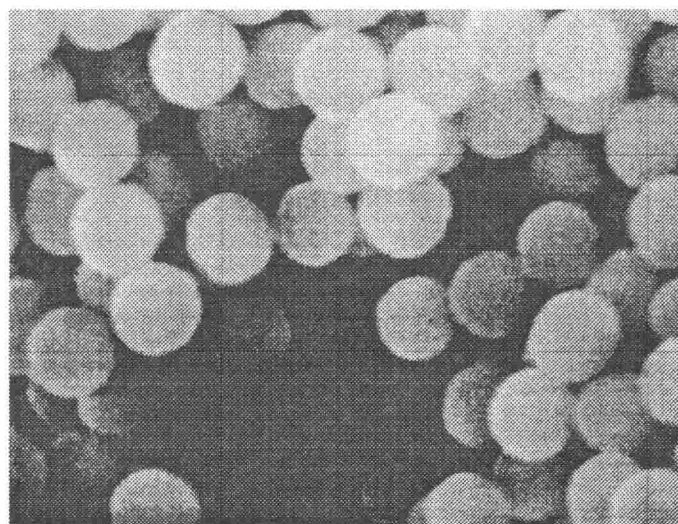
Figure 1.3. Typical SEM photograph of poly-2EGDM microspheres. 10 vol % of 2G with ethyl acetate, 4 kGy h^{-1}.
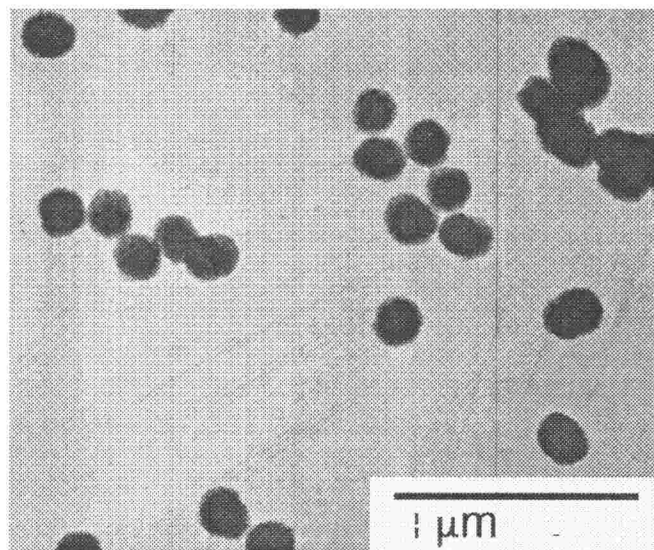
Figure 1.4. TEM photograph of poly (*N,N* -methylenebisacrylamide) fine particles.

between two methacrylate groups. This result suggests that the distance or the three dimensional position of two vinyl groups in the solutions is an important factor.

Esters gave good results, but alcohols and hydrocarbons gave poor results in general. These suggest that the good solvents are suitable for the microsphere preparation, since 2EGDM monomer is also a kind of esters.

1.3.2　Poly (*N,N'*–Methylenebisacrylamide) Fine Particles

The cross-linking reaction seems to cause the formation of the microspheres. Therefore, it is expected that the monomers having two vinyl groups give microspheres in suitable solvent. As described above, 2EGDM type monomers (1EGDM, 3EGDM, and so on) did not give good result except 2EGDM. In order to confirm that 2EGDM is the special monomer to give microspheres, divinyl benzene is commonly used as clossl-inking reagent for the polymerization. Samples of *p*-divinyl benzene in benzene, toluene and ethyl acetate solutions are irradiated, but they did not give particles.

N,N'- methylenebisacrylamide is also commonly used as closs-linking reagent. The solubility of *N,N'*- methylenebisacrylamide in various solvents is tested, since good solvent is suitable for the preparation of microspheres. The solvents are acetonitrile, ethyl acetate, methanol, *n*-propylamine, pyridine, THF, triethylamine, and water. *N,N'*-methylenebisacrylamide is dissolved in methanol and *n*-propylamine, but the irradiation of the solutions resulted in gel formation. Fine particles were obtained only from the THF solution.

Figure 1.4 is the TEM photograph of the poly (*N,N'*-methylenebisacrylamide) particles obtained from THF solution. The shape of particles is almost sphere but the surface is rather rough compared with the 2EGDM microspheres. The narrow size distribution suggests that the mechanism

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is the same as the 2EGDM microsphere case. The measured size is 0.22 μm. The size of the particles is smaller than that of the 2EGDM microspheres. More suitable solvent must be found for the effective preparation of poly (*N,N'*-methylenebisacrylamide) fine particle. The formation of poly (*N,N'*-methylenebisacrylamide) fine particles is another example for the preparation of particle from cross-linking monomers.

1.3.3 Irradiation Time Dependence

Figures 1.5(a) and 1.5(b) show the SEM photographs of the microspheres prepared in ethyl acetate. The microspheres both obtained at 15 min as Fig. 1.5(a) and 2 h as Fig. 1.5(b) have a complete spherical shape. The diameter increases with irradiation time. This means that the microspheres grow independently during the polymerization.

Figure 1.6 shows the time-conversion curve for the microspheres. Figure 1.7 shows the irradiation time dependence of the size of the microspheres. The monodisperse microspheres are obtained with the yields more than 80 %. The size of the microspheres can be controlled by irradiation time as well as by selecting solvents. 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 1.8 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 becomes constant at the conversion below 10 % within the
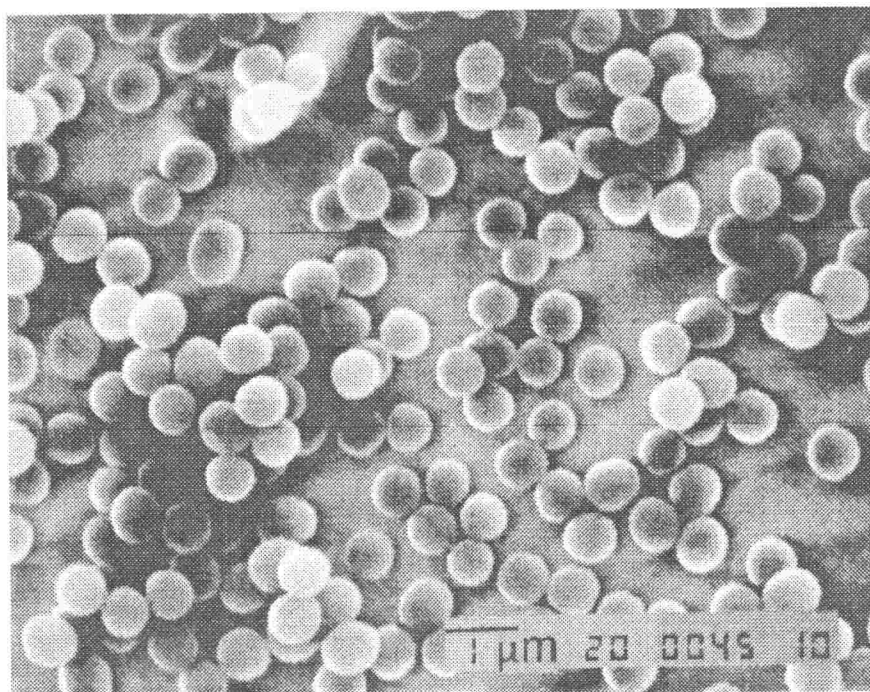
(a)
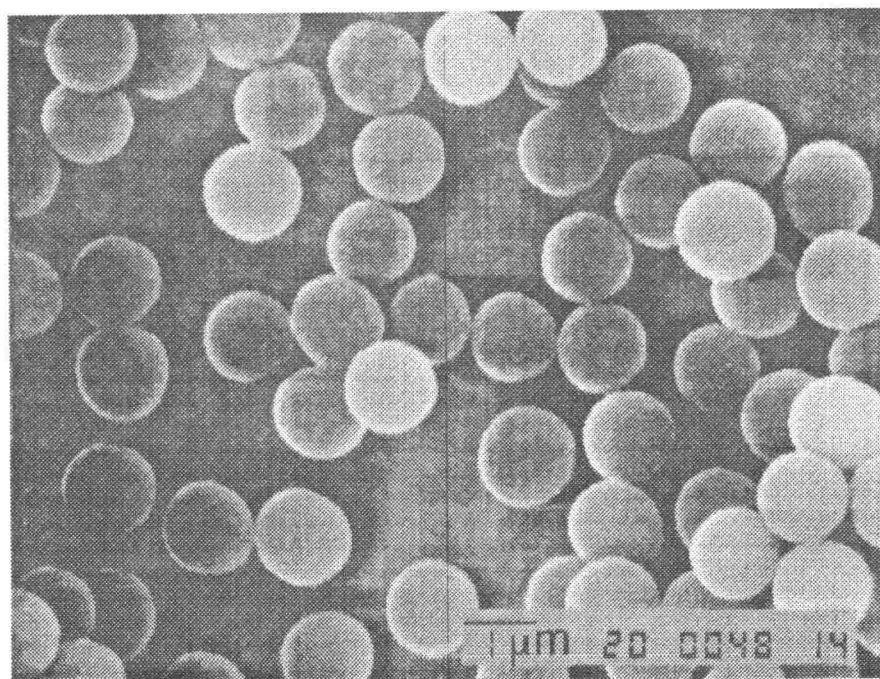
(b)

Figure 1.5. SEM photographs of poly-2EGDM microspheres.
(a) 15 min, (b) 120 min. 4 kGy h^{-1}. 10 vol % of 2EGDM
monomer in ethyl acetate.
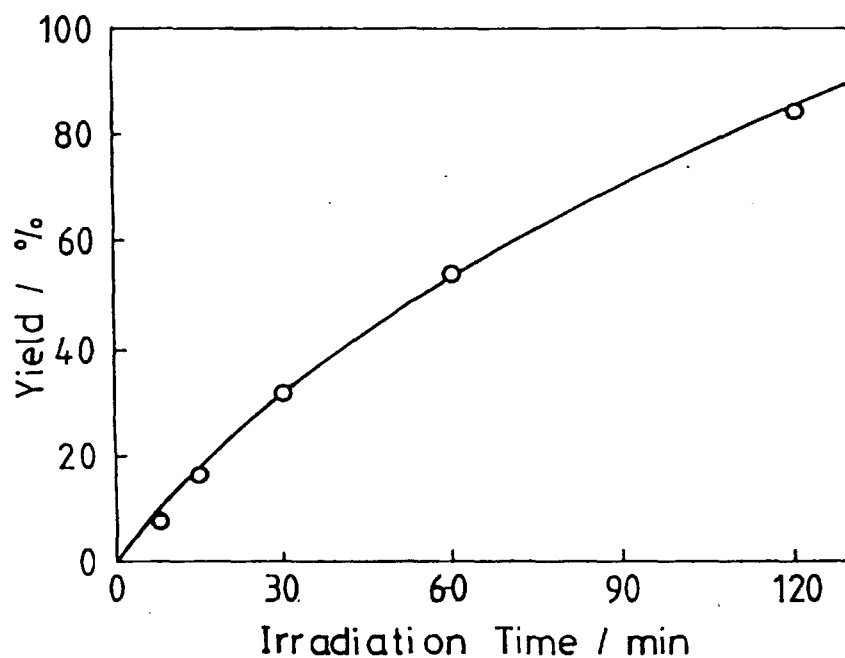
Figure 1.6. Irradiation time dependence of microsphere yield. 10 vol % of 2EGDM monomer with ethyl acetate, 4 kGy h⁻¹.
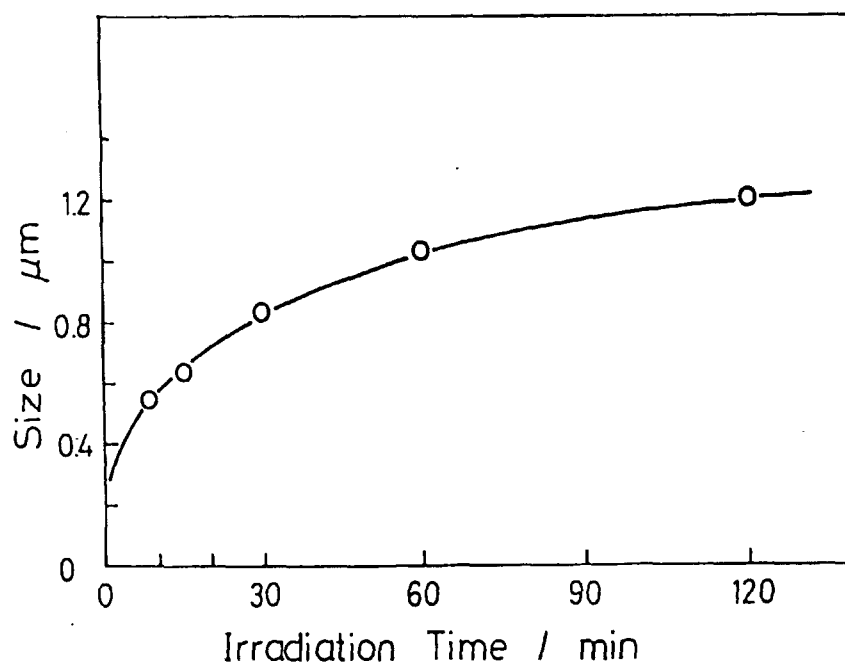
Figure 1.7. Irradiation time dependence of microsphere size. 10 vol % of 2EGDM with ethyl acetate, 4 kGy h⁻¹.
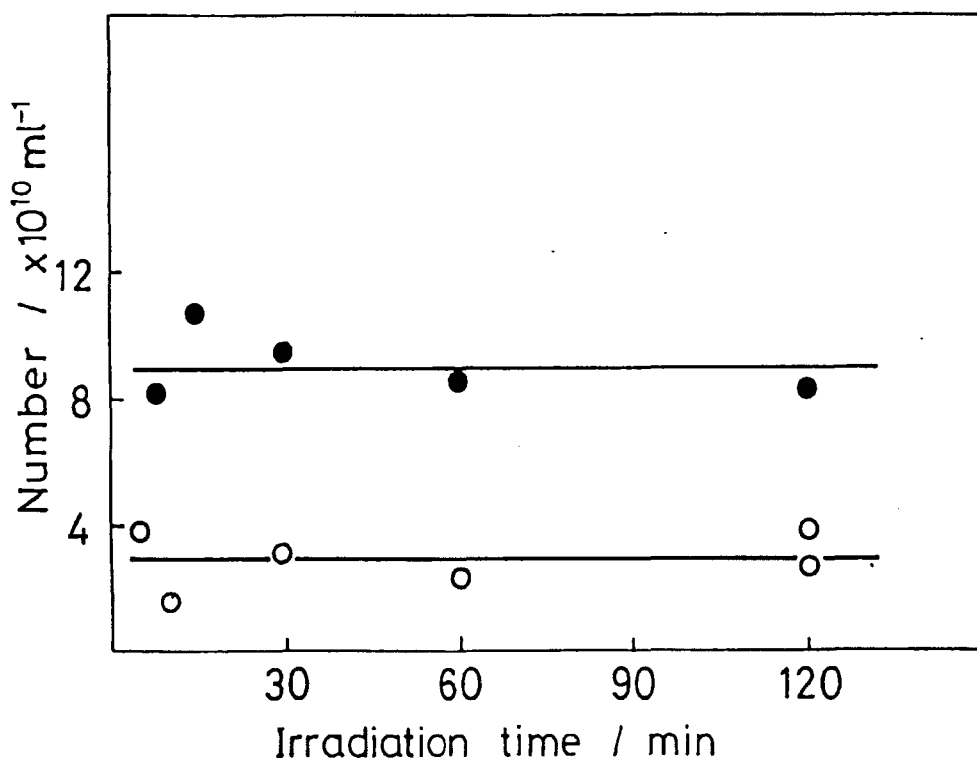
Figure 1.8. Relationship between irradiation time and number of microspheres. The number didn't change during the polymerization. (●) 10 vol %, at room temperature, (○) 5 vol % at 40 °C, with ethyl acetate. 4 kGy h^{-1}.

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 number of the monomer units contained in a single polymer particle was also calculated from the specific gravity and the size of the microspheres. Figure 1.9 shows the irradiation time dependence of the number of the monomer units in a polymer particle. It gives a straight line of which slope is unity. The number of monomer for the initial nuclei is estimated as 10^4 to 10^6 based on the distance of carbon to carbon bond length and the space for the one microsphere. The polymerization time for this number of monomer is 10^{-2} to 1s from Fig. 1.9. The formation of the nuclei is completed in a very short period compared to the whole

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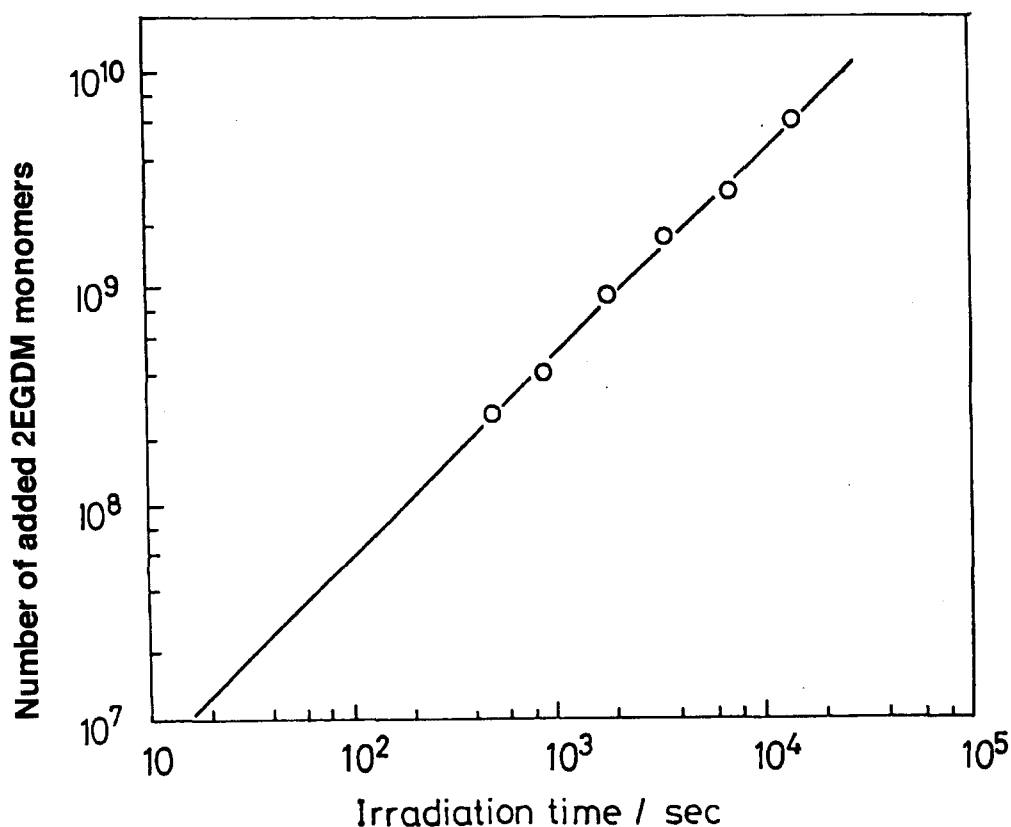
Figure 1.9.   Relationship between irradiation time and number of
2EGDM segment in a microsphere. 10 vol % of 2EGDM, at room
temperature, 4 kGy h⁻¹.

irradiation time.

The volume of the solution per polymer particle is 2.2 μm^3 for the
polymerization in ethyl acetate. The rate of the formation of radicals for the
volume is 3×10^5 s⁻¹ at the dose rate of 4 kGy h⁻¹ taking 11 as the G value of the
formation of radicals for ethyl acetate.[34] The rate of the radical formation is large
enough for each microsphere to grow under the same conditions. The average
time when the first radical appeared in the space for one microsphere is calculated
to be 3×10^{-6} s. This value has the same order as the value obtained from the
intercept of Fig. 1.9. Therefore, it is considered that the number of radicals which
contribute to the formation of a nucleus is very small, and that the formation of the
nuclei is finished within a very short period.
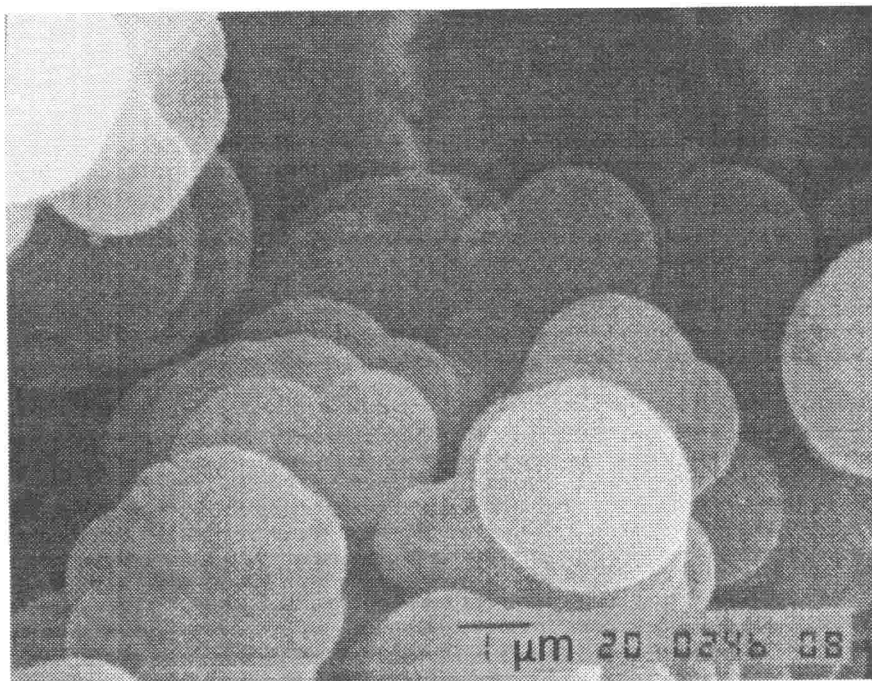
Figure 1.10. SEM photograph of poly-2EGDM microspheres, prepared with stirring. Dose was 8 kGy, 10 vol % of 2EGDM monomer in ethyl acetate.
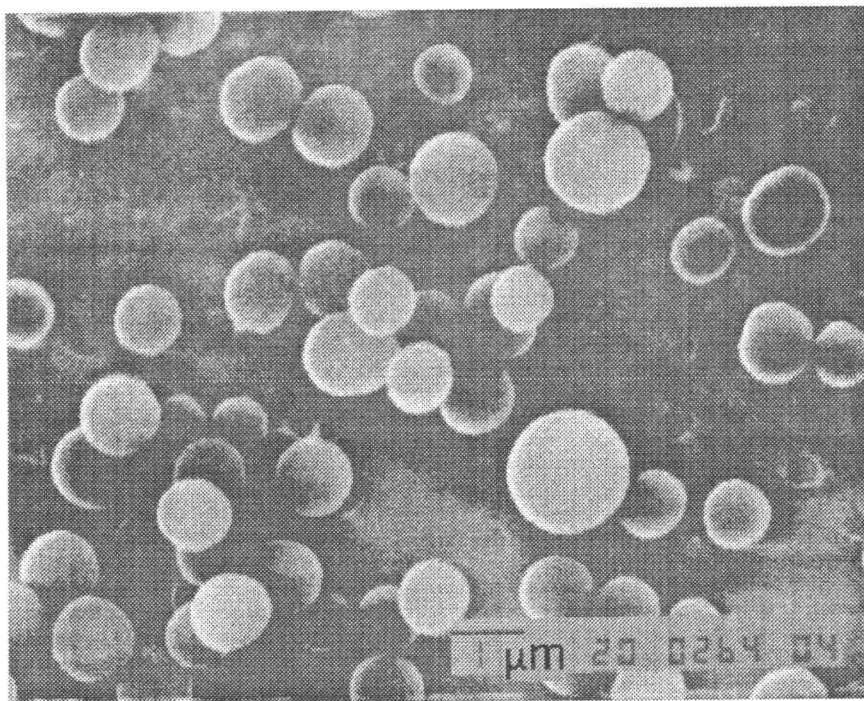
Figure 1.11. SEM photograph of microspheres prepared by photo initiated reaction instead of γ rays. 10 vol % of 2EGDM, at room temperature.

1.3.4   Stirring and Photo-Initiation

Figure 1.10 shows the SEM photograph of the 2EGDM polymer particles prepared with stirring during the irradiation. Aggregated particles were observed in the products. It is considered that a contact of two microspheres was caused by stirring, and that the propagating radicals on the surface of the microsphere joined these aggregated microspheres. Therefore, it is essential to keep the solutions stationary during the irradiation to avoid the contact of the propagating microspheres in the radiation-induced polymerization. The homogeneous initiation of the polymerization without stirring is one of the characteristics of the radiation- induced polymerization, and this is a difference from the other methods such as dispersion polymerization.

Figure 1.11 shows the SEM photograph of the microspheres obtained by the irradiation with UV light. There are different sizes of microspheres in the SEM photograph. The size distribution is not monodisperse. This can be attributed to the light absorption and scattering caused by the polymer particles. The monodispersion of the product is attained by the irradiation with γ rays with a high permeability capable of homogeneous initiation of the polymerization even in the presence of the opaque polymer particles.

1.4 Conclusion

The combination of closs-linking monomer such as 2EGDM, good solvent and radiation-induced polymerization is effective to obtain monodisperse microsphere. The formation of nuclei of the microspheres is completed within a very short period. Each microsphere grows independently. The number of microspheres are constant during the polymerization after the nuclei formation step. These are the reasons for giving monodisperse microspheres by this method.

Chapter 2

Solvent Effects

2.1 Introduction

The γ rays enable the homogeneous initiation of polymerization because of their strong transmission ability. The photo-initiation also gives microspheres, but the size distribution is wide because of the heterogeneous initiation in the course of the polymerization. Heating of the solutions gives homogeneous initiation, when the solutions are stirred. The stirring causes the contacts between growing particles and gives aggregated particles.

It is a characteristics of the present method that the simple mixtures consisting of only monomer and solvents give monodisperse microspheres. Since the polymerization is carried out in organic solvent, the method may be regarded as a kind of the dispersion polymerization. But the mechanism is considered to be completely different from the conventional dispersion polymerization, [27] because the preparation of the microspheres can be carried out in the absence of stabilizers and the polymer microspheres are obtained in good solvents. Many kinds of solvents can be used for the preparation of microspheres. The good solvents seem to make growing microspheres stable in the solution and to avoid the aggregation of the microspheres. The poor solvents seem to help the phase separation, but the low affinity of the surface of particles to the solvents causes the aggregation of the particles. The details of the solvent effects on the formation of the microspheres are described in this chapter.

2.2 Experimental

Hydroxy ethyl methacrylate (HEMA), purchased from Wako Pure Chemicals, was used after distillation. Reagent grade solvents and carbon tetrabromide, purchased from Wako Pure Chemicals, were used without further purification. All other reagents used in this chapter are the same as those described in chapter 1.

2.3 Results and Discussion

2.3.1   Microspheres Obtained in Various Solvents

The results of the radiation-induced polymerization of 2EGDM monomer in various solvents are presented in Table 2.1 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.[35] The solubility parameter of the 2EGDM monomer was calculated to be 8.9 according to the literature.[34,36] The solvent of which solubility parameter is close to 8.9 is considered to be a good solvent for 2EGDM monomer.

Monodisperse microspheres, polymeric gel, and soluble polymer 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 2.2. Solvent Effect on the Formation of the Microspheres[a]

Run Number	Solvents	Result	Yield %	Size μm	Distribution[b] %	δ[c]	Viscosity[d] cp (25°C)
7	Methyl formate	Microspheres	50.4	4.80	2.9	10.2	0.33
4	2-Butanone	Microspheres[i]	64.1	4.01	0.7	9.4	0.38
10	THF	Microspheres	72.6	2.81	11.0	9.9	0.46
17	DEGDME[e]	Microspheres	85.9	1.60	33.1	8.7[f]	0.98
5	Ethyl acetate	Microspheres	82.3	1.30	4.6	9.1	0.43
14	DMP[g]	Microspheres	72.8	1.18	20.3	8.0	0.56[h]
15	Methyl orthoformate	Microspheres	88.6	1.16	6.8	8.3[f]	
11	Ethyl caprylate	Microspheres	94.7	1.01	5.9	7.3	
12	Ethyl propionate	Microspheres	85.2	0.98	10.2	8.4	0.56[h]
69	Diethyl succinate[i]	Microspheres		0.41	7.3	9.1[f]	
67	Diethyl phthalate	Gel				10.0	
8	Benzene	Gel				9.2	0.87
9	Ethanol	Gel				12.8	1.08
18	1,4-Dioxane	Gel				10.1	1.08[h]
70	Acetic anhydride[j]	Gel				10.3	0.78[h]

a Concentration of 2EGDM was 5 vol %. Dose rate and irradiation time were 4 kGy h⁻¹ and 4 h, respectively.
b Coefficient of size variation. Standard deviation divided by the size.
c Solubility parameter (cal⁻¹/² cm⁻³/²) from the reference 34,35,36
d Viscosity from the reference
f Calculated value
e Diethylene glycol dimethyl ether
g 2,4-Dimethyl-3-pentanone
h 30 °C
i Irradiation time was 2h.
j 4-Hydroxy-4-methyl-2-pentanone

Table 2.2. Solvent Effect on the Formation of the Microspheres II [a]

Run Number	Solvents	Result	Yield %	Lost %	Size μm	Distribution %	δ[c]
273	Methyl formate	Ms + Agg[d]	68.3	14.9	4.59	9.6	10.2
284	Ethyl formate	Microspheres	77.3	6.8	1.98	10.3	9.4
285	Propyl formate	Aggregated particles	84.9	6.7	2.89		9.2
286	Methyl acetate	Microspheres	75.8	4.1	1.85	4.1	9.6
297	Ethyl acetete	Microspheres	84.9	2.0	1.28	4.0	9.1
289	Propyl acetete	Microspheres	90.7	0.8	1.11	5.3	8.8
288	Butyl acetete	Microspheres	90.1	1.0	0.76	6.2	8.5
291	Metyl propionate	Microspheres	86.1	2.4	1.48	2.9	8.9
290	Ethyl propionate	Microspheres	88.2	0.2	1.11	3.8	8.4
292	Methyl butylate	Gel					8.9
293	Ethyl caprylate	Gel					7.3
296	Dimethyl malonate	Gel					11.0
68	Diethyl malonate	Gel					9.9
295	Diethyl succinate	Ms + Agg[d]	92.6	6.5	0.48	10.2	9.5[e]
67	Diethyl phthalate	Gel					10.0
280	Acetone	Microspheres	73.3	10.8	2.38	30.6	10.0
294	Methyl ethyl ketone	Microspheres	75.0	12.5	2.49	6.8	9.3
283	Diethyl ketone	Microspheres	66.4	8.1	1.95	27.0	8.8
330	DMSO	Gel					12.0
329	Acetonitrile	Microspheres	81.8	N.D.[f]	1.96	5.6	12.1
246	Propanol	Gel					11.9
357	tert -Butyl alcohol	Particles	92.3	2.3	0.51	12.0	10.6

a Concentration of 2EGDM was 10 vol%. Dose rate and irradiation time were 4kGyh[-1] and 2h, respectively.
b Coefficient of size variation. Standard deviation divid by the size.
c Solubility parameter (cal$^{-1/2}$cm$^{-3/2}$) from the reference 34, 35, and 36.
d Microspheres with aggregated particles
e Calculated value
f The soluble polymer was observed, but could not be recovered.

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.

2.3.2 Microspheres Obtained in Ester Solvents

Esters seem to be suitable solvents among the good solvents (Table 2.1). The results of the microsphere formation in various esters are shown in Table 2.2. The microspheres are obtained from esters listed above ethyl propionate. The esters in the Table 2.2 can be classified into three groups according to their sizes, i.e., the small, middle and large size esters.

The small esters, such as formates, are good to give the large microspheres, but some aggregated particles are observed in the SEM photograph (Fig. 2.1). There are some basins suggesting a contact with another particle. The soluble polymer is a by-product of polymerization as described in chapter 3. The percentage of the soluble polymer in the total recoverd polymer are higher for the small esters than for the other esters. The small esters also give wide distribution in size of microspheres (standard deviation divided by the average size). The conditions for the high yields of the soluble polymer give also poor result in shape and monodispersity.

The middle size esters, such as acetates and propionates gave the best results among the esters. The size of the microspheres varies with the size of the solvent molecules. The shape of the microspheres is a complete sphere as shown in Fig. 2.2. The losts in the microsphere formation due to the soluble polymer formation are low and the size distributions are narrow. Especially, propyl acetate, butyl
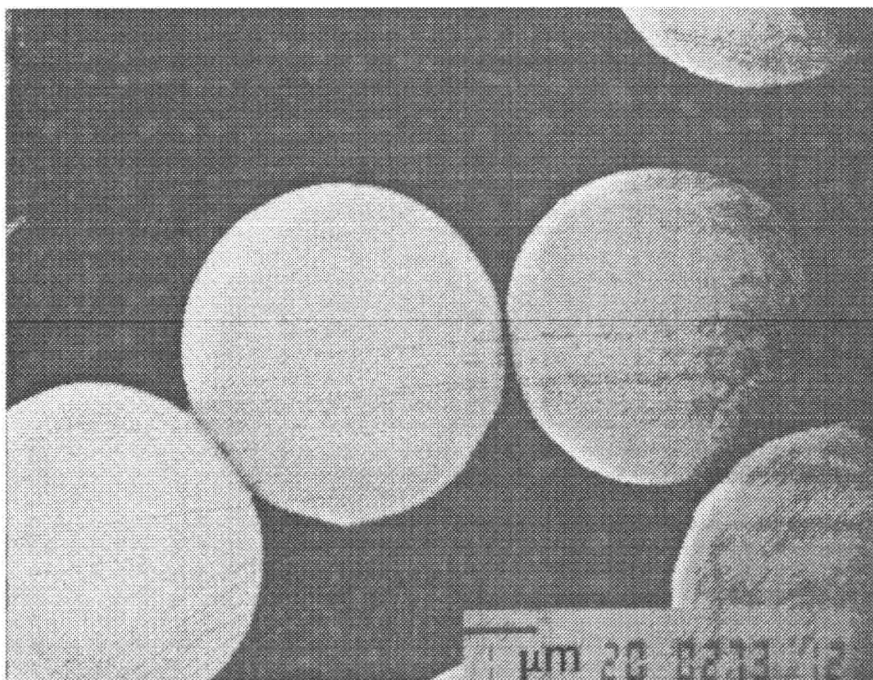
Figure 2.1. SEM photograph of particles obtained in methyl formate. Dose rate and irradiation time was 4 kGy h^{-1} and 2h, respectively.
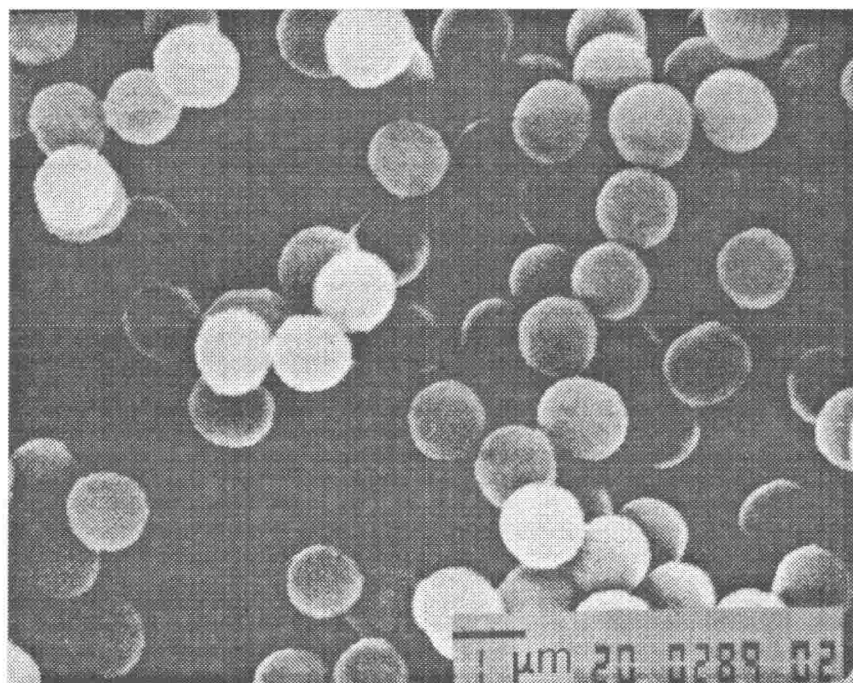

Figure 2.2. SEM photograph of microspheres obtained in propyl acetate. Dose rate and irradiation time was 4 kGy h^{-1} and 2h, respectively.

acetate and ethyl propionate gave good results, i.e., high yield and low lost. The size of propyl acetate, butyl acetate and ethyl propionate are almost similar to the half of 2EGDM. The form of the monomer molecules in the solvents seems to be an important factor.

The large size esters tend to result in gelation. Methyl butylate and ethyl caprylate gave microspheres for 5 vol % solution (Table 2.1), but not for 10 vol% solution (Table 2.2). Although ethyl acetate gives microspheres for wide range of 2EGDM concentration (2-24 vol %) as described in Chapter 3, the large esters are not favorable for the preparation of microspheres. The characteristics of the large size esters become close to that of hydrocarbons with an increase in their size.

The good solvents for 2EGDM monomer are favorable to prepare microspheres. Esters and ketones seem to satisfy this requirement. Since the monomer, 2EGDM, is an ester, esters are good solvents for 2EGDM and give good results for the microsphere preparation. It is no doubt that good solvents are essential for preparing microspheres by this method.

2.3.3   Form of 2EGDM Monomer in Solvets.

The solubility parameter is one of the indicators to know the solubility of the solute in the solvent. The problem of the solubility parameter is that it is an average of a whole molecule, but it does not express any local affinity of monomer molecules to solvent. Thus, it is not appropriate to apply it to other types of solvents. In spite of the solubility parameter, not close to 8.9, acetonitril (d = 11.9) gave microspheres (Fig. 2.3). Benzene, toluene and hexane (d = 0.91, 8.9, and 7.3, respectively) did not give particles. The solubility parameter is not an absolute factor. The difference in effect on the microsphere preparation between the hydrocabons and the esters may be attributed to the polarity of the solvents. Both the hydrocarbons and the esters are good solvents for 2EGDM, but the forms of
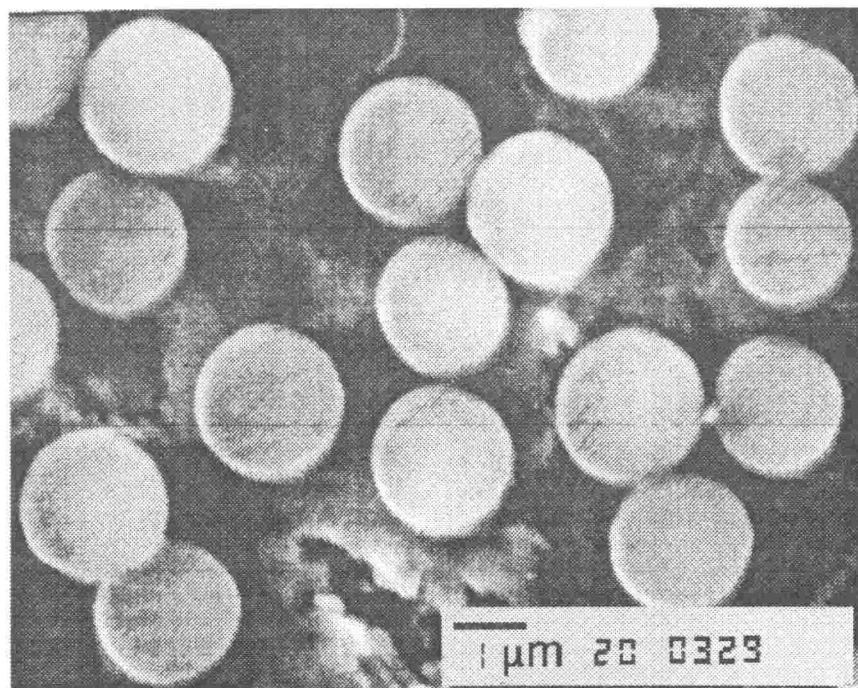
Figure 2.3.   SEM photograph of microspheres obtained in acetonitrile. Dose rate and irradiation time was 4 kGy h^{-1} and 2h, respectively.

2EGDM molecules in the solvents may be different. The structure of 2EGDM can be divided into two parts, i.e., methacrylate and ethyleneoxide moieties. The two methacrylate groups of the 2EGDM molecule may be solvated independently and separated from each other in the ester solvents. So the 2EGDM monomer takes a stretched form in the esters as shown in Fig 2.4(a). On the other hand, the two methacrylate groups of the 2EGDM molecule may be close each other in nonpolar hydrocarbon solvents. The 2EGDM monomer is considered to take a bended form in hydrocarbons as shown in Fig 2.4(b). In this form, the distance between two vinyl groups of the same molecule is short. The approaching two vinyl groups of the same 2EGDM molecule become contained in the same propagation chain. Consequently, this causes the reduction in the cross-liking probability of 2EGDM and no cross-linking microspheres were obtained in benzene.

Even if the solubility of 2EGDM is the same in esters and hydrocarbons, the forms of the monomer molecules in the solvents may be different. The solvent
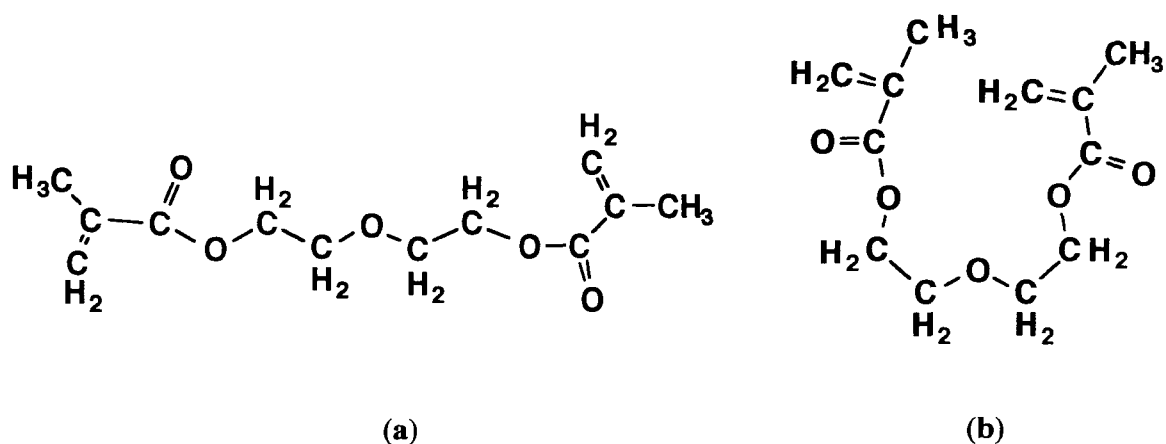
25

Figure 2.4.   Form of 2EGDM monomer; (a) stretched form, (b) bended form.

properties appropriate for the microsphere preparation are not only the good solubility for 2EGDM but also making the 2EGDM molecule expanded in the solution to take the stretched form. Propyl acetate, butyl acetate and ethyl propionate gave good results. This is probably related to the spread of 2EGDM monomer in the solvents. In order to obtain the microspheres, the solvent must keep the two vinyl groups of the 2EGDM molecule separated.

2.3.4   Solvent Effect of Diethyl Succinate and Diethyl Malonate

In spite of the resembling structures, ethyl succinate and ethyl malonate gave different results as shown in Tables 2.1 and 2.2. Diethyl succinate gave microspheres but diethyl malonate did not . Both diethyl succinate and diethyl malonate have two ester groups and the solubilities of 2EGDM in these solvents are almost the same (ethyl succinate d = 9.1; ethyl malonate d = 9.0). The difference in the structure between these two solvents is in the length of the hydrocarbon chain between the ester groups. Since the size of diethyl malonate is

smaller than that of diethyl succinate, the former was expected to give microspheres. An occurrence of the hydrogen abstraction from the solvent may inhibit the formation of microspheres

The hydrogens of the methylene (-CH$_2$-) of diethyl malonate are easily abstracted compared with those of diethyl succinate. The active hydrogens of the methylene interposed by the two ester moieties of diethyl malonate cause the termination of the propagation of the polymer chain and interferes the formation of microspheres.

$$
-CH_2-\underset{\underset{\displaystyle CO}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}\cdot \;+\; \underset{\underset{\underset{\displaystyle OC_2H_5}{|}}{\overset{\displaystyle CO}{|}}}{H}\overset{\overset{\overset{\displaystyle OC_2H_5}{|}}{CO}}{C}H \longrightarrow -CH_2-\underset{\underset{\displaystyle CO}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{CH}} \;+\; \cdot \underset{\underset{\underset{\displaystyle OC_2H_5}{|}}{\overset{\displaystyle CO}{|}}}{\overset{\overset{\overset{\displaystyle OC_2H_5}{|}}{CO}}{C}}H
$$
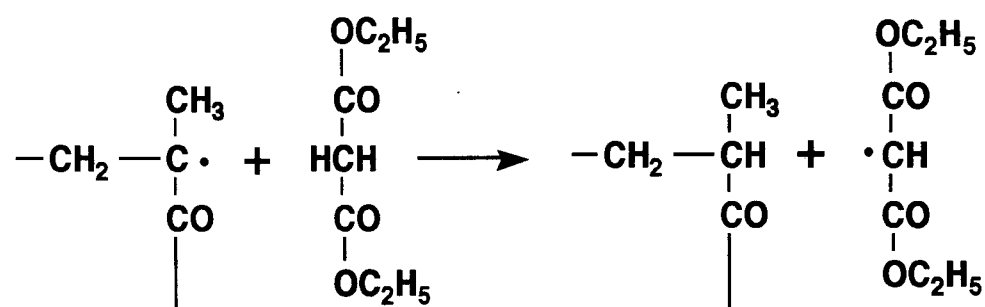
On the other hand, the effect of ester moieties on the hydrogens of the methylene chain of diethyl succinate is considered to be smaller than that of diethyl malonate. Thus the hydrogen abstraction is less probable in diethyl succinate.

$$
-CH_2-\underset{\underset{\displaystyle CO}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}\cdot \;+\; \underset{\underset{\underset{\underset{\displaystyle OC_2H_5}{|}}{\overset{\displaystyle CO}{|}}}{\overset{\displaystyle HCH}{|}}}{H}\overset{\overset{\overset{\displaystyle OC_2H_5}{|}}{CO}}{C}H \longrightarrow \text{No Reaction}
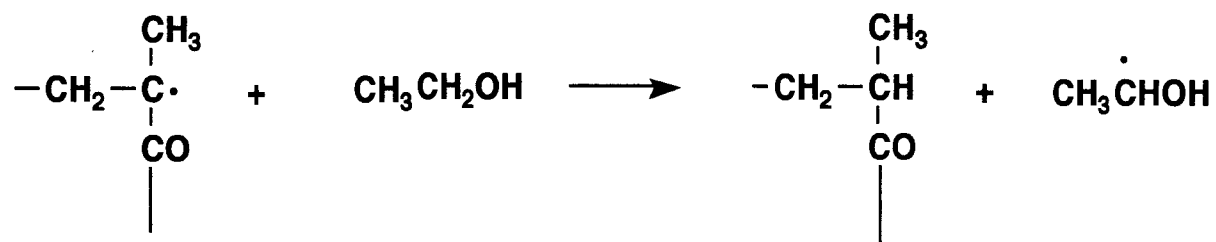$$
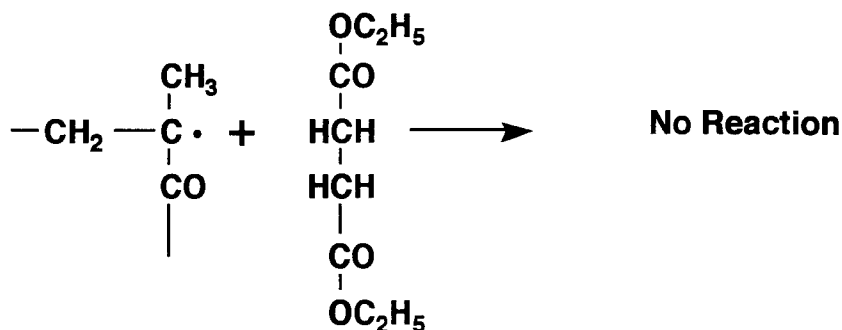
The chain transfer reaction due to the hydrogen abstraction from the solvents

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causes the reduction of the chain length of the polymer. This is considered to be the reason for the gelation instead of the microsphere formation.

2.3.5   Solvent Effect of Alcohols

Although alcohols are used commonly in the preparation of microspheres by the dispersion polymerization, no particles were obtained by the method described in this paper as shown in Table 2.1. It has been described that alcoholic solvents are not favorable for the microsphere preparation by this method because of their solubilities and viscosities (Table 2.1). Furthermore, it has been found that the chain transfer reaction caused by the hydrogen abstraction from alcohols interferes the formation of microspheres. For example, ethanol has two α hydrogens which are easily abstracted by radicals. The chain transfer reaction terminates the propagation reaction and interferes the formation of microspheres.

$$-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle |}{CO}}{C}}\cdot \quad + \quad CH_3CH_2OH \quad \longrightarrow \quad -CH_2-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle |}{CO}}{CH}} \quad + \quad CH_3\overset{\displaystyle \cdot}{C}HOH$$

This effect, the interference by the hydrogen abstraction, can be confirmed by using 2-methyl-2-propanol (*tert* -butyl alcohol) as a solvent having no α hydrogen . Figure 2.5 shows the SEM photograph of the particles obtained from the 2-methyl-2-propanol solution. The result indicates that the hydrogen abstraction interferes the microsphere formation. The obtained particles are partially aggregated. The aggregation may occur after the irradiation.
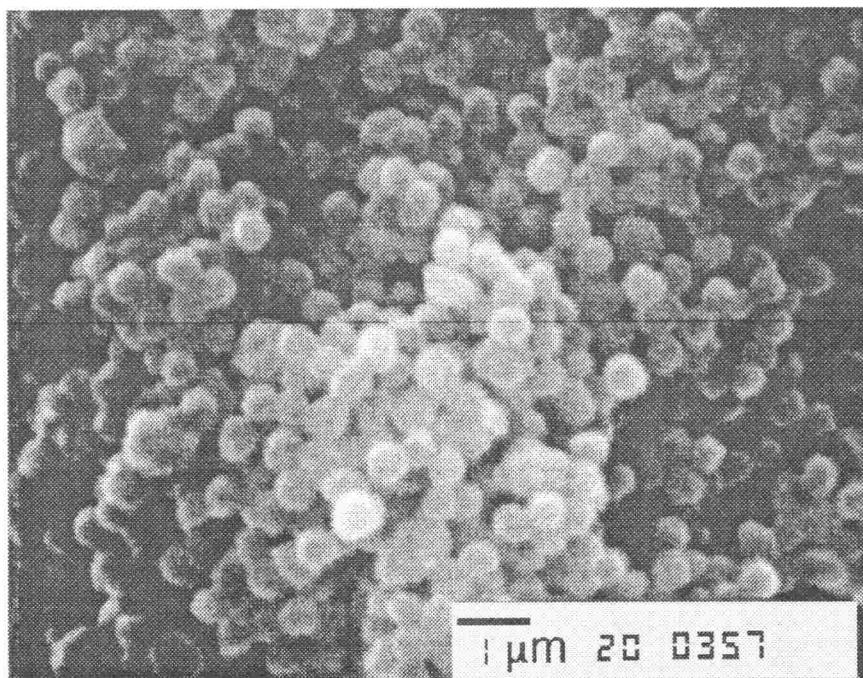
Figure 2.5.   SEM photograph of microspheres obtained in 2-methyl-2-propanol (*tert* -butyl alcohol). Dose rate and irradiation time was 4 kGy h^{-1} and 2h, respectively.

2.3.6   Copolymerization of 2EGDM and HEMA

The reactivity of 2EGDM is considered to be the same as MMA. Some monomers are expected to form copolymer microspheres with 2EGDM as described in chapter 4. The copolymerization with hydroxy ethyl methacrylate (HEMA) provides the hydrophilicity to the microspheres. The copolymerizations of 2EGDM - HEMA do not give microspheres as shown in Table 2.3. All of the feed solutions containing HEMA result in gelation. That is, the presence of HEMA leads to the gelation. This is considered to be the same as the alcohols having α hydrogen. The hydrogens of the hydroxy ethyl group can be easily abstracted by the propagating radicals similar to the case of alcohols. HEMA is not favorable as the comonomer for the preparation of microspheres.
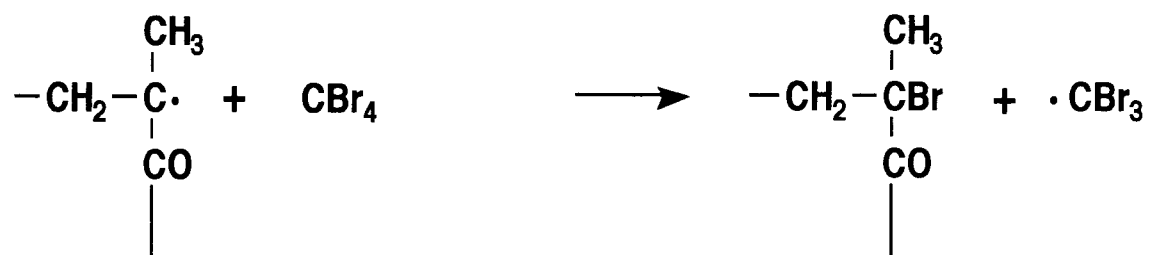
Table 2.3.	Copolymerization of 2EGDM and HEMA. [a]	
Run Number	Mole fraction of HEMA	Result
219	0	Microspheres
220	0.1	Gel
221	0.2	Gel
224	0.5	Gel
233	1.0	Gel

a   Concentration of monomer mixture was 10 vol %. Dose rate was 4 kGy h^{-1} and irradiation time was 2 h. Temperature was 23 °C.

2.3.7   Addition of CBr₄

Carbon tetrabromide (CBr$_4$) is known as a strong chain transfer reagent in radical polymerization. [37] It is expected that the addition of CBr$_4$ interferes the microsphere formation by the chain transfer reaction.

$$-CH_2-\underset{\underset{CO}{|}}{\overset{\overset{CH_3}{|}}{C}}\cdot \ + \ CBr_4 \ \longrightarrow \ -CH_2-\underset{\underset{CO}{|}}{\overset{\overset{CH_3}{|}}{C}}Br \ + \ \cdot CBr_3$$

Its addition results in decrease in the microsphere yield and in the gelation. The yield decreased with increasing CBr$_4$ concentration as shown in Fig. 2.6. Gelation is observed for the 15 vol% 2EGDM solution by the equimolar addition of CBr$_4$. The propagation chain length becomes short by the chain transfer to CBr$_4$. The use of halogenated solvents, such as CCl$_4$, CH$_2$Cl$_2$ and so on, was not favorable for the preparation of microspheres.
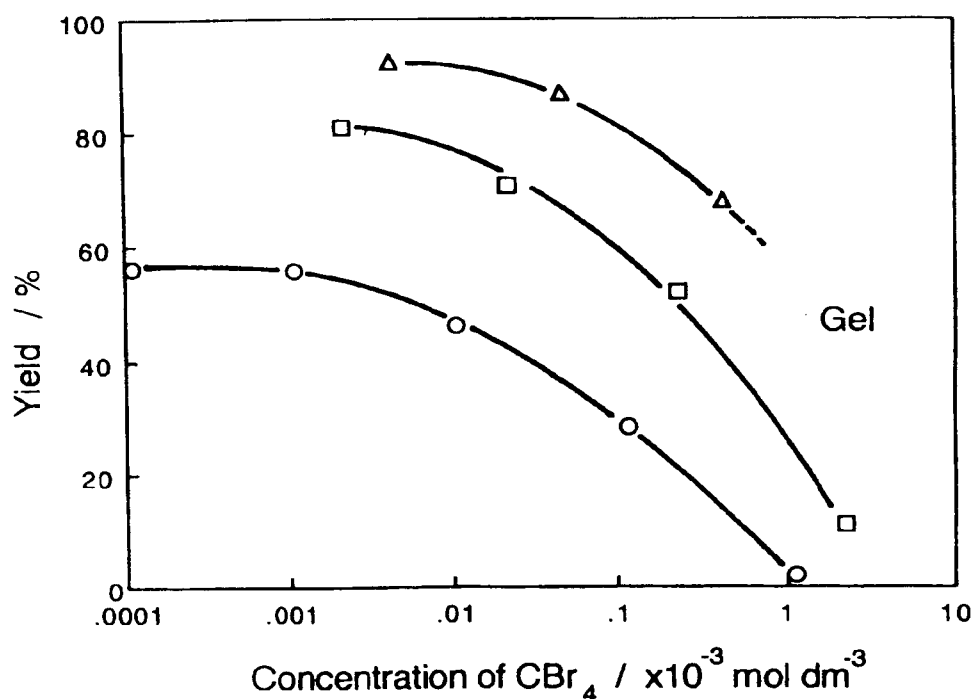
Figure 2.6. Effect of CBr₄ on the yield of microspheres. Concentrations of 2EGDM were ($\bigcirc$) 5 vol %, ($\square$)10 vol %, and ($\triangle$) 15 vol %, respectively. Dose rate was 4 kGy h⁻¹ and irradiation time was 2 h.

2.4 Conclusion

The good solvents for 2EGDM monomer, especially samll ester, are favorable to prepare microspheres. The conformation of the monomer in the solvents is important for the preparation of the microspheres. The chain transfer reaction interferes the formation of microspheres.

Chapter 3

Mechanism of the Microsphere Formation

3.1 Introduction

Dispersion and emulsion polymerizations are used for the preparation of polymer fine particles, "microspheres". Among these methods, surfactants in aqueous solution[14,15,17] and stabilizers in organic solution[18-20] play an important role. One of the roles is the stabilization of the polymer phase in the solution, and another is to avoid the aggregation of particles.[21] The use of a stabilizer makes it possible to obtain the products in high yield. This is because the adhesion is prevented by the surfactant. There was another effort to prepare microspheres without using surfactants.[28-30] Some kinds of additives are used to give stability to the microspheres in the solution. The stabilization of the interface between the monomer or polymer phase and the liquid phase is essential to for the preparation of sphere-shape particles.

The characteristics and the advantages of the diethylene glycol dimethacrylate (2EGDM) microspheres are that the preparation can be carried out in the absence of the stabilizer. The mixture of only monomer and solvent gives the monodisperse microspheres. This suggests that the mechanism for the microsphere formation is different from the dispersion and emulsion polymerizations.

The reason for the monodispersity in size is described in chapter 1 and the solvent effects on the formation of the monodisperse microspheres are discribed in

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chapter 2. Eethyl acetate is used as a solvent in these series of experiments, because it gives microspheres in high yields and with good shape. The effects of some conditions, such as temperature, irradiation time and monomer concentration are described in this paper. Attention is paid to the number of the microspheres in the solution to explain the growth mechanisum of microspheres in this chapter.

3.2 Experimental

Materials and Polymerization. Distilled ethyl acetate was used as a solvent. Polymerization temperature was kept at 25±1 °C in a dewar vessel. All the other conditions were the same as described in Chapter 1.

Separation. After separating microspheres, methanol (100 cm^3) was added to the filtrate to precipitate the soluble polymer. The precipitated soluble polymer was separated after keeping overnight. Both the microspheres and the soluble polymer were dried under vacuum.

Hydrolysis. The microspheres (50 mg) were dissolved in sulfuric acid (2 cm^3) and were stored over night at room temperature. Acetic acid (7 cm^3) was added to the solution of the completely dissolved microspheres. The solution was stored over night and then kept for one hour at 60 °C in the oven. The hydrized polymer was precipitated by adding 100 cm^3 distilled water and filtrated using Teflon filter (2 μm). The polymer were washed by a sulfuric acid solution (0.1 mole dm^{-3}). The recovered polymer were further hydrolyzed with almost the same method as described above except for the added amount of acetic acid (20 cm^3).

Measurements. IR spectra of the polymers were measured by IR spectrophotometer (Shimadzu, IR-408). Moleculer weights were measured by a gel permeation chromatograph (GPC, Toyo soda, HLC-802A), for soluble

polymer; TSK gel G2000H column, THF 1 cm^3 min^{-1}, 40 °C, for hydrolyzed polymer; TSK gel #G3000PW$_{XL}$ column, water / acetenitril (1:9) containg 0.1 mole dm^{-3} of sodium carbonate, 1 cm^3 min^{-1}, at 40 °C.

3.3 Results and Discussion

3.3.1 Temperature and Irradiation Time

Figure 3.1 shows the temperature effect on the yields of the microspheres and the soluble polymer. Although the yields were different, all the experimental runs with 5 and 10 vol % solutions give microspheres in the wide range of temperature from -15 to 50 °C at 10 vol % and from 0 to 50 °C at 5 vol %. The yields of the microspheres for both the 5 and 10 vol % solutions increase with increasing temperature. Temperature strongly affects the yield of the microspheres. The yield for the 10 vol % solution is higher than that for the 5 vol % solution under the same conditions. This suggests that the 2EGDM concentration also affects the microsphere yield.

The yield of the soluble polymer, which was deposited from the solution by methanol, did not change with temperature. The yield of the soluble polymer for the 10 vol % solution is lower than that for the 5 vol % solution. This is different from the case of the microspheres.

Figure 3.2 shows the time yield curves of the microspheres and the soluble polymer. The time-conversion curves are similar for the soluble polymer and the microspheres. The ratio of the conversion of the microspheres to that of the soluble polymer is almost constant during the irradiation. The conversion of the microspheres for the 10 vol % solution is higher than that for the 5 vol % solution. On the other hand, the conversion of the soluble polymer from the 10 vol % solution is lower than that for the 5 vol % solution. The difference in
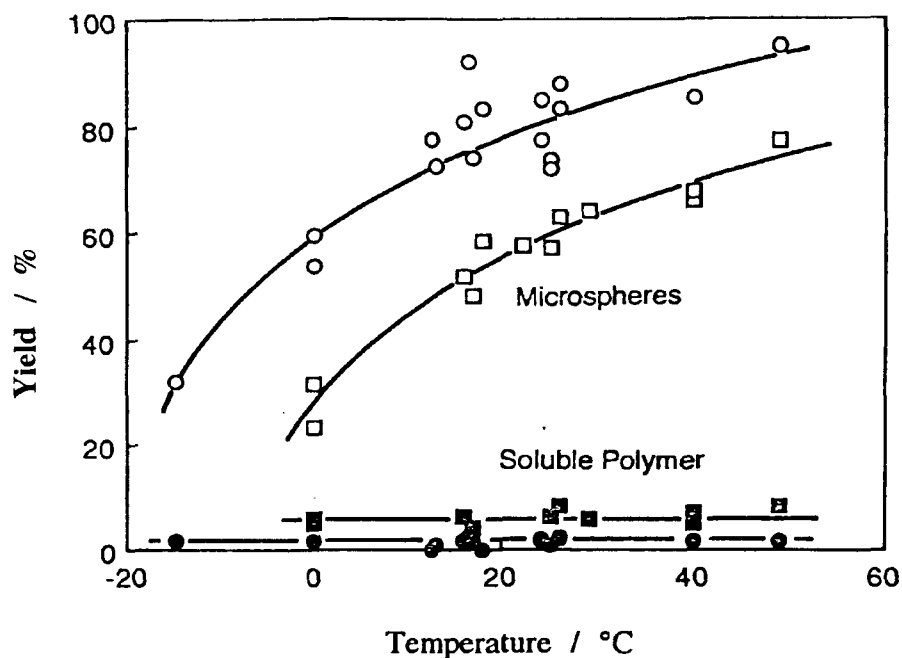
Figure 3.1. Effect of temperature on the yield of the microspheres and the soluble polymer. Dose rate and irradiation time was 4 kGy h^{-1} and 2h, respectively. Concentrations of 2EGDM monomer were (□, ■) 5 vol % and(○, ●)10 vol %.
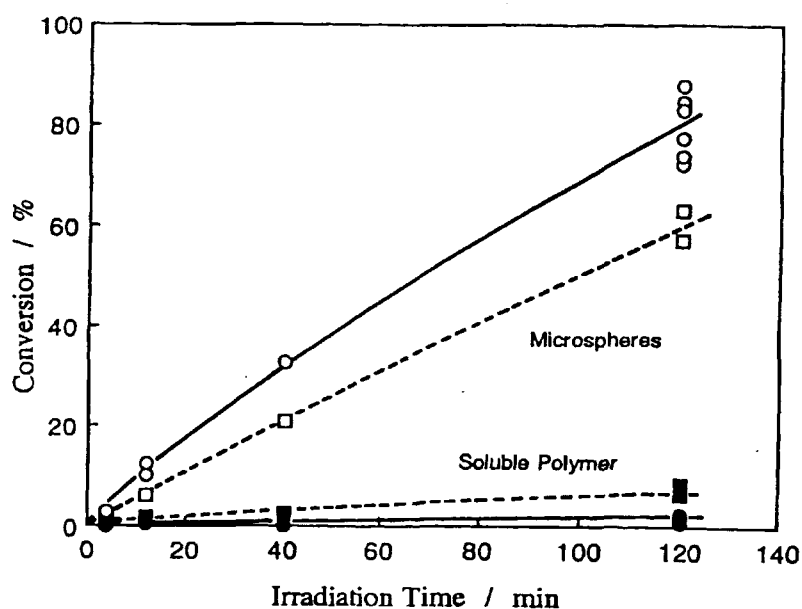

Figure 3.2. Time-conversion curve of the microspheres and the soluble polymer. Concentrations of 2EGDM monomer were (□, ■) 5 vol % and(○, ●)10 vol %. Dose rate was 4 kGy h^{-1}. Temparature was 25 °C.

concentration dependence of the microspheres and the soluble polymer is considered to be important for the discussion of the microsphere growth in this method.

## 3.3.2   Effect of Monomer Concentration

Figures 3.3(a), 3.3(b), 3.3(c), and 3.3(d) show the shapes of the particles at 10, 20, 22, and 24 vol % of 2EGDM monomer, respectively. The shape of the particles obtained from the 10 vol % solution is completely spherical, but those from the solutions of more than 20 vol % concentrations are not sphere. Here the name "microsphere" is used only for the completely spherical praticles; "particle" includes "microsphere". The surface of the microspheres becomes rough with increasing monomer concentration. Some particles, obtained at the concentrations higher than 20 vol %, show the aggregated shapes.

Figures 3.4(a), 3.4(b), and 3.4(c) show the monomer concentration effect on the yields of the particles and the soluble polymers at 25, 17, and 0 °C, respectively. The yield of the particles increases with increasing concentration of 2EGDM monomer. The concentration effect blow 10 vol % is significant. No microspheres were obtained from the 1 vol % solution. Gelation is observed at high 2EGDM concentrations. The critical concentration between particles and gel is shown in Table 3.1. The critical concentration is laid on between 24 and 26 vol % at 25 °C. Gelation is observed at the high concentrations more than 26 vol % at 25 °C. Microspheres or particles were obtained at the wide range of 2EGDM concentrations, from 2 to 24 vol %. This concentration range was the same even at different temperatures.

The yield of the soluble polymer decreases with an increase of 2EGDM monomer concentration. The yield of the microspheres is less than that of the soluble polymer at 17°C and 0°C, at the lowest monomer concentration of the
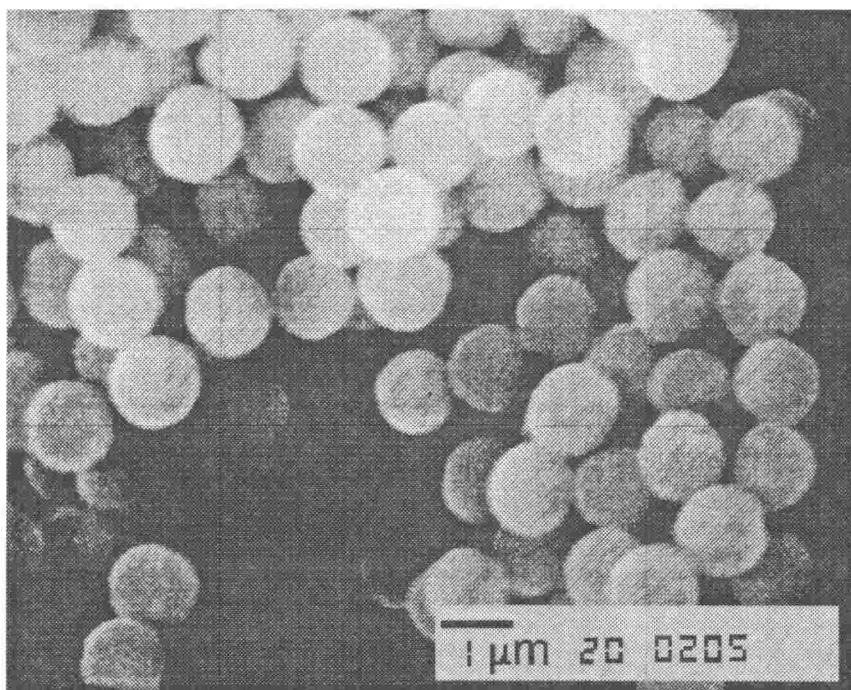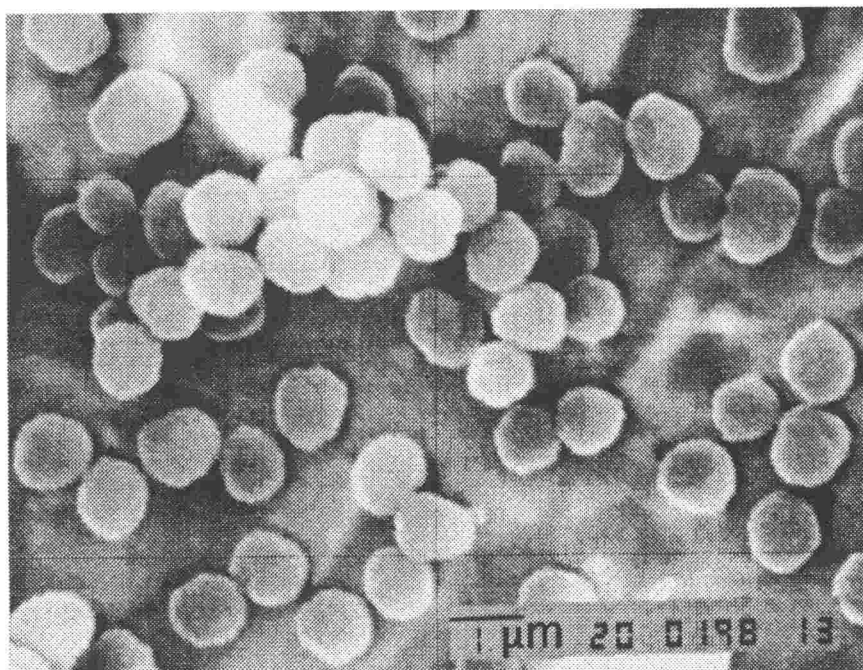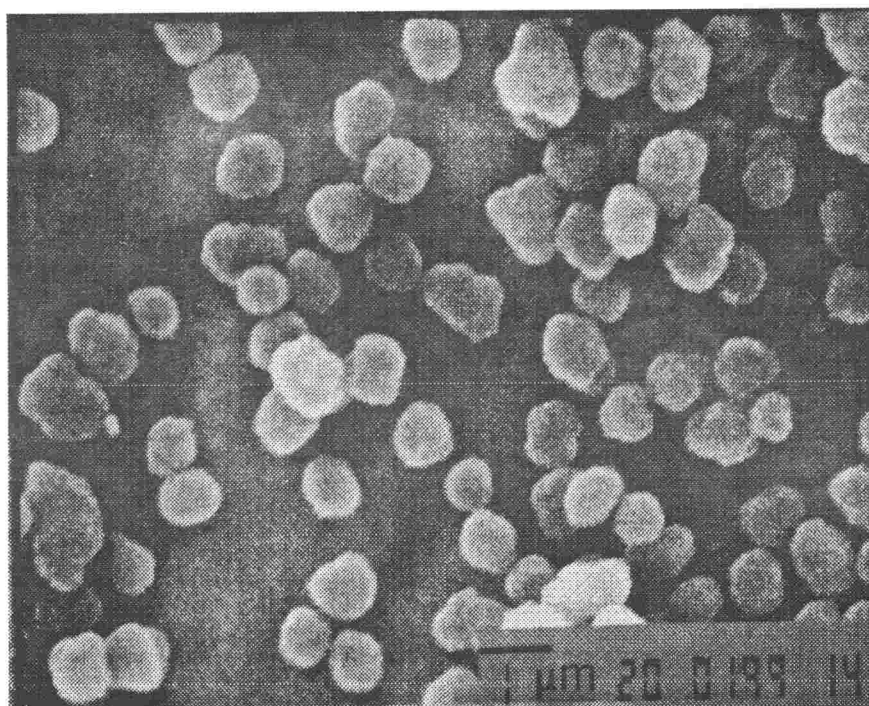
(a)
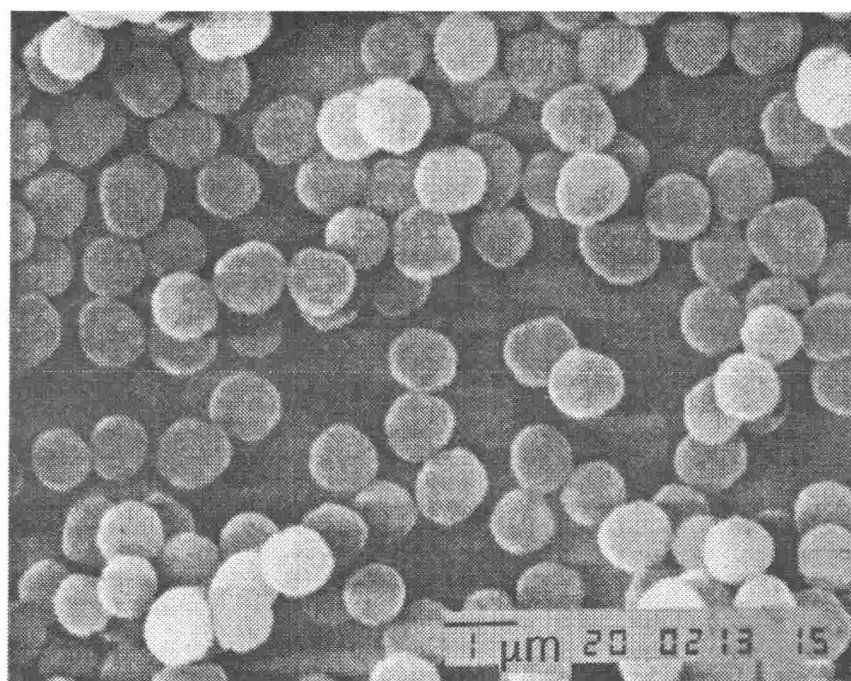
(b)

Figure 3.3.   SEM photograph of poly 2EGDM microspheres and particles. Concentrations of 2EGDM monomer were (a) 10 vol %, (b) 20 vol %, (c) 22 vol %, and (d) 24 vol %. Dose rate and irradiation time were 4 kGy h^{-1} and 2h, respectively. Temparature was 25°C.
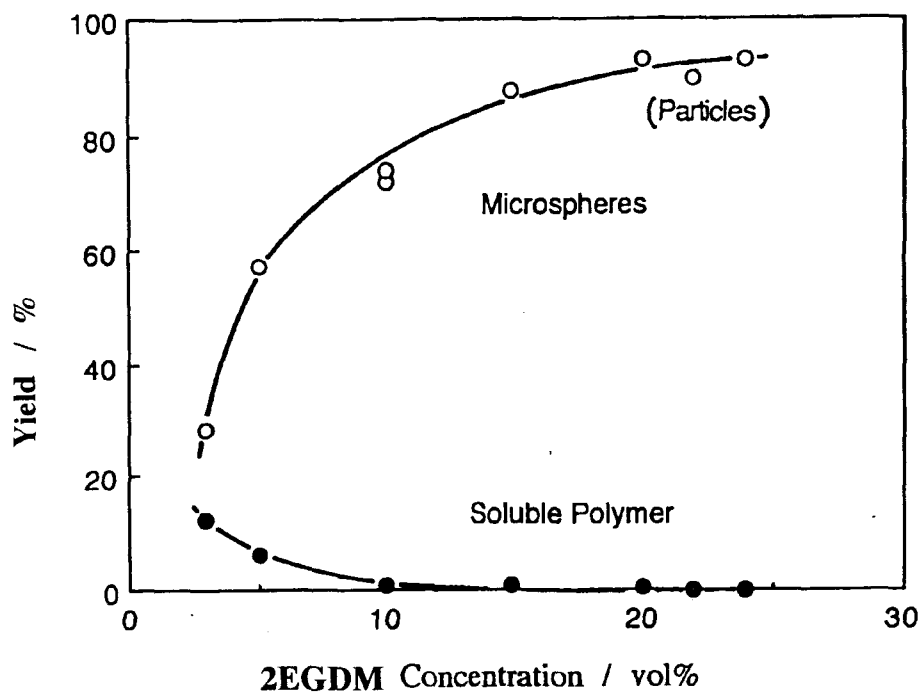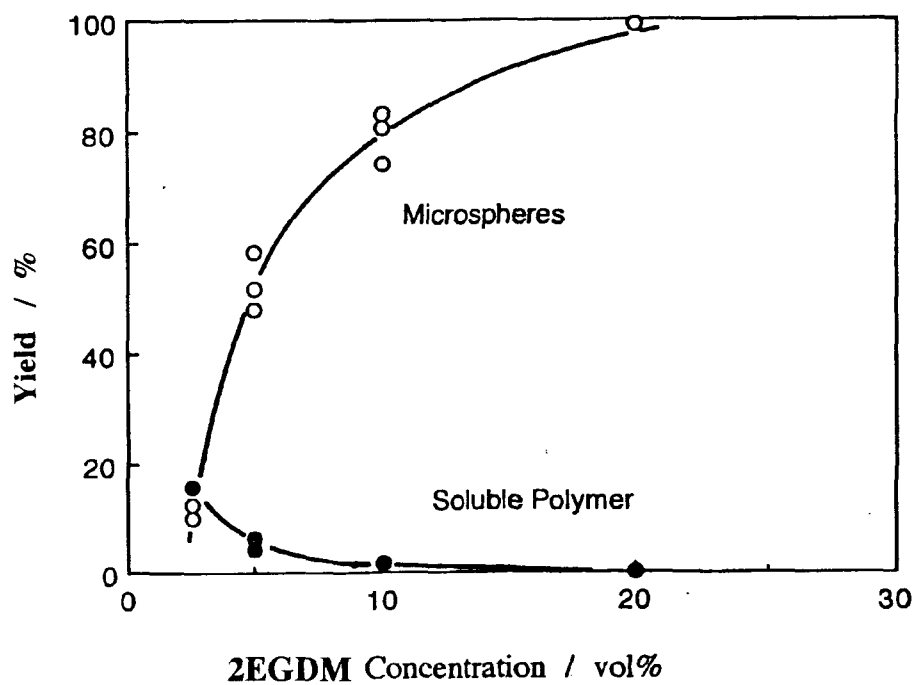
(c)

(d)

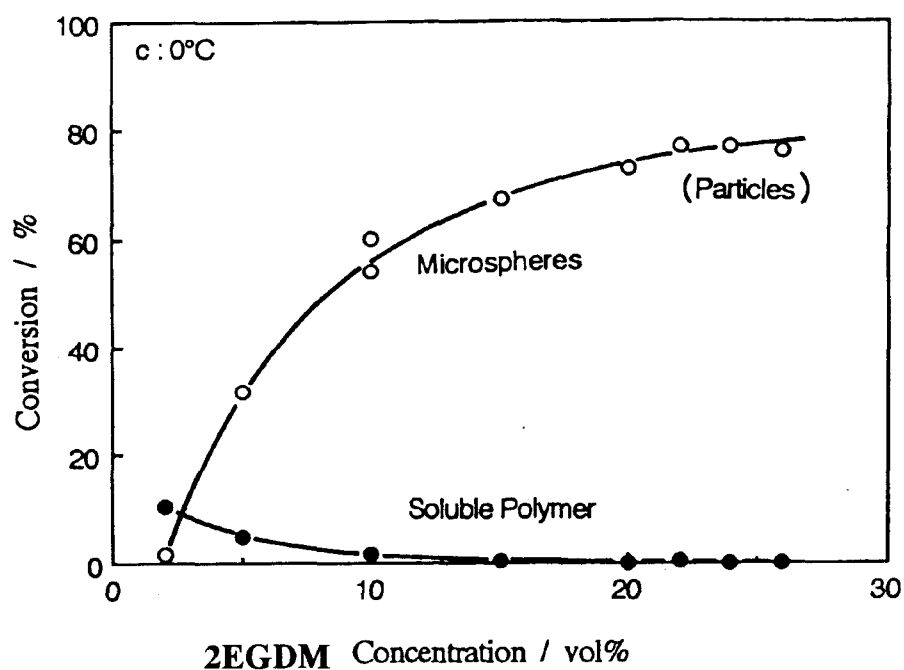Figure 3.3.   (Continued from the previous page)

(a)

(b)

Figure 3.4.   Effect of monomer concentration on the conversions to the microspheres and the soluble polymer. Dose rate and irradiation time were 4 kGy h^{-1} and 2h, respectively. Temparatures were: (a) 25°C, (b)17°C, and (c) 0 °C.

(c)

Figure 3.4.   (Continued from the previous page)

Table 3.1.   Critical Concentration of 2EGDM Monomer for the Microsphere
Formation.[a]

Run Number vol%	2EGDM Concentration	Results %	Conversion
198	22	Particles	88.2
199	24	Particles	90.2
217	26	Gel	
201	28	Gel	

a   Dose was 4 kGy. Temperature was 25 °C.

experiments. The concentration dependence of the soluble polymer completely differs from that of the microspheres.

The yield of the particles increases with increasing 2EGDM concentration. For example, the weights of particles obtained from the 5, 10, and 20 vol % solutions were 30, 78, and 196 g dm^{-3}, respectively. The yield in the 20 vol % solution was 6 times higher than that in the 5 vol % solution. In order to obtain particles in high yield, the high monomer concentration is favorable.

The yield of the particles increases with increasing monomer concentration, but the surface of the particles becomes rough . Although, the critical concentration between microspheres and particles with rough is not clear, the optimum concentration of 2EGDM monomer for the preparation of the spherical microsphere having smooth surface with high yields is considered to be 10 vol %
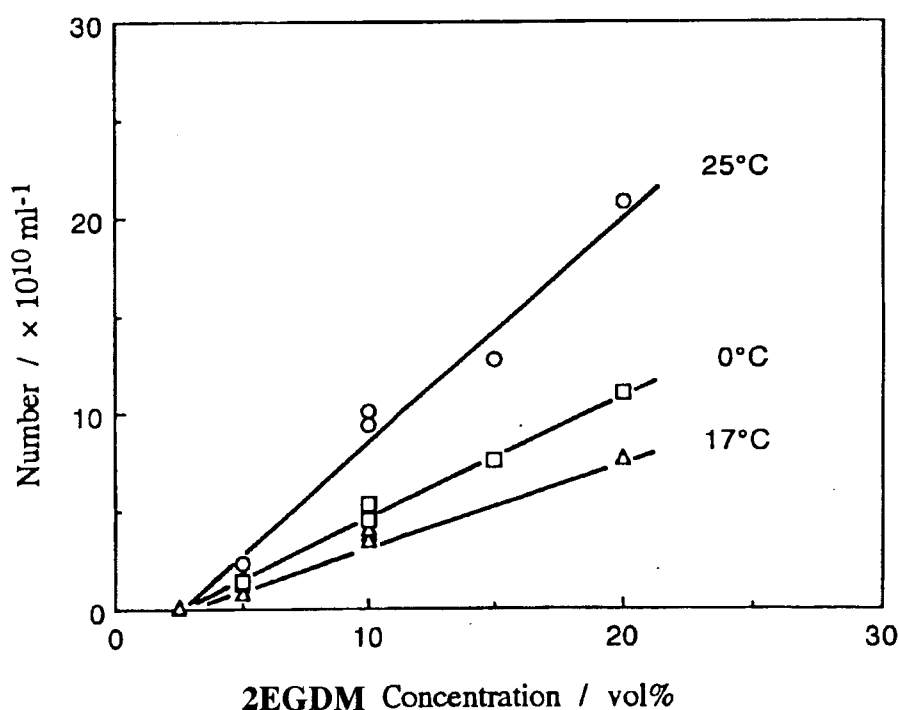

Figure 3.5.   Concentration effect on the number of particles. Number of particles was calculated from the size and the product yield. Particles were assumed to be spheres. Dose rate and irradiation time were 4 kGy h^{-1} and 2h, respectively.

in ethyl acetate. High concentration of the monomer is not favorable for the preparation of the microspheres, but it is good for the preparation of particles with a large surface area.

Figure 3.5 shows the monomer concentration effect on the number of particles in the solution. The number of particles increases linearly with the monomer concentration. The intercepts of the plots to the abscissa are the same, ca. 2 vol %. The extrapolation of the three lines meets at almost the same point, 2 vol %. This value is regarded as the lower limit of the monomer concentration for the preparation of the microspheres.

3.3.3 Critical Concentrations for Particles and Gel

The microspheres are considered not to move in the solution during the propagation otherwise it occur to give aggregated particles as descrived in Chaspter 1. The distance between the microspheres in the solution can be calculated under an assumption that all the microspheres have the same distance to
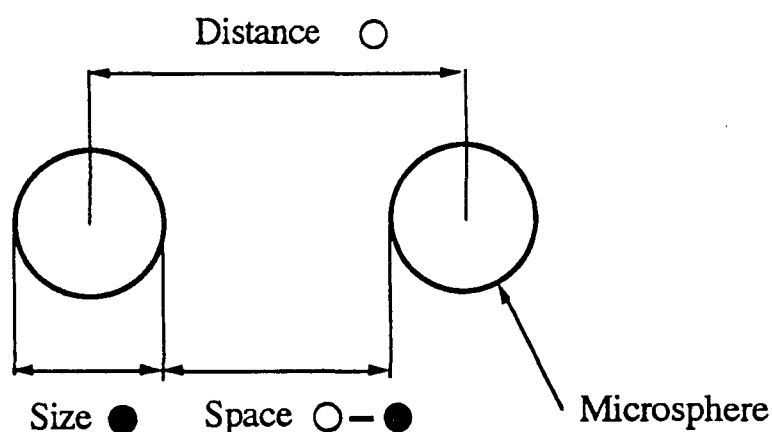

Figure 3.6. Difinition of size, distance and space.

the neighboring particles (Fig. 3.6). The center to center distance is calculated using the following equation for the hexagonal closest packing,

$$\text{Distance} = \sqrt[3]{\frac{4V}{n}} \times \frac{1}{\sqrt{2}}$$

where V and n are the volume of the solution and the number of the particles, respectively. Figures 3.7(a), 3.7(b), and 3.7(c) show the size of the particles and the distance between two neighboring microspheres at different monomer concentrations at 0, 17, and 25 °C, respectively. The size of the microspheres is not affected by the monomer concentration. On the other hand, the distance decreases rapidly with increasing monomer concentration. The vertical difference between two curves represents the space between surfaces of neighboring particles at the end of irradiation (Fig. 3.6). The space decreases with increasing monomer concentration, and seems to reach zero when the gelation occurs. However, the sintering of particles caused by the contact due to the decrease in space is not reason for the gelation as described below.

There were three different results depending on the monomer concentration, i.e., no polymerization and the productions of particles and gel. The critical concentration for the formation of particles or gel is located between 24 and 26 vol % (Table 3.1). This concentration is low if the contact between microspheres results in the gelation, because the theoretical maximum total volume of solid spheres is 74 % under the hexagonal closest packing. If the contact of the growing microspheres is not considered to restrict the formation of microspheres during the propagation, there should be another possibility for the preparation of smaller microspheres even at high monomer concentration and at low conversion.

The sizes of the microspheres increase with increasing irradiation time, and is considered to be small enough to avoid the contact between microspheres in the beginning of polymerization. The size of microspheres and the distance between neighbouring microspheres for the 5 min irradiation are predicted to be 0.5 μm
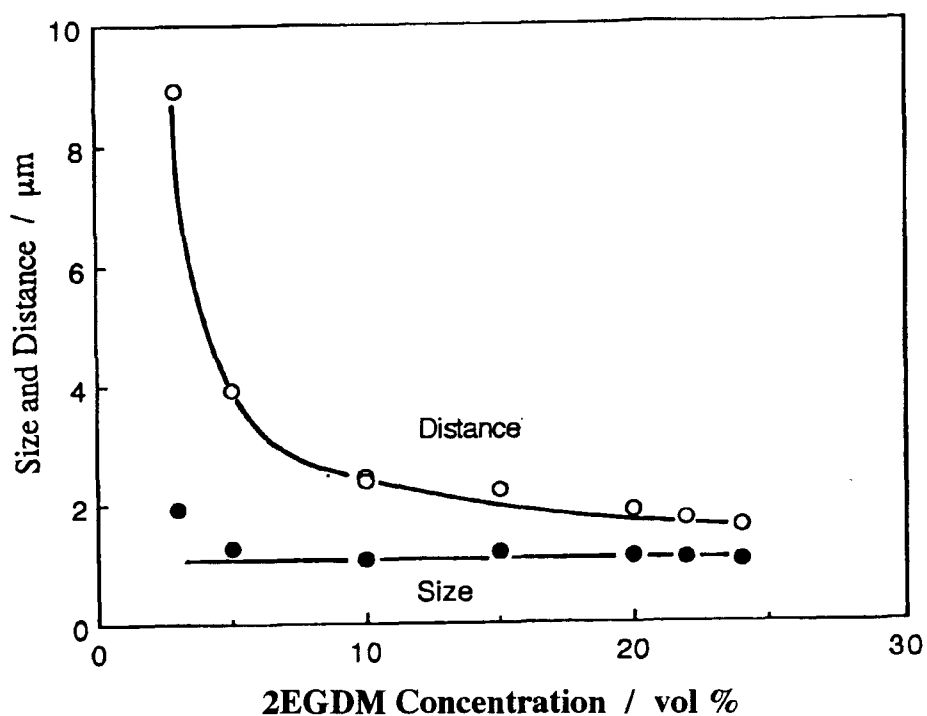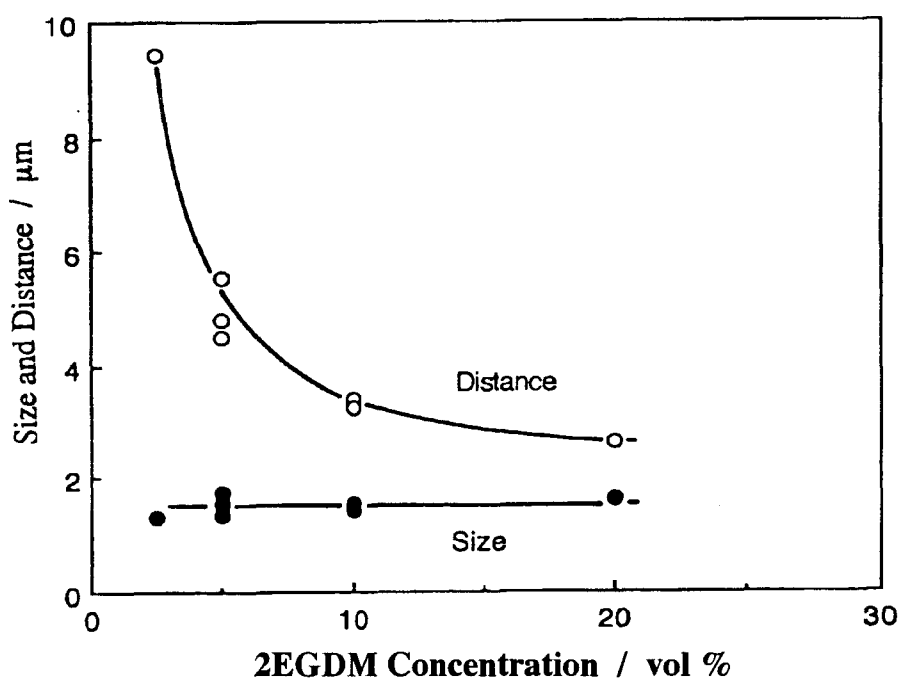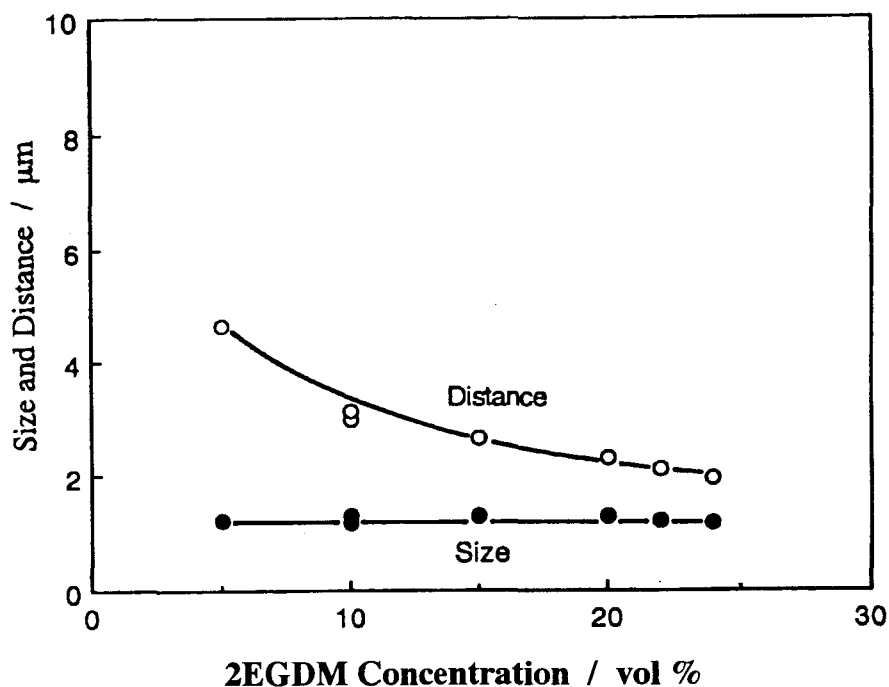
Figure 3.7. Concentration effect on the size of microspheres (particles) and the distance between two microspheres at (a) 25°C, (b)17°C, and (c) 0°C. Dose rate and irradiation time were4 kGy h^{-1} and 2h, respectively.

Figure 3.7.   (Continued from the previous page)

and 2 μm, respectively. Therefore, it can be expected to obtain the small microspheres, when the propagation is stopped in a short period, even if monomer concentration is high.   The gelation occurs at the high monomer concentrations even at the short irradiation times as showen in Table 3.2. To avoid the gelation, the concentration of the 2EGDM monomer must be low.

Although the decrease of space causes the contact between particles, the gelation is not caused only by the decrease of space at high monomer concentration. The gelation observed at high monomer concentration is caused not by the particles sintering due to the contact, but by the formation of the polymer networks occuring in a very short period. Thus, the polymer chain spreads over a wide area in a very short period. A possible growth mechanism of microspheres is proposed below.

Table3.2. Gel Formation of 2EGDM Monomer at High Monomer Concentration.[a]

Run Number	2EGDM Concentration	Time	Results
vol%	min		
178	30	5	Gel
184	30	5	Gel
186	40	5	Gel
188	50	5	Gel

a   Dose rate was 1 kGy h⁻¹. Temperature was 25°C.

3.3.4   Difference from Conventional Radical Polymerization

The emulsion and dispersion polymerizations need some kinds of stabilizer to prevent the contact and aggregation of growing particles. Surfactants give the field of the particle growth, that is, the micelle in the emulsion polymerization. Surfactants enable polymers to exist in a stable polymer phase in the solution. Thus, the fields for the polymer phase are already prepared before the polymerization is initiated. The polymerization starts in a homogeuous system in the dispersion polymerization. The decrease of solubility of the produced polymer in the solution causes the phase separation. Therefore, the solvent is selected from poor solvents for the producing polymer. The stabilizer helps the formation of particles and prevents the aggregation.

Since the radiation-induced polymerization of the present method is carried out in the organic solvent, it is regarded as a kind of the dispersion polymerization. But the mechanism is considered to be completely different from the conventional dispersion polymerization. First, the polymerization does not need any kind of stabilizer, and the polymer microspheres are created in good solvents such as ethyl acetate, tetrahydrafuran, and so on. as described in Chapter 2. Therefore, the

solubility change due to the polymerization in the solvent is not the reason for the phase separation.

In the cases of the emulsion and dispersion polymerizations, the stirring contributes to the stabilization of the microspheres and helps the homogeneous initiation reaction under heating. On the other hand, in the case of the present method, the stirring disturbs the formation of the microspheres as described in Chapter 1. The stirring causes the contact of the growing particles resulting in an aggregation, because there is stabilizer preventing the aggregation. It is important that the present method dose not need stirring to consider the mechanism.

The monomer used in the present method is 2EGDM having two vinyl
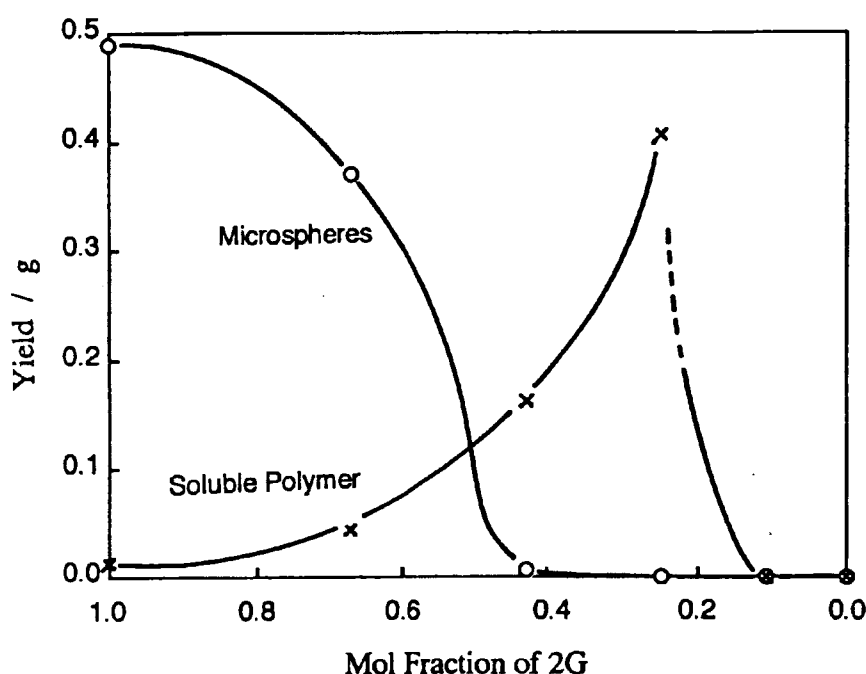

Figure 3.8.   Effect of bi-functional monomer on the formation of microspheres. The concentration of 2EGDM and EMA are controlled to keep constant vinyl group concentration in the solution, 4.4 mol dm^{-3} . Dose rate and irradiation time were 4 kGy h^{-1} and 2h, respectively. Temparatures was 25°C.

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groups, whereas uni-functional monomer such as styrene and methyl methacrylate are used in the emulsion and dispersion polymerization. Figure 3.9 shows the effect of the copolymerization on the formation of microspheres. Ethyl methacrylate (EMA) was used as a comonomer, because its structure is almost half of 2EGDM. The total concentration based on vinyl groups was kept constant to be 0.88 mol dm^{-3}. The yield of microspheres decreases with decreasing mole fraction of 2EGDM monomer, especially, at mole fraction below 0.8. At mole fraction of 0.4, the yield ofthe microspheres is almost zero. The solution with mole fraction of 0.4 has still enough concentration (4 vol %) for the production of the homopolymer microspheres. This shows the importance of the use of the bi-functional monomer.
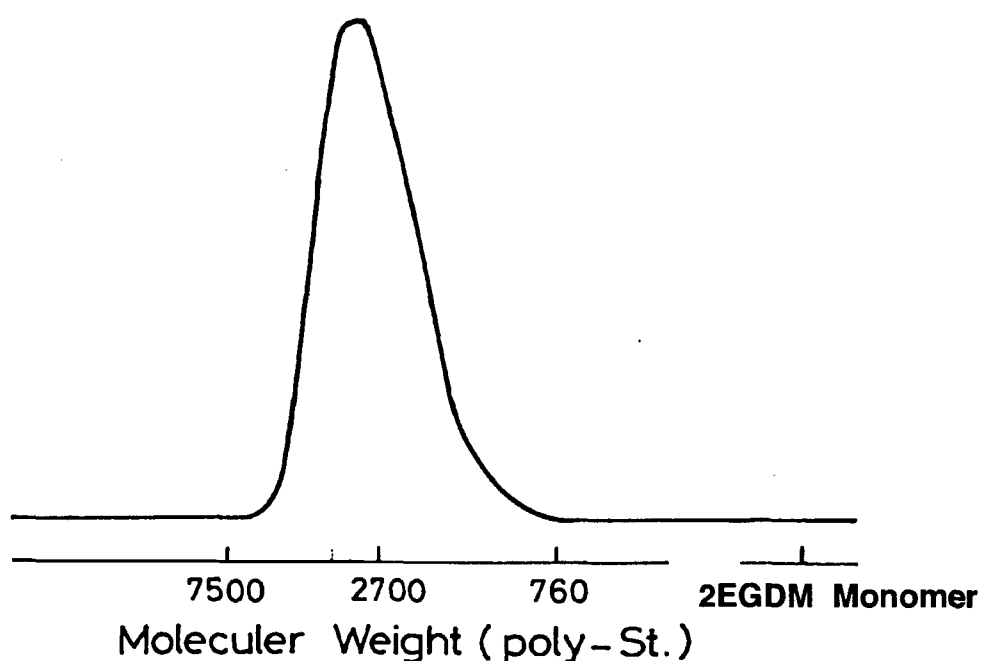

7500	2700	760	2EGDM Monomer

Moleculer Weight (poly – St.)

Figure 3.9. Typical GPC curve of the soluble polymer.

3.3.5   Soluble Polymer

The yield of the soluble polymer decreases with increasing 2EGDM concentration in contrast to that of the microspheres as shown in Figs. 3.4. It should be expected that the soluble polymer is an intermediate for the microsphere formation. On the other hand, the soluble polymer exhibits the same trend in the time-conversion curves as the microspheres; its yield increases with irradiation time (Fig. 3.2). If the soluble polymer were the intermediate of the microspheres, the time-yield curve of the soluble polymer should have a peak in time-conversion
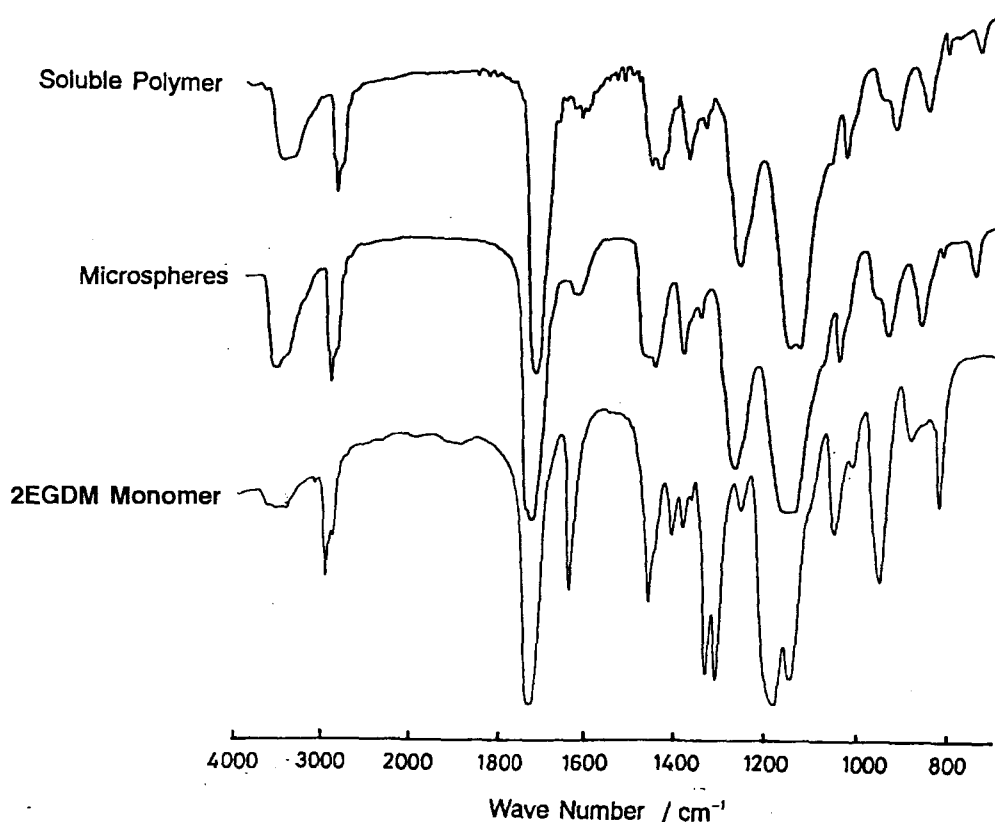
Soluble Polymer

Microspheres

2EGDM Monomer

4000   3000   2000   1800   1600   1400   1200   1000   800

Wave Number / cm⁻¹

Figure 3.10.   IR spectra of poly-2EGDM microspheres and soluble polymer. The absorption band at 1640cm⁻¹ is assigned to the vinyl group. Both microspheres and soluble polymer were prepared under the following conditions. Dose rate and irradiation time were 4 kGy h⁻¹ and 2h, respectively. Temparature was 17°C.

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curves. Therefore, the soluble polymer is considered as the byproduct of the preparation of the microspheres.

Figure 3.10 shows the GPC curve of the soluble polymer. The molecular weight of the soluble polymer is estimated to be in the range of 1000 to 5000 based on standard polystyrene. Figure 3.11 shows the IR spectra of the soluble polymer, the microspheres and 2EGDM monomer. The absorption at $1640 cm^{-1}$, which is assigned to vinyl group, has almost the same intensity as those for the microspheres and soluble polymer and is very week compared with that for 2EGDM monomer. The low absorption intensities of vinyl group for both the microspheres and the soluble polymer suggest almost all of the second vinyl groups are consumed. Although the basic structure of both the soluble polymer and the microspheres are the same, it seems to reasonable to consider that the soluble polymer and microspheres are independently produced. Even if, the soluble polymer acted as stabilizer on the microsphere, it should be uptaken in the microspheres during the polymerization. And it does not exist no more separated soluble polymer in the solution.

3.3.6   Region of Microspheres

Since the number of microspheres does not change during the polymerization, each microsphere should have a region in which the creation of another nucleus is inhibited (Fig. 3.12). It can be called as the territory of a microsphere. The half value of the distance between neighbouring microspheres represents the diameter of the inhibiting region. It is interesting that the space of inhibiting region of a microsphere decreases with increasing monomer concentration. But this tendency does not agree with the length of the polymer chain. It is natural to consider that the kinetic chain length of the propagation reaction increases with increasing monomer concentration since the rate of the
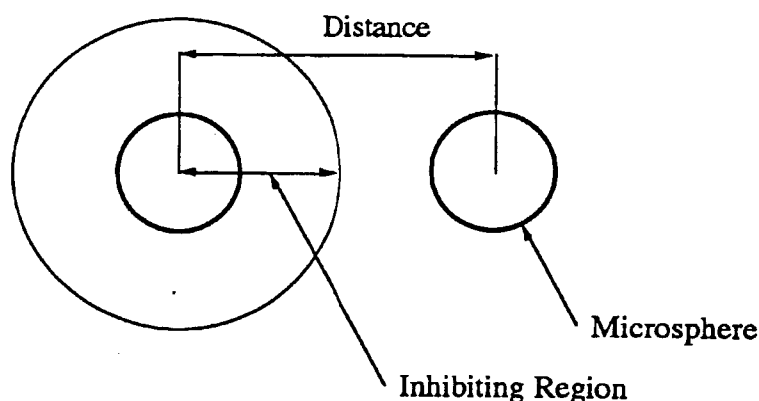
Figure 3.11.   Difinition of the inhibiting region.

initiation reaction is constant at the same dose rate.

This disagreement suggests the contribution of some kind of force which suppresses the expansion of the polymer chain due to the propagating reaction and leads the polymer chain toward the nuclei or the surface of the microsphere. If the polymer chain continues to grow without the any kind of contruction forces, the contact of the neighboring polymer is unavoidable. The "shrinkage force" is proposed to explain the suppression of the gelation and the aggregation of the microspheres. This force must be an important factor for the microsphere formation.

The shrinkage force is not due to the phase separation by the decrease of solubility, because particles are obtained in good solvents as described in Chapter 2. This shrinking is caused because of the bi-functional monomer. The number of the vinyl groups, which belong to the propagating polymer, increases one by one with proceeding the propagating reaction of the bi-functional monomer (Fig.
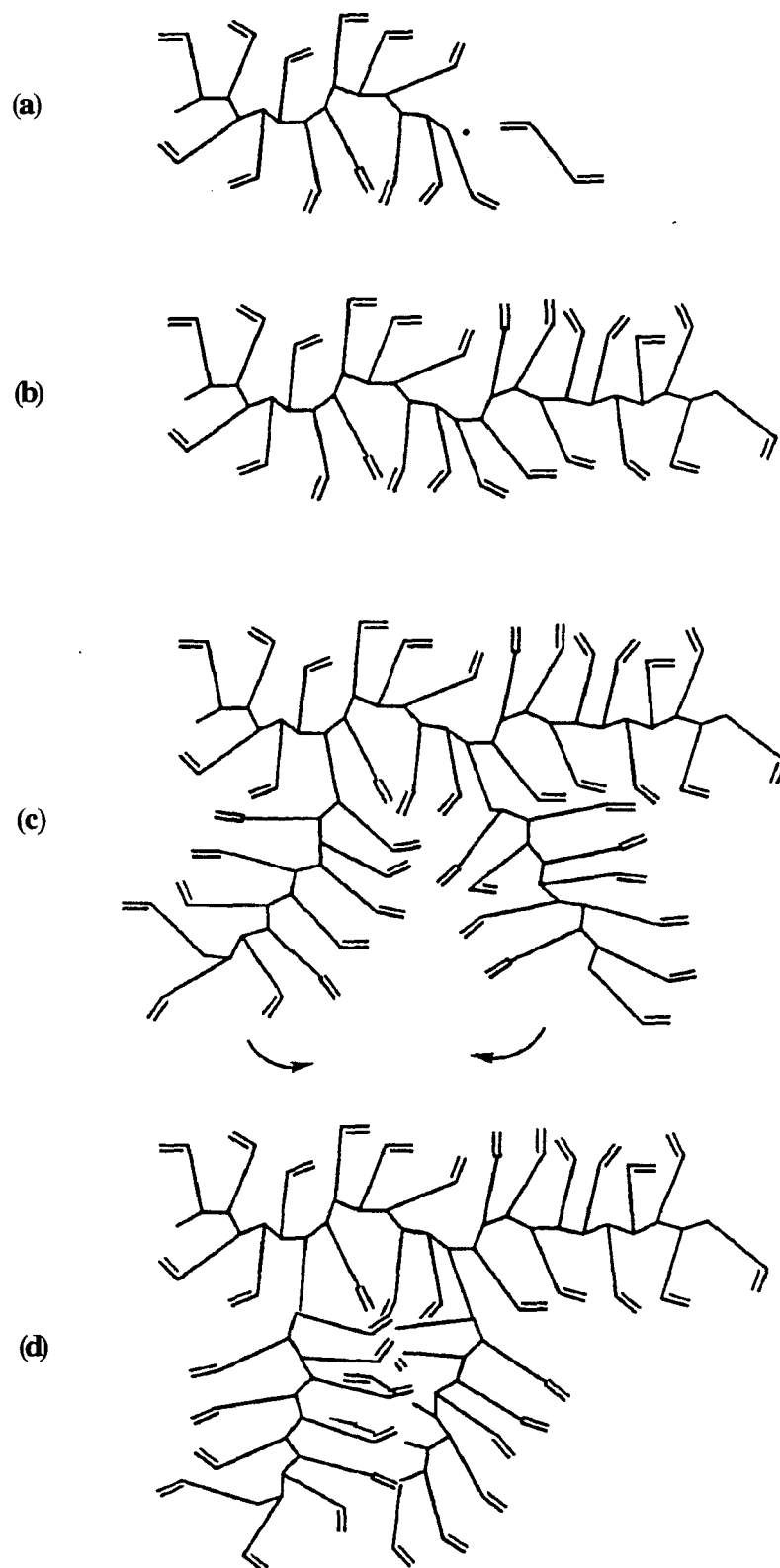
51

Figure 3.12.   Scheme for the expanding by the propagation and the shrinking by the cross-linking reaction.

3.12). The number of the vinyl groups included in a propagating polymer radical is equal to the number of the monomer units in the chain if there is no cross-linking. Figures 3.12(a) - 3.12(d) are the scheme of the shrinking mechanism. Figures 3.12(a) and 3.12(b) illustrate the propagation step and the termination step, respectively. The number of the remaining vinyl group is equal to the number of 2EGDM monomer units in the 2EGDM polymer. Figure 3.12(c) is the branch propagation. Although the number of the remaining vinyl groups decreases with increasing number of the branches, the 2EGDM polymer still has a large amount of the remaining vinyl groups. The polymer chain, including the each branched chain, can move or swing like seaweed in the solution because a good solvent is used. When two chains or branches move and approach together, the local concentration of the vinyl groups becomes high in this area shown as Fig. 3.12(d), the rate of chain reaction is expected to become extremely high. After this reaction, these chains can not leave. The shrinking force is caused by these processes.

3.3.7 GPC Analysis of Hydrolyzed Microspheres

The 2EGDM microspheres are not dissolved in any solvent except concentrated sulfuric acid. The 2EGDM monomer has two acryl acid groups linked by one diethylene glycol with two ester bond. Concentrated sulfuric acid destroyes the polymer structure by the hydrolysis of the ester bond. Although the hydrolysis of 2EGDM microsphere destroyes original sturcture, the hydrolyzed polymer remains polymer chain produced by the polymerization.

Figure 3.13 shows the GPC chromatogram of the hydrolyzed 2EGDM microspheres. Each chromatogram are normalized as their peek areas. Two peaks are observed in all the chromatograms. The first peak is observed at 16.5 min and the number-average molecular weight at the peak is ca. 2×10^5 as
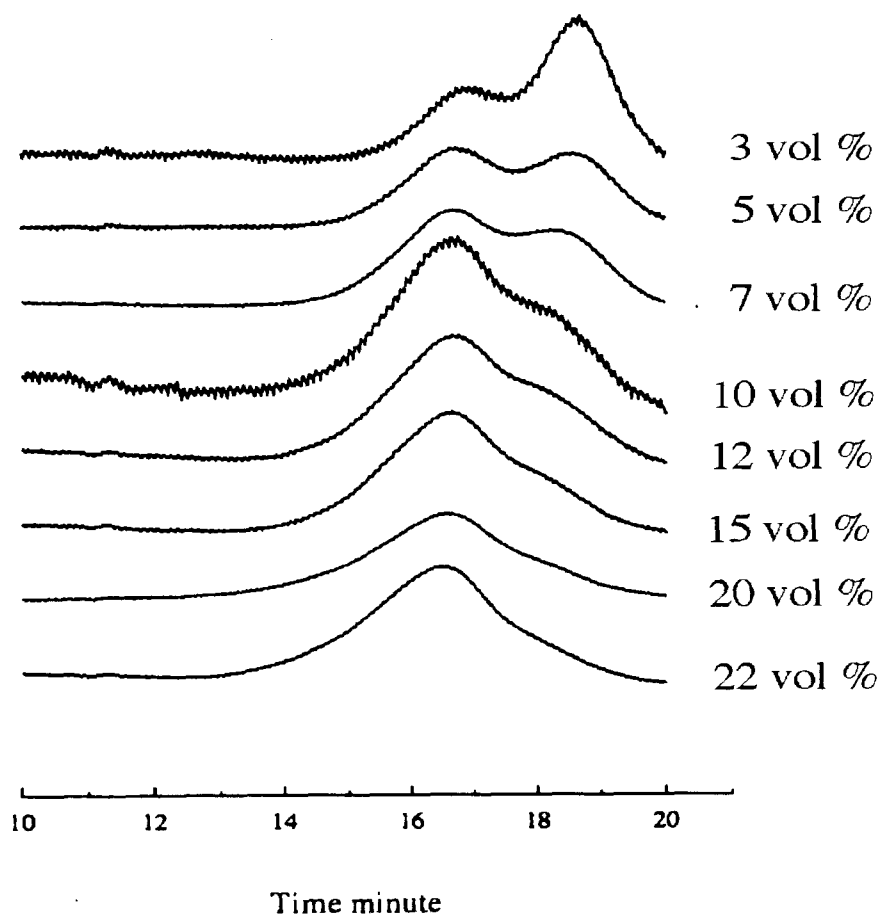
Figure 3.13. GPC curve of the hydrolyized poly 2EGDM microspheres. Dose rate and irradiation time were 4 kGy h^{-1} and 2h, respectively. Temparature was 25°C.

poly(methacrylic acid). The second peak appears at 18.2 to 18.7 min and the molecular weight at the peak is 2×10^4 to 3×10^4 as poly(methacrylic acid). The peeks of the lower molecular weight are shifted with increasing monomer concentration. The peeks of the higher molecular weight are not shifted with the monomer concentration. The relative peak area of the higher molecular weight polymer increases with increaseing monomer concentration. The second peak in the sample obtained in 3 vol % solution is very large. The second peak for the 22
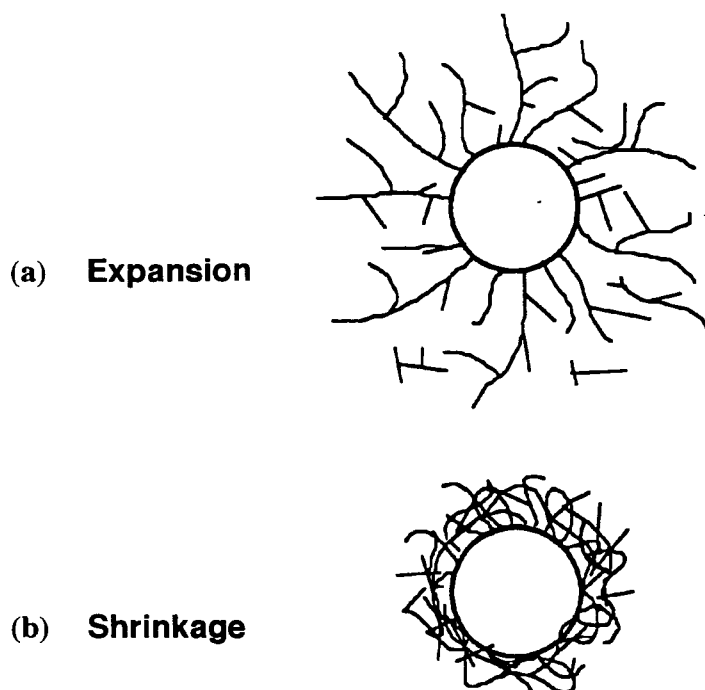
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(a) **Expansion**

(b) **Shrinkage**

Figure 3.14.   Two element process of the microsphere formation.

vol % solution almost disapears. Two peaks in the GPC chromatograms show that the two types of processes contribute to the formation of the 2EGDM microsphere.   Microspheres were obtained in the range 2 to 24 vol % of the 2EGDM monomer concentration for the ethyl acetate solution.   No precipitated polymer was obtained below 2 vol %.   The first peak seems to disapear below 3 vol %.   The monomer solution turned to gel when the monomer concentration exceeds 24 %.   Both of the lower and higher molecular weight polymers are the hydrolysis products of the microspheres.   Each peak is not directly assigned to the two processes, such as propagation reaction and cross-linking reaction, because the propagating radicals react with both the monomer and the remaining vinyl

groups of polymer chains. It is clear that the microsphere formation stands on the contribution of two processes.

3.3.8   Formation of Microspheres

The mechanism is divided into the two processes in order to explain the formation of the microspheres, i.e., the expanding and the shrinking of the polymer chains (Fig. 3.14). The simultaneous progresses of these two reactions cause the growth of the microspheres. It is impossible to distinguish clearly between the propagation reaction by the first vinyl group and the cross-linking reaction by the second vinyl group.

However, it can be considered that the growth of particles is controlled by the competition of the propagation and cross-linking reactions.

3.4 Conclusion

The monomer concentration strongly affects the formation of microspheres, such as yield, shape and number. The uses of the bi-functional monomer, such as 2EGDM, make it possible to prepare microspheres by this method. The formation of the microspheres is caused by the competition between the propagation and the cross-linking reactions.

Chapter 4

Copolymer Microspheres

4.1 Introduction

Microspheres are used mainly in the biological fields.[8-12,38] The usage of microsphere can be expanded by adding functional groups on microspheres. Copolymerization is the one of the methods for introducing functional groups into polymer.[12,13,24-26]

Diethylene glycol dimethacrylate (2EGDM) gives microspheres from organic solution by radiation-induced polymerization in the absence of stabilizers. The mixture of only monomer and solvent gives the microspheres. It is expected that the monomers soluble in 2EGDM feed solutions give copolymer microspheres. The reactivity of 2EGDM is considered to be the same as that of MMA, and hence many mononers are expected to give copolymer microspheres with 2EGDM. This chapter is concerned with the copolymerization of 2EGDM with some comonomers not only to prepare microspheres but also to get general information on copolymer microspheres.

Ethyl methacrylate (EMA), acrylamide, maleic anhydride and styrene were used as comonomers with 2EGDM. EMA was used because of its structure. The size of EMA is a half of 2EGDM monomer, and the reactivity of vinyl group of EMA is considered to be the same as that of 2EGDM. The differences between EMA and 2EGDM are in mobility in the solution and in number of the vinyl groups. Therefore, the copolymerization of 2EGDM and EMA is expected to give

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copolymer with constant uptaking ratio during the whole polymerization period and to give general information on the copolymerization of the 2EGDM microspheres.

Copolymerization of maleic anhydride and 2EGDM was used because of two reasons. One is to introduce the carbonyl group into the microsphere, and another is for the sake of comparison with EMA. Maleic anhydride is known as the comonomer that gives alternative copolymers. Therefore, it is expected to give microspheres without a significant influence of copolymerization. Acrylamide was used to introduce hydrophilic group into the 2EGDM microspheres. Both maleic anhydride and acrylamide are expected to obtain further possibilities for the modification of the microspheres. Styrene is expected to be uptaken with a high ratio in the polymer according to its monomer reactivity ratio to MMA.

The conditions giving the copolymer microspheres and the effects of the comonomer structures on the formation of the microspheres are discussed.

4.2 Experimental

Materials. Ethyl methacrylate (EMA), styrene, maleic anhydride, acrylamide and ethyl acetate, were purchased from Wako Pure Chemical. Ethyl methacrylate and styrene were purified by distillation. Maleic anhydride and acrylamide were purified by recrystallization from benzene. Ethyl acetate was used without further purification. All other conditions were the same as described in Chapter 1.

Polymerization. In a series of runs, the feed solutions were prepared as they contain constant amounts of 2EGDM monomer. The solvent, ethyl acetate, was added to keep the volume constant. The volume change by mixing 2EGDM and the comonomers is assumed to be negligible. In a typical experimental run, 0.5

cm^3 of 2EGDM monomer, 0.069 cm^3 of EMA and 4.43 cm^3 of ethyl acetate were poured into glass vessel with 10 mm I.D. (2EGDM concentration, 10 vol %: mole fraction of EMA, 0.2). The feed solutions were degassed on the vacuum line by repeating a freeze-melt cycle. The samples were irradiated with ^{60}Co γ rays at room temperature without stirring. The dose rate was 4 kGy h^{-1} and the irradiation time was 2 h otherwise noted.

Measurements. The formation of copolymer was confirmed by the IR spectrophotometer (Shimadzu, IR-408). The ratio of copolymerization in the microspheres is determined by elemental analysis (Perkin Elmer 240C).

4.3 Results and Discussion

4.3.1   Copolymerization with Ethyl Methacrylate

Figure 4.1 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 (the same marks in the figure) contains the same concentration of 2EGDM monomer. (This is because the decrease of 2EGDM concentration also causes the decrease of the microsphere yield as described in Chapter 3. It is difficult to distinguish the effect whether by decreasing 2EGDM concentration or by decreasing 2EGDM mole fraction if the total monomer concentrations are kept constant.)

Figures 4.2(a) and 4.2(b) show the IR spectra of the 2EGDM microspheres and 2EGDM - EMA copolymer microspheres, respectively. Since the structures of both 2EGDM and EMA are analogous, the change in the IR spectrum due to the EMA units is very small, except for the appearance of new week absorption at
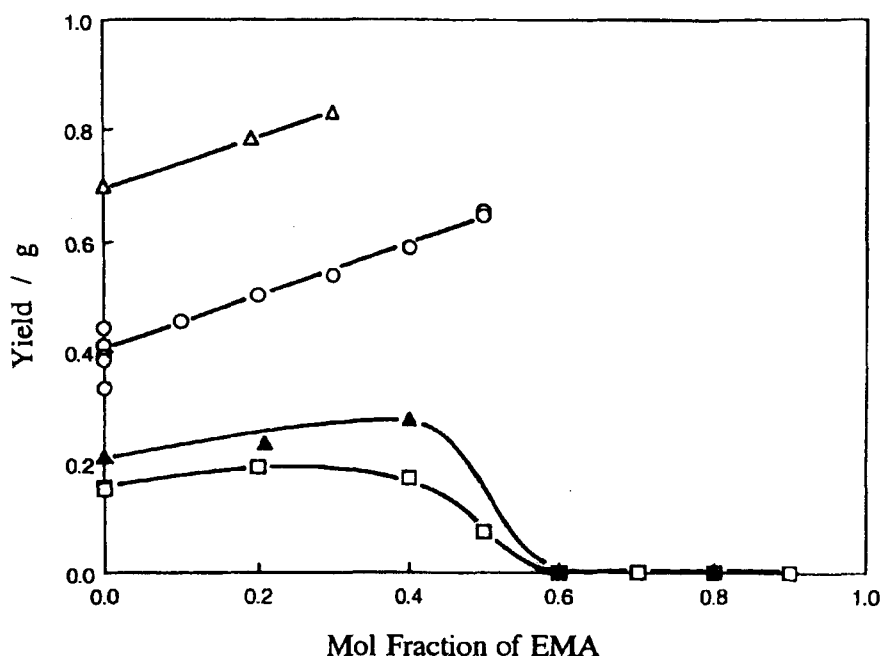
Figure 4.1.   Effect of EMA on the yield of 2EGDM based copolymer
microspheres. Each feed solution contains (□) 5 vol %, (▲) 7 vol %,
(○) 10 vol %, and (△) 15 vol % 2G.

1480 cm^{-1} and 1030 cm^{-1}. The increase of yield by adding EMA in Fig. 4.1 suggests the formation of copolymer microspheres. 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
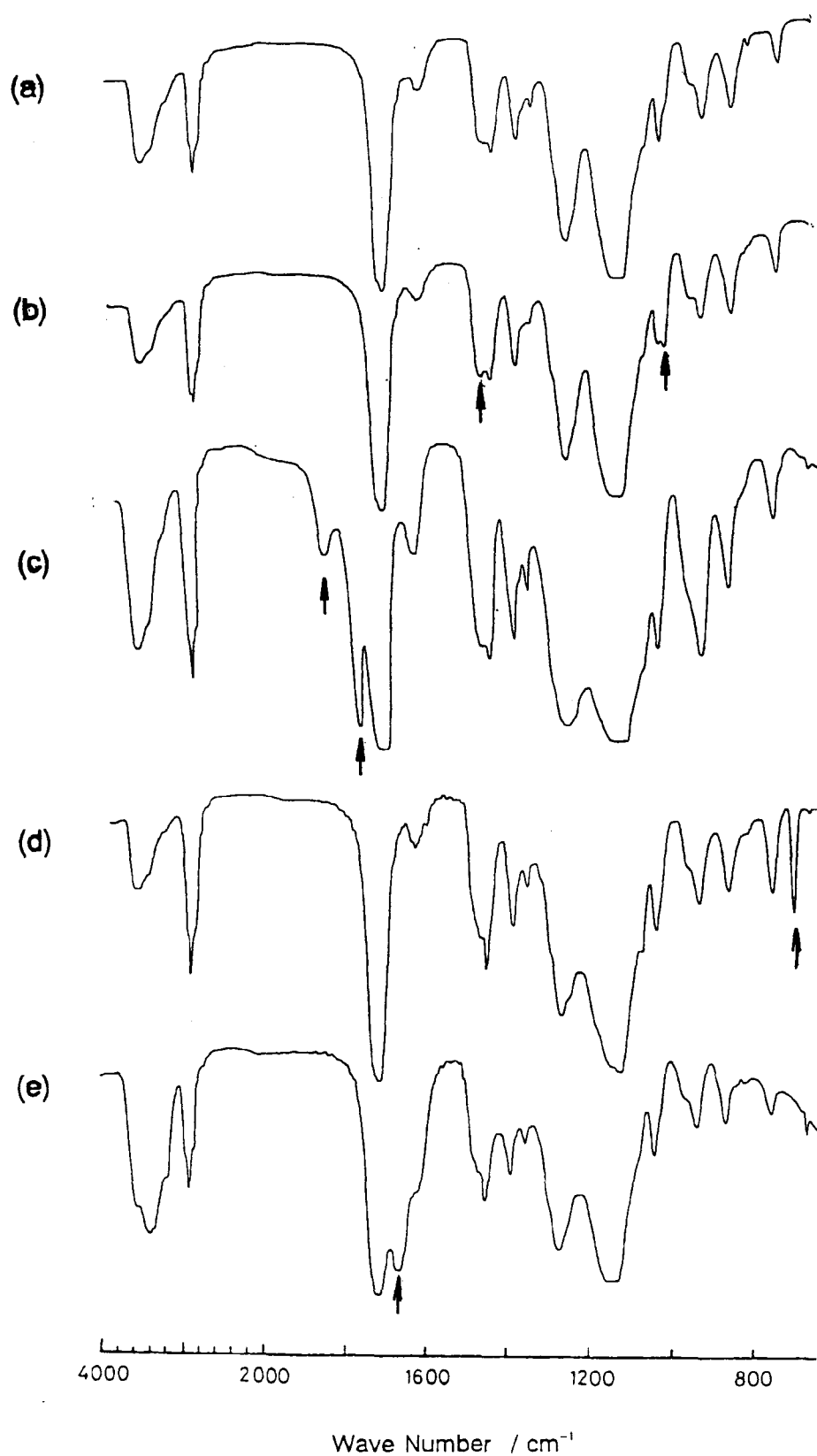
Figure 4.2.   IR spectrum of the microspheres: (a) 2EGDM, (b)
2EGDM - EMA, (c) 2EGDM - maleic anhydride, (d) 2EGDM -
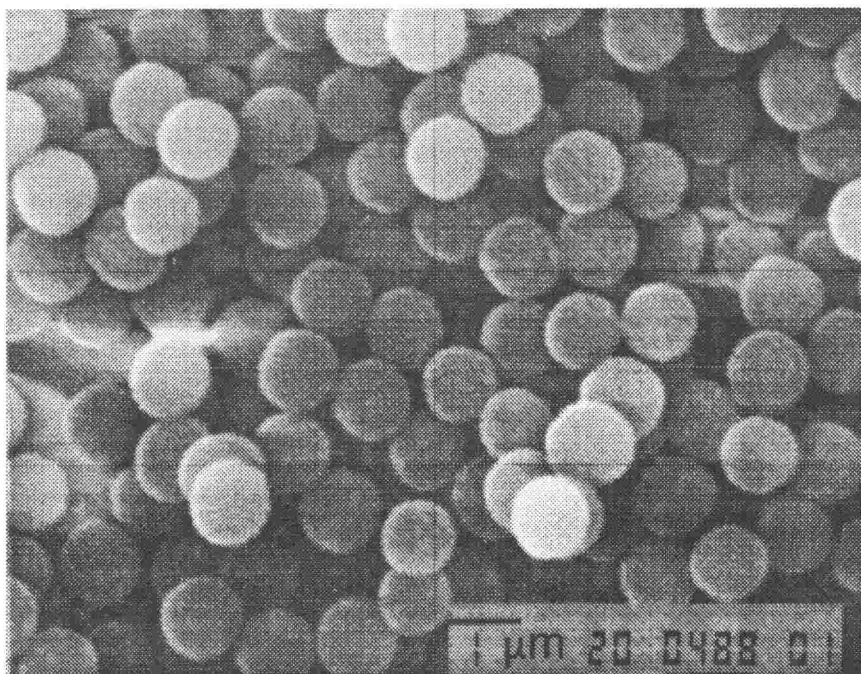styrene, (e) 2EGDM - acrylamide.

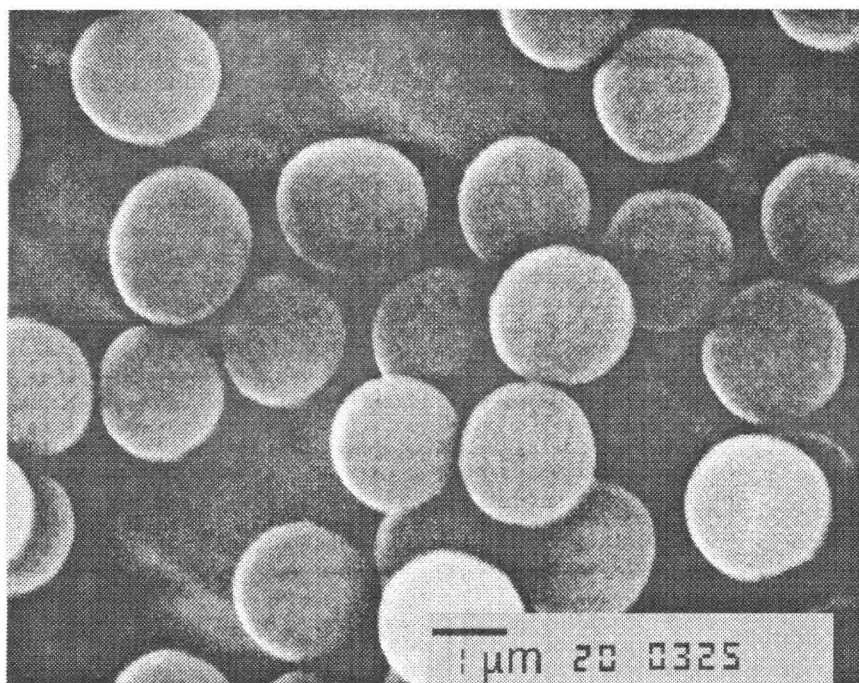Figure 4.3.   SEM photograph of 2EGDM microspheres from the 10 vol % solution

Figure 4.4.   SEM photograph of 2EGDM - EMA copolymer microspheres. Mole fraction of EMA, 0.3: 2EGDM concentration, 10 vol %.

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 %.

Figures 4.3 and 4.4 are the SEM photographs of the 2EGDM homopolymer microspheres and the 2EGDM - EMA copolymer microspheres, respectively. The size of the 2EGDM - EMA microspheres became large compared with that of the 2EGDM microspheres keeping monodispersity. The shape of the 2EGDM - EMA microspheres turned to somewhat nonspherical with increasing fraction of EMA. Figure 4.5 shows the copolymerization effect of EMA on the size of microspheres. The size of microspheres increased with increasing fraction of EMA. The
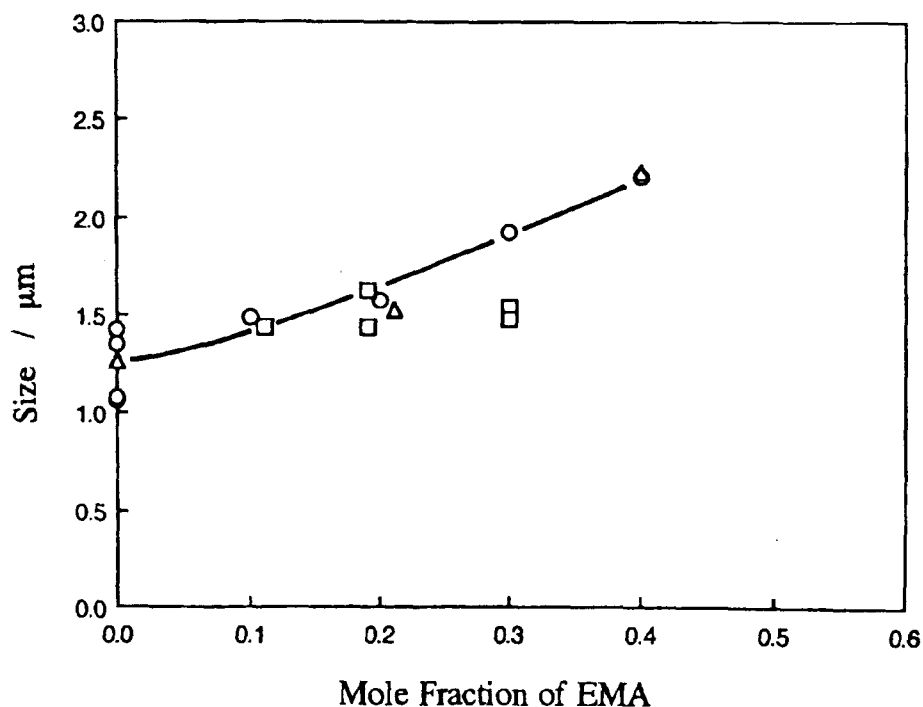

Figure 4.5.   Effect of copolymerization with EMA on the size of microspheres. Feed solutions contain (△) 7 vol % , (○) 10 vol %, and (□) 15 vol % 2EGDM.

copolymerization of 2EGDM and EMA gives large size monodisperse microspheres without a decrease in yield. There is no difference due to 2EGDM concentration. The change in size depends on the mole fraction of the monomers.

4.3.2 Copolymerization with Maleic Anhydride

Figure 4.6 shows the copolymerization effect for 2EGDM and maleic anhydride on the formation of microspheres. The weight yield of microspheres was not affected by the addition of maleic anhydride, but the IR spectrum suggests the formation of the copolymer microspheres consisting of 2EGDM and maleic anhydride as shown in Fig. 4.2(c). The absorption bands at 1780 cm^{-1} and 1850
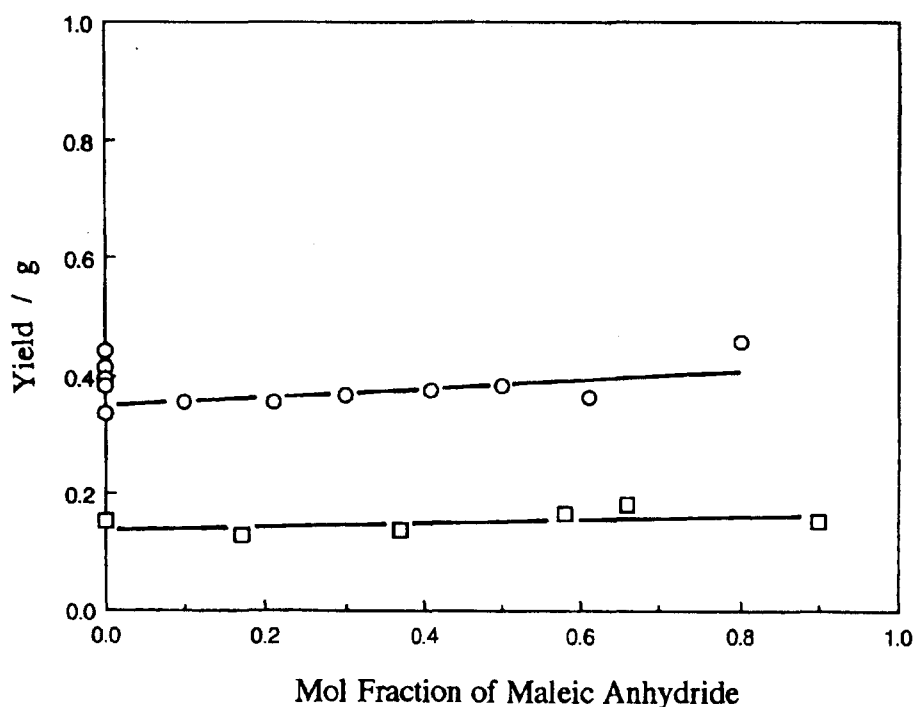
Figure 4.6. Effect of maleic anhydride addition on the weight yield of copolymer microspheres. Feed solutions contain (○) 10 vol % 2EGDM and (□) 5 vol % 2EGDM.

cm^{-1} indicate the formation of copolymer of 2EGDM and 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.

Figure 4.7 is a typical SEM photograph of the 2EGDM-maleic anhydride copolymer microspheres. The microspheres keep the sphere shape and the size distribution is narrow. Figure 4.8 shows the effect of maleic anhydride on the size of microspheres. The size of microspheres is affected neither by the fraction of maleic anhydride nor by the 2EGDM concentration. The copolymerization of
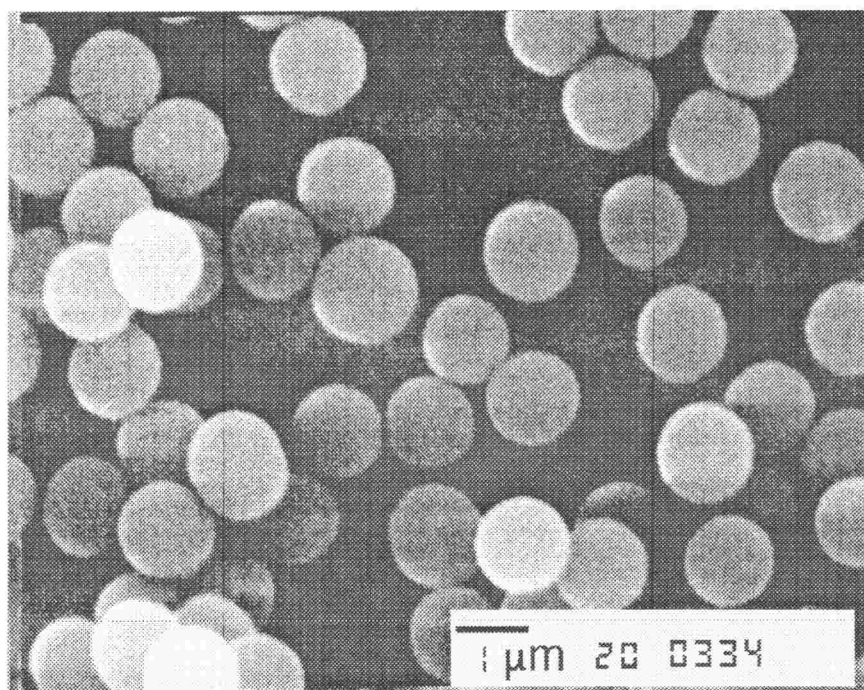

Figure 4.7.   SEM photograph of 2EGDM-maleic anhydride copolymer microspheres. Feed solution contains 10 vol % 2EGDM and 0.2 mole fraction of maleic anhydride
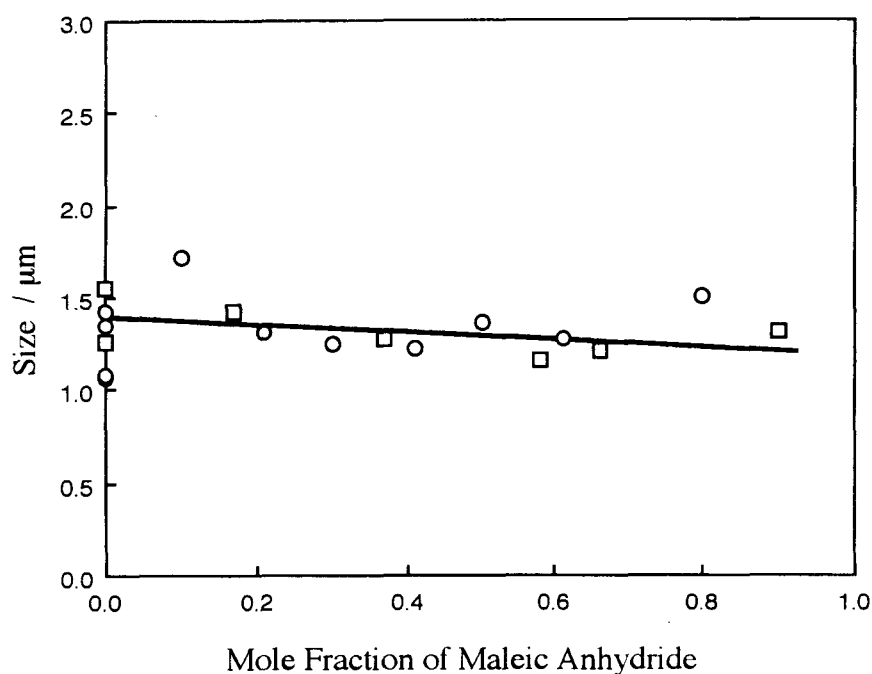
Figure 4.8. Effect of copolymerization with maleic anhydride on the size of microspheres. Feed solutions contains (○)10 vol % 2EGDM and (□) 5 vol % 2EGDM.

2EGDM and maleic anhydride gives the functional microspheres easily without changing their shape.

4.3.3 Copolymerization with Styrene

Figure 4.9 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.
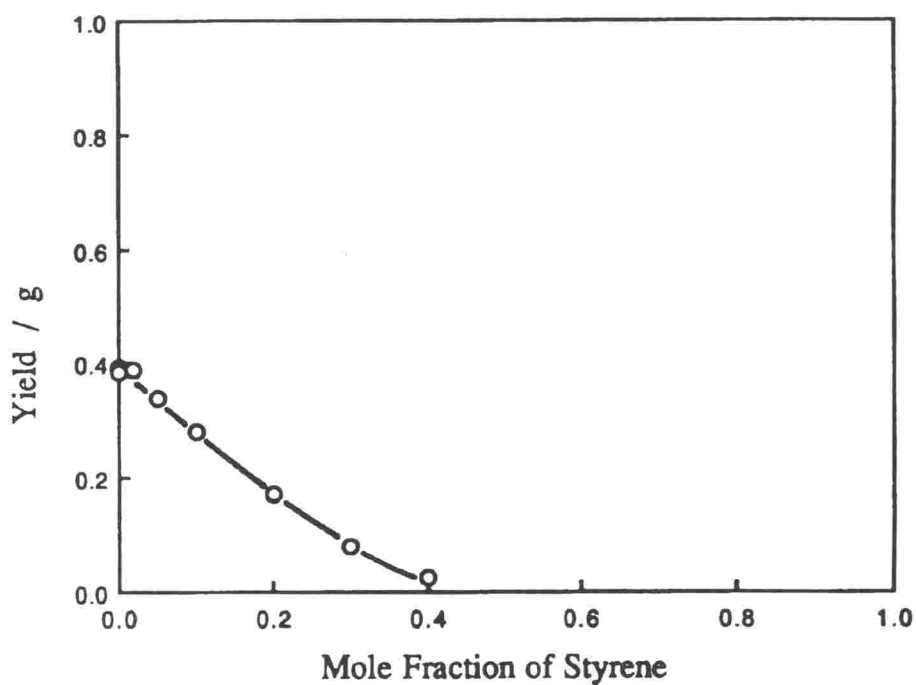
Figure 4.9.   Effect of styrene on the weight yield of copolymer microspheres. Feed solution contains 10 vol % 2EGDM.
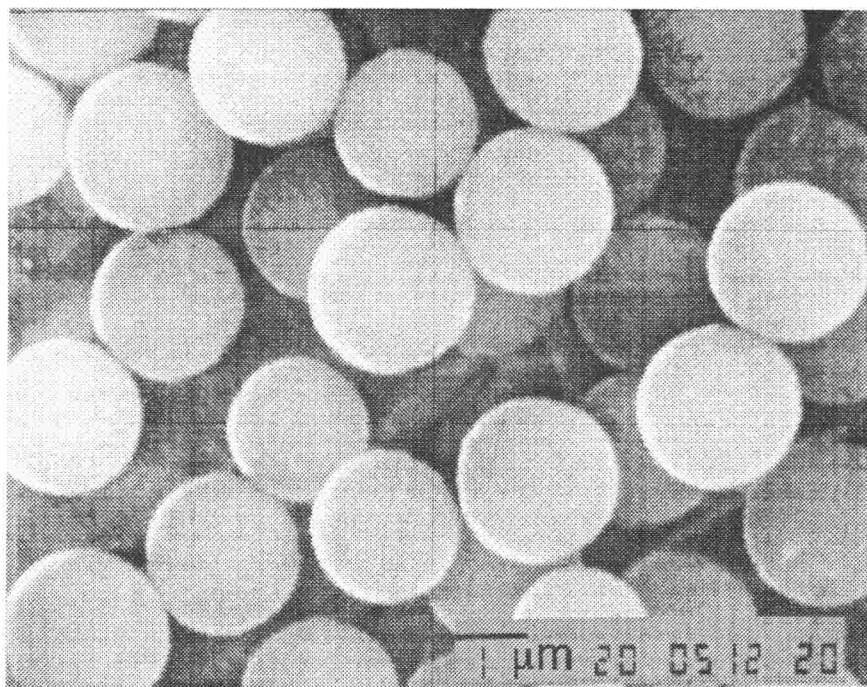

Figure 4.10.   SEM photograph of 2EGDM-styrene copolymer microspheres. Feed solution contains 10 vol % 2EGDM and 0.3 mole fraction of styrene.

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The IR spectrum suggests that the copolymer microspheres consist of 2EGDM and styrene as shown in Fig. 4.2(d). The absorption band at 700 cm^{-1} indicates the formation of copolymer of 2EGDM and styrene.

Figure 4.10 shows the SEM photograph of the 2EGDM-styrene copolymer microspheres. The shape of microspheres is also kept spherical and the size distribution is narrow. The size of the microspheres is larger than those of the 2EGDM homopolymer and 2EGDM-EMA copolymer microspheres. Figure 4.11 shows the effect of styrene fraction on the size of microspheres. The size of microspheres increases with increasing mole fraction of styrene in the feed solution. The microspheres obtained from the 0.3 mole fraction feed solution have the maximum size. The effect is more significant than the case of EMA. For
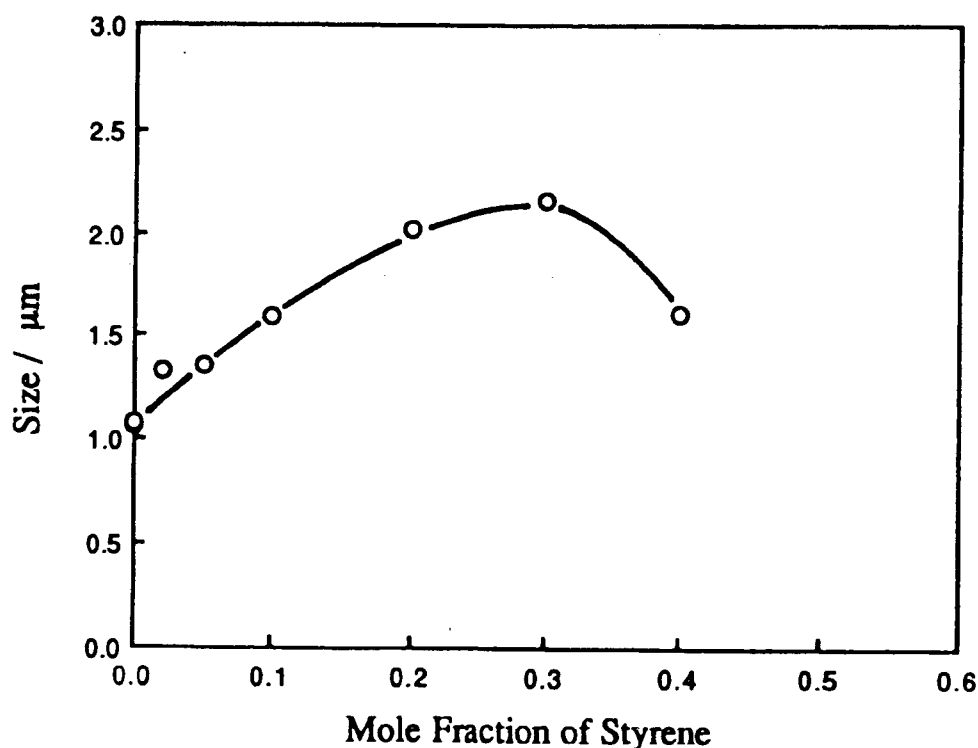

Figure 4.11.   Effect of styrene on the size of microspheres. Feed solution contains 10 vol % 2EGDM.

example, the sizes obtained from the feed solutions containing 0.2 mole fraction of EMA and styrene are 1.5 and 2.0, respectively (the both feed solutions contain 10 vol % 2EGDM).

The copolymerization of 2EGDM and styrene is 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. Figure 4.12 is the SEM photograph of the copolymer microspheres obtained from the feed solution of 10 vol % 2EGDM containing 0.2 mole fraction of styrene by 4 h irradiation. The size is 2.6 μm and the weight yield is 60 %.
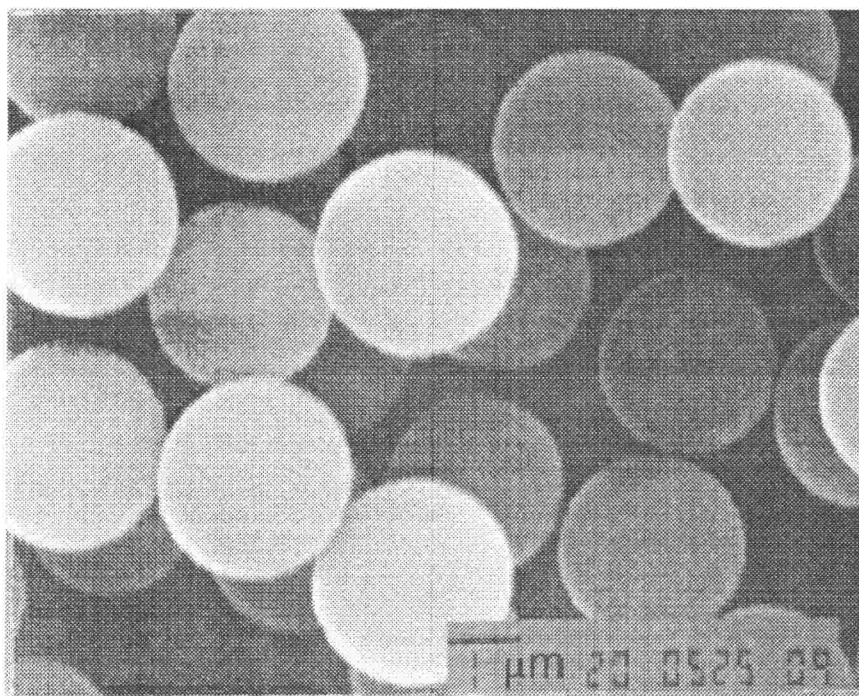

Figure 4.12. SEM photograph of 2EGDM-styrene copolymeric microspheres. Feed solution contains of 10 vol % 2EGDM and 0.2 mole fraction of styrene. Irradiation time was 4 h.
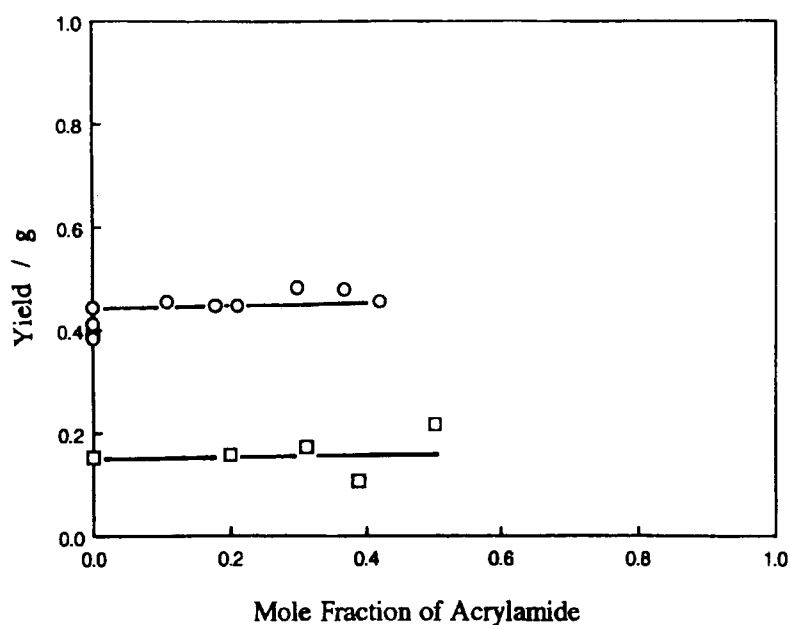
Figure 4.13. Effect of copolymerization with acrylamide on the formation of 2EGDM based microspheres. Feed solutions contain (○) 10 vol % 2EGDM and (□) 5 vol % 2EGDM.

4.3.4 Copolymerization with Acrylamide

Figure 4.13 shows the effect of copolymerization with acrylamide on the formation of 2EGDM based microspheres. The weight yield increases slightly with increasing mole fraction of acrylamide for both the feed solutions containing 5 and 10 vol % 2EGDM monomer. The decrease of weight yield was not observed, but gelation was observed when the mole fraction of acrylamide exceeded about 0.5 for the solution containing 10 vol % 2EGDM. The mole fraction of acrylamide at which the gelation occurred in the solution containing 10 vol % 2EGDM is lower than that in the 5 vol % 2EGDM solution.

Figure 4.14 is the SEM photograph of the 2EGDM-acrylamide copolymer microspheres. The shape of the microspheres is spherical and the size distribution is narrow. Figure 4.15 shows the effect of acrylamide on the size of microspheres.
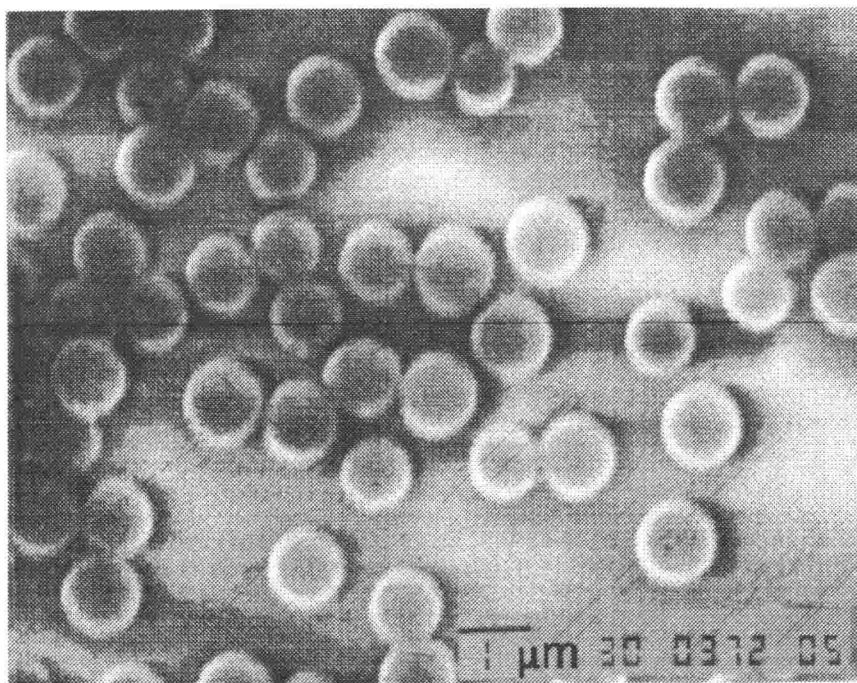
Figure 4.14. SEM photograph of 2EGDM-acrylamide copolymeric microspheres. Feed solution contains 10 vol % 2EGDM and 0.2 mole fraction of acrylamide
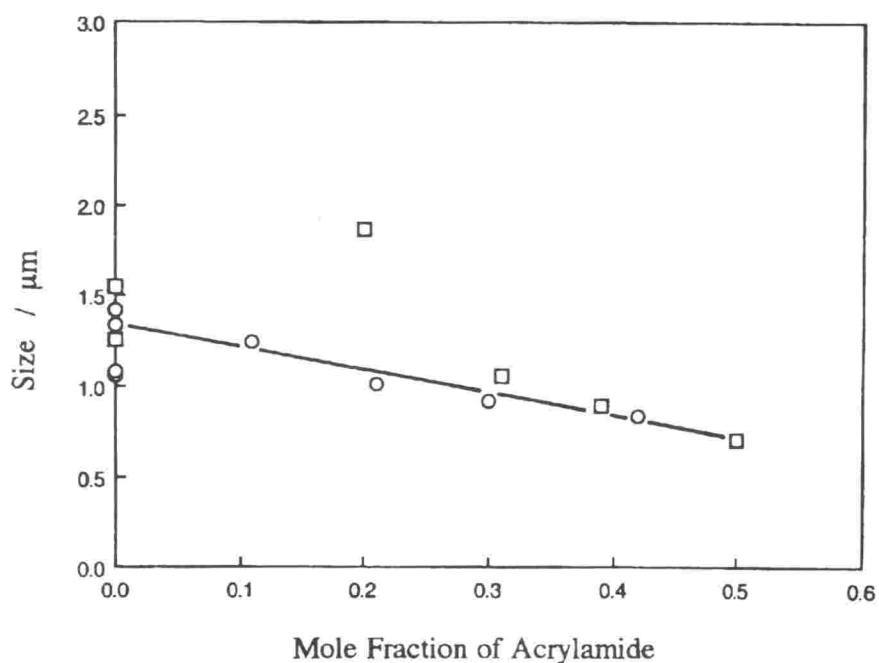

Mole Fraction of Acrylamide

Figure 4.15. Effect of acrylamide on the size of microspheres. Feed solutions contain (○) 10 vol % 2EGDM and (□) 5 vol % 2EGDM.

The size of the microspheres decreases with increasing amount of acrylamide. The addition of acrylamide causes the reduction in size. In this case, the size is not affected by the 2EGDM concentration. The change in size depends on the mole fraction of monomers similarly to the 2EGDM-EMA case (Fig. 4.5).

Figure 4.2(e) is the IR spectrum of the 2EGDM-acrylamide copolymer microspheres. The absorption band at 1675 cm^{-1} indicates the introduction of the amide group into the microspheres. Table 4.1 shows the mole fraction of monomer units in the copolymer microspheres determined from the nitrogen contents by elemental analysis. The values for the samples 311 and 313 are somewhat higher than the predicted value from monomer reactivity ratio as described below. The fractions of acrylamide unit in the microspheres are almost equal to the feed fractions of acrylamide monomer at about 80 % of conversion.

4.3.5 Cross-linking Ability

The mechanism of the microsphere formation for the homogenous 2EGDM polymerization, is quite different from the dispersion and the suspendion polymerization as described in Chapter 3. That is to say, the solubility of polymer do not contribute to the phase separation, but the cross-linkig reaction drives the particle formation. Here the effect of the copolymerization on the microsphere

Table 4.1. Elemental analysis of 2EGDM-acrylamide copolymer microspheres [a]

Run Number	Acrylamide fraction in feed	Acrylamide fraction in polymer
311	0.21	0.25
313	0.30	0.34
314	0.42	0.33

a   Solutions contain 10 vol % of 2EGDM.

formation is considered.

The observed effects of the copolymerization are the changes in microsphere size and in yield. The copolymerization gives two effects on the microsphere preparation, where bi-functional and mono-functional monomers are used. One is the effect of cross-linking ability of the mixed monomers in the feed solution. The cross-linking ability, a qualitative factor introduced here, is related to the fraction of bi-functional monomer in the feed solution and the ratio of the uptake into the polymer. The cross-linking ability decreases with increasing fraction of mono-functional monomer. The cross-linking caused by the radiation-induced polymer fragmentation is ignored. Another is the the effect of the rate of polymerization. Combination of monomers with different reactivities affects not only the overall rate of polymerization but also the ratio of monomer units in the polymer. Since one of monomers is bi-functional, both the linear propagation and cross-linking reactions are affected by mixing the monomers. The formation of the copolymer microspheres is considered to be affected by the cross-linking ability and/or polymerization rate.

In the case of the copolymerization of 2EGDM and EMA, the reactivities of the vinyl groups of the both monomers are considerd to be almost the same. The solubility parameters of 2EGDM and EMA are 8.9 (estimated in Chapter 2) and 8.3,[36] respectively. The change in solubility by varying fraction of monomers is small. Therefore, the solubilty change can be negligible. Two EMA molecules are stipulated to be one 2EGDM monomer divided into almost equal parts. The change caused by the copolymerization is due to the cross-linking ability depending on the ratio of di-vinyl and mono-vinyl monomers.

Figure 4.16 shows the three-component diagram for the microsphere formation. The area that gives microspheres is small. The formation of microspheres seems to be the special case of gelation. Homogeneous 2EGDM monomer solutions give microspheres in the range 2 to 24 vol % in ethyl acetate.
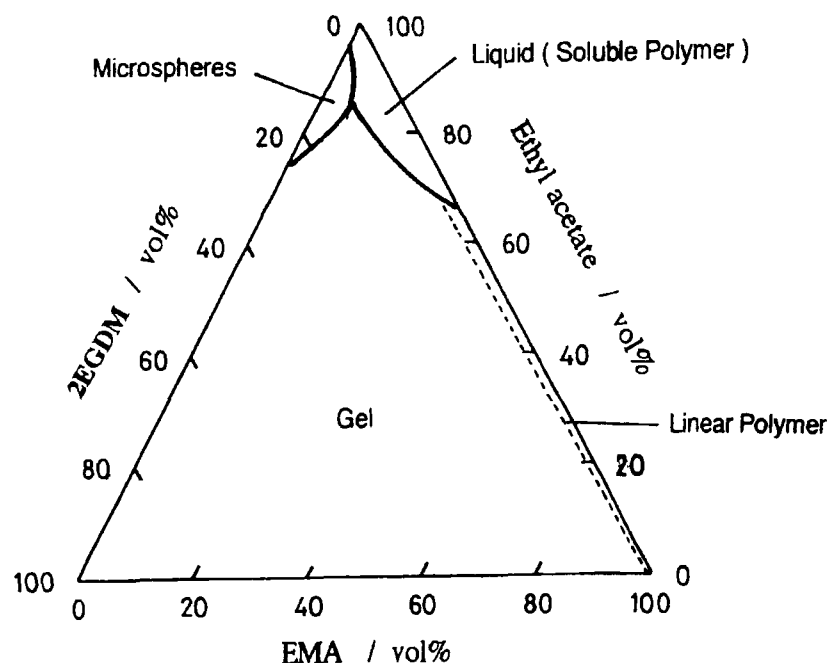
Figure 4.16.   Three-component diagram for the microsphere
formation.

The allowed region for the formation of the copolymer microspheres of 2EGDM
and EMA is rather narrow compared to that for the homogenueous 2EGDM
system. In Fig. 4.1, the gelation is observed at 0.6 of EMA mole fraction for the
10 vol % 2EGDM solution and at 0.4 for the 15 vol % 2EGDM solution. The total
monomer volume concentrations of these feed solutions are 13.7 vol % and 18.2
vol %, respectively. These concentrations are lower than the upper limit of
monomer concentration giving microspheres for the 2EGDM homogeneous
solution, 24 vol %. The total concentrations of vinyl groups of the above solutions
correspond to 1.54 and 1.76 mol dm^{-3} for the EMA mole fraction of 0.6 and 0.4,
respectively. These concentrations are also lower than 2.12 mol dm^{-3} (the vinyl
group concentration of 2EGDM homogeneous solution at 24 vol %). These
results indicate that the addition of monomer with a single vinyl group gives the
gelation more easily than the addition of the monomer with double vinyl groups.
These suggest that the increase of the total monomer concentration is not the

reason for the gelation, and that the solution with high cross-linking ability easily gives microspheres. Although the excess concentration of 2EGDM causes the gelation, 2EGDM is more favorable for the microsphere formation than the monomer with single vinyl group. Thus, the comonomer acts like as an inhibiter to the formation of microspheres.

Thus, It is considered that the cross-linking ability is a very important factor for the formation of the microspheres. The first vinyl group (one vinyl group of 2EGDM monmer) contributes to the propagation reaction, and second vinyl group (remaining vinyl group of 2EGDM monmer unit in the polymer), to the cross-linking reaction. The growing mechanism consists of two processes proceeding simultaneously, that is, expanding and shrinking processes as described in Chapter 3. Although it is difficult to distinguish these two processes in the actual polymerization, it seems reasonable to consider that the expanding and shrinking processes are due to linear propagation and crosslinking reactions, respectively.

4.3.6   Effect on the Size

The factor that affects the size of microspheres is the ratio of 2EGDM and comonomer, but not 2EGDM concentration as shown in Figs. 4.5 and 4.13. This indicates that the character of microspheres depends on the ratio of monomers. An increase of the EMA ratio in the feed solution reduces the cross-linking ability. By assuming the reactivity of 2EGDM and EMA are comparable, the major effect of EMA is the decrease of the cross-ininking ability. The decrease of the cross-linking ability is considered to result in the decrease of shrinking and then the expanding of the region of a microsphere.

The number of microspheres in the solutions can be calculated from the weight yield and the size of microspheres. Since it is very difficult to know the density of copolymer microspheres, I assume that the density of copolymer

microspheres is constant and equal to that of bulk 2EGDM polymer, 1.24 (the calculation error caused by this estimation is at most 10%). Figure 4.17 shows the relations between mole fractions of comonomers and numbers of microspheres in the suspension during the polymerization. The number of microspheres obtained from the 2EGDM and EMA solutions decreases with increasing mole fraction of EMA. It is proper that the region occupied by one microsphere determines the number of microspheres in the solution.[16] Thus, the region of one microsphere in the solution expands with increasing mole fraction of mono-vinyl comonomer such as EMA and styrene.

The reason for the gelation of the solution containing high concentration of 2EGDM monomer (10 and 15 vol %) are considered to be that the expanding exceeds the shrinking and then the region of one particle reachs to that including the neighboring particles. The decrease in weight yield with increasing mole fraction of EMA for the feed solution containing low concentration of 2EGDM (5 and 7 vol %), shown in Fig. 4.1, suggests that the decrease of the cross-linking ability reduces the ability of the particle formation. Perhaps the termination reaction became predominant compared to the cross-linking reaction for the solution containing low concentration of 2EGDM monomer.

Table 4.2. Estimated monomer reactivity ratio and monomer ratio in polymer.

Monomer1	Monomer2	$r_1{}^a$	$r_2{}^a$	Ratio in polymer [b]
$[M_1] = 0.8$	$[M_2] = 0.2$			$d[M_1] : d[M_2]$
MMA	EMA	1.0	1.0	0.80 : 0.20
	Maleic anhydride	4.0	0.01	0.94 : 0.06
	Acrylamide	3.0	0.8	0.92 : 0.08
	Stylene	0.45	0.52	0.71 : 0.29

a   Estimated value from the reference 36

b $\dfrac{d[M_1]}{d[M_2]} = \dfrac{[M_1]}{[M_2]} \times \dfrac{r_1[M_1]+[M_2]}{[M_1]+r_2[M_2]}$, from the reference 38

The microspheres obtained are monodisperse in their sizes (Figs. 4.3, 4.4, 4.8, 4.11, 4.12, 4.15). This suggests that the number of microspheres in the solution does not change during the polymerization period. The number of microspheres is determined in a very early stage of the polymerization.[32] Therefore it is considered that the initial conditions, i.e., monomer compositions in the feed solution, determine the feature of microsphere. It is easy to know the initial ratio of monomer units in the polymer from the monomer reactivity ratio.[36] Table 4.2 shows an estimation of the monomer reactivity ratio (r_1, r_2) for the monomers used in this study and the calculated initial ratio of monomer units in the polymer. There seems to be no relation between the monomer reactivity ratio and the characteristics of microspheres.

Maleic anhydride is well known as a comonomer that gives an alternative copolymer. The monomer reactivity ratio, r_1 and r_2, are about 5 and 0.01, respectively. Therefore the maleic anhydride unit never appears next to maleic anhydride units. The cross-linking ability is almost constant even if maleic anhydride is added. The cross-linking ability is not reduced in the copolymerization with maleic anhydride. In the case of the copolymerization of 2EGDM and EMA, the number of monomer units in EMA blocks is greater than one, thus the decrease of the cross-linking ability is greater than that predicted from the feed solution. In spite of the formation of the copolymer microspheres, the effect of copolymerization with maleic anhydride is small. This result also suggests the importance of cross-linking for the formation of microspheres.

The order of the rate constant of the propagation reaction, k_p, for the homopolymerization system is:[36]

$$Acrylamide > EMA > Styrene.$$

The reactivity of styrene is the lowest among the monomers used in this study.

Since the rate of styrene is low, the weight yield of the microspheres is decreased by copolymerization. The calculated ratio of styrene units in the polymers, 0.29, is higher than the ratio of styrene in the feed solution, 0.2, (Table 4.2). Therefore the effect of copolymerization with styrene is larger than those with the other monomers. Both the low reactivity of styrene and the high ratio of monomer units in the polymer cause the rapid decrease in yield in Fig. 4.9.

On the other hand, in spite of the low reactivity of styrene, the size of microsphere obtained from the copolymerization of 2EGDM and styrene is extremely large. This result is explained as follows. The decrease of the cross-linking ability by styrene is the highest, and the spread of region of a microspheres is also the largest. The spread of region of a microsphere causes the extreame decrease of the number of the microsphere (Fig. 4.17). The effect of the decreased
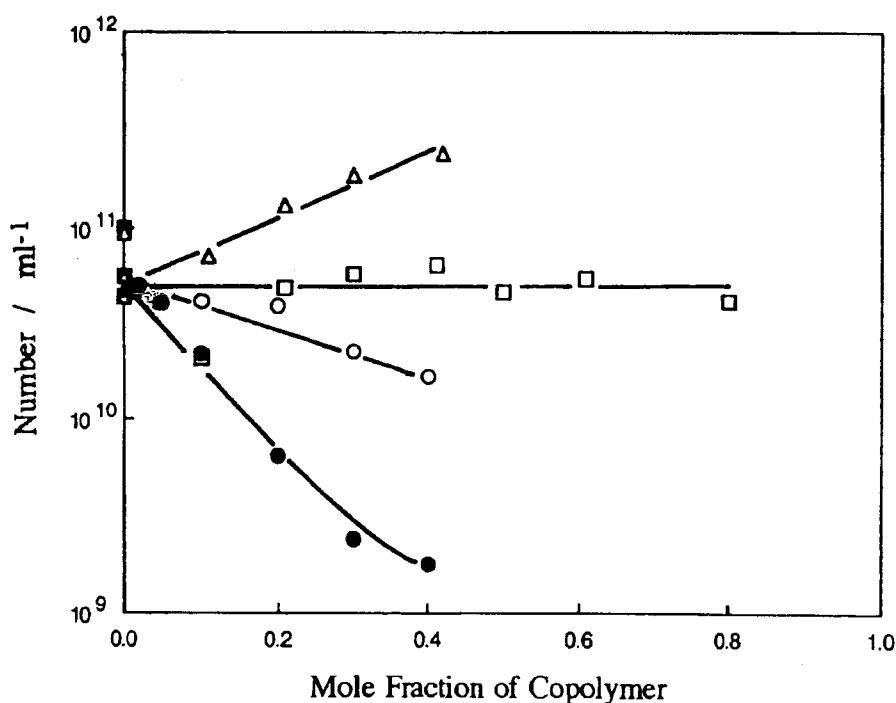

Figure 4.17. Relation between mole fraction and the number of microspheres. ($\square$) 2EGDM - maleic anhydride, ($\triangle$) acrylamide, ($\bigcirc$) EMA, and ($\bullet$) styrene.

number is larger than the decrease of the polymerization rate.

The size of the microspheres obtained from 2EGDM and acrylamide is small. The reason for the decrease in size by the copolymerization with acrylamide is considered to be an increase of shrinking. The number of microspheres decreases with incresing mole fraction of acrylamide (Fig. 4.17). The calculated initial ratio of acrylamide units in the polymers, 0.08, is lower than the ratio in the feed solution, 0.2, (Table 4.2). Therefore the effect of the copolymerization with acrylamide is not so important. On the other hand, the rate constant of propagation reaction of acrylamide, k_p, is the highest among the monomers used in this study. It is considered that the high reactivity of acryl amide enhances the shrinking ability. Perhaps, this causes the suppression of the expanding of the region of a microsphere and increases the number of microspheres. The result in Fig. 4.13 (mark □) that the weight yield does not decrease for the feed solution containing 5 vol % 2EGDM can be explained by this effect, i.e., by the increased ability of shrinking by copolymerization with acrylamide.

4.4 Conclusion

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. The factors affecting the formation of microspheres are the cross-linking ability due to the copolymerization with mono-functional monomer and the reactivities of the comonomers.

Chapter 5

Preparation of Nonspherical Fine Particles

5.1 Introduction

Dispersion polymerization or emulsion polymerization are commonly used to prepare the micrometer range size polymer particles.[13-26] Seed polymerization is a well known method for producing monodisperse large polymer particles.[39] It consists of two polymerization processes: (1) the preparation of seed particles by emulsion polymerization, (2) the second polymerization of seed particles that include swelled monomer. The added monomer spreads from inside to outside of the seed partilce and serve to grow particles to larger microspheres. Giving dimension stability by adding a small amount of a cross-linking agent to the seed at the first stage, the added monomer spreads from one point of the surface and gives non-spherical particles instead of large spherical particles.[40-46]

As described in the previous chapters, the formation process of the diethylene glycol dimethacrylate (2EGDM) microsphere is quite different from other common methods, e.g., dispersion polymerization or emulsion polymerization. Having two vinyl groups on 2EGDM monomer causes the formation of microspheres. The stirring during the polymerization gives aggregated particles as described in Chapter 1. A contact of the particles causes joining and gives aggregated particles. It is expected that the suitable vibration gives an joined particle from two microspheres. Ultrasonic vibration is used to cause suitable contact between the microspheres during the polymerization. A

short vibration during the polymerization is expected to give information about the microsphere formation.

5.2 Experimental

Materials and Polymerization. The sealed samples were prepared as described in the previous chapters. A ultrasonic vibration washer (frequency is around 50 k Hz with little fluctuation) is used as a vibration apparatus (Fig. 5.1). The power supply unit is separated from vibration and protected from γ radiation. The samples were irradiated with ^{60}Co γ rays. The dose rate was 4 kG h^{-1} and the irradiation time was 2 h at room temperature. All other treatments were the same as described in the previous chapters
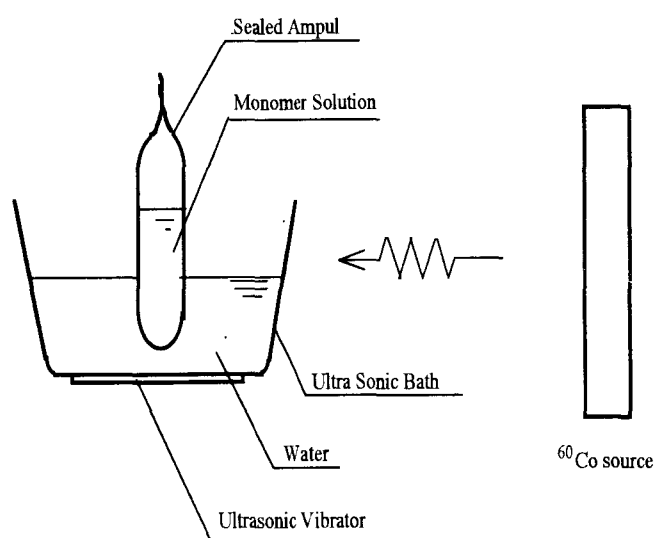
Figure 5.1.   Radiation-induced polymerization with ultrasonic vibration. Frequency of the ultrasonic vibration is around 50 kHz.

5.3 Results and Discussion

5.3.1   Monomer Concentration

Figure 5.2(a) shows the SEM photograph of the particles obtained from the polymerization with ultrasonic vibration applied for 10 min from the beginning of the polymerization. The shape of the obtained particle is the same as that of the microsphere obtained from the normal method. There is no effect of the ultrasonic vibration. When the ultrasonic vibration is applied from 20 to 30 min during the polymerization, some nonspherical particles are observed as shown in Fig. 5.2(b).
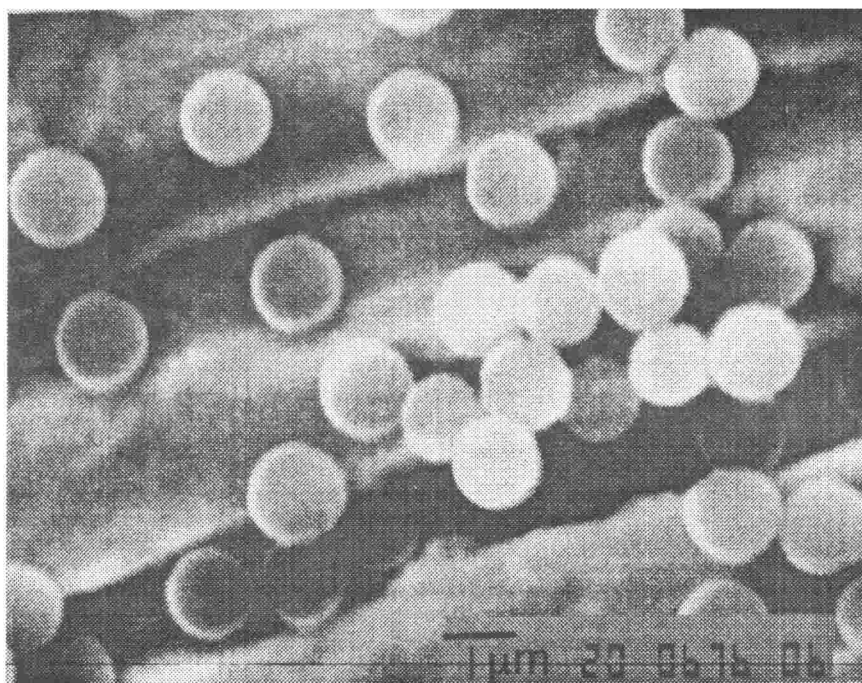
(a)

Figure 5.2.   SEM photographs of particles obtained from the solution of 5 vol % monomer. Ultrasonic vibration was applied (a) 0-10 min, (b) 20-30 min, (c) 40-50 min, (d) 60-70 min, and (e) 80-90 min.
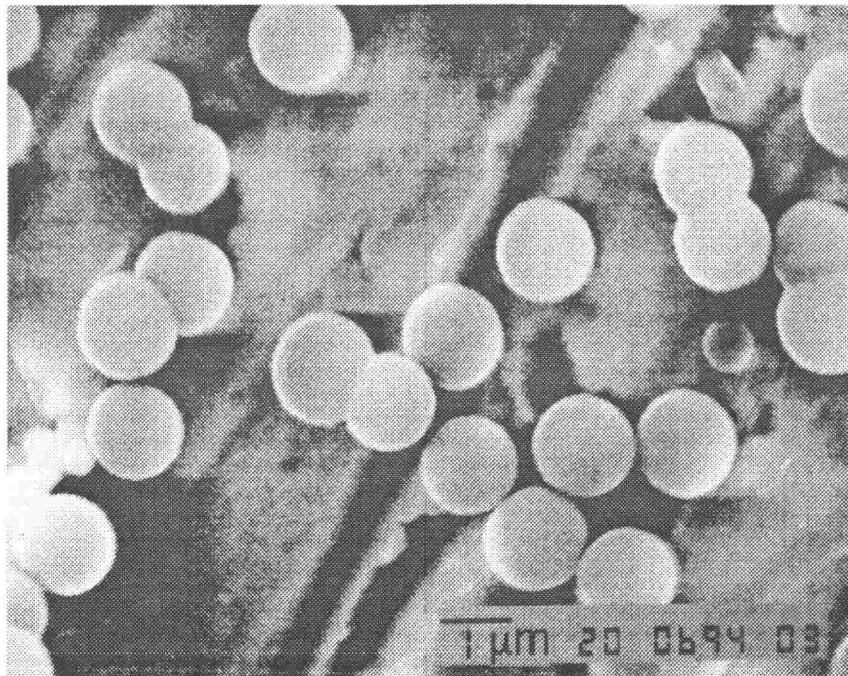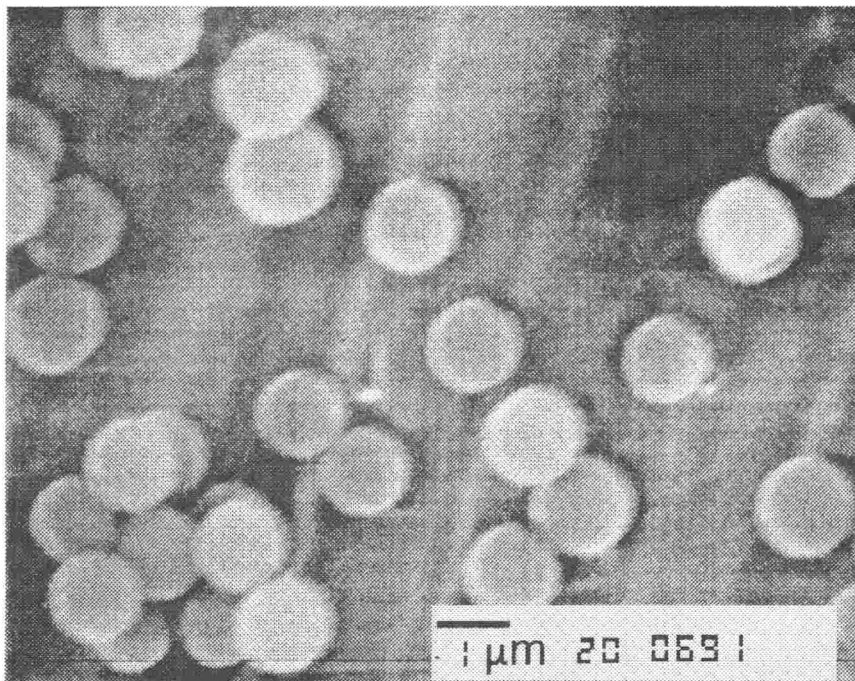
(b)
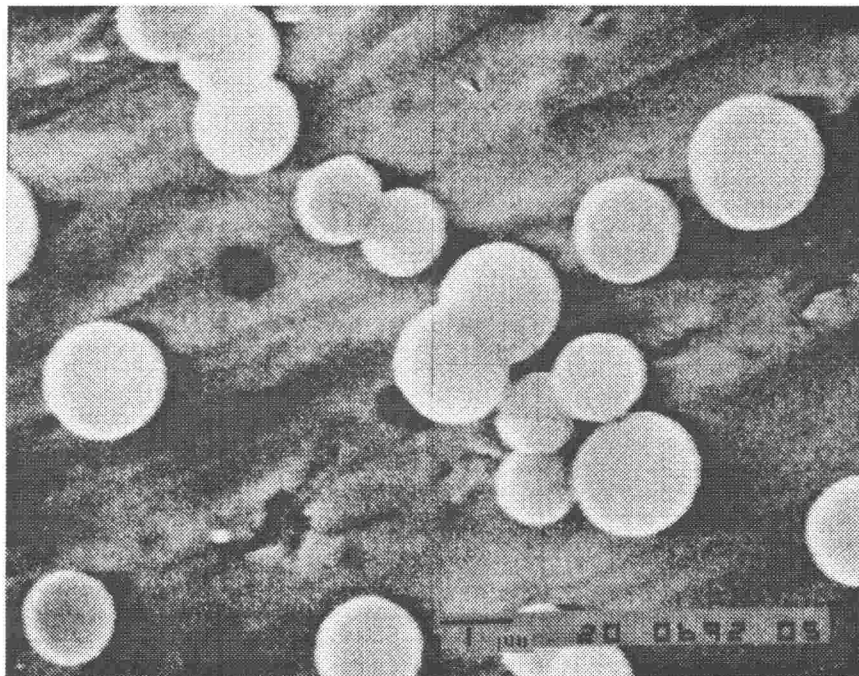
(c)

Figure 5.2.   (Continued from the previous page)
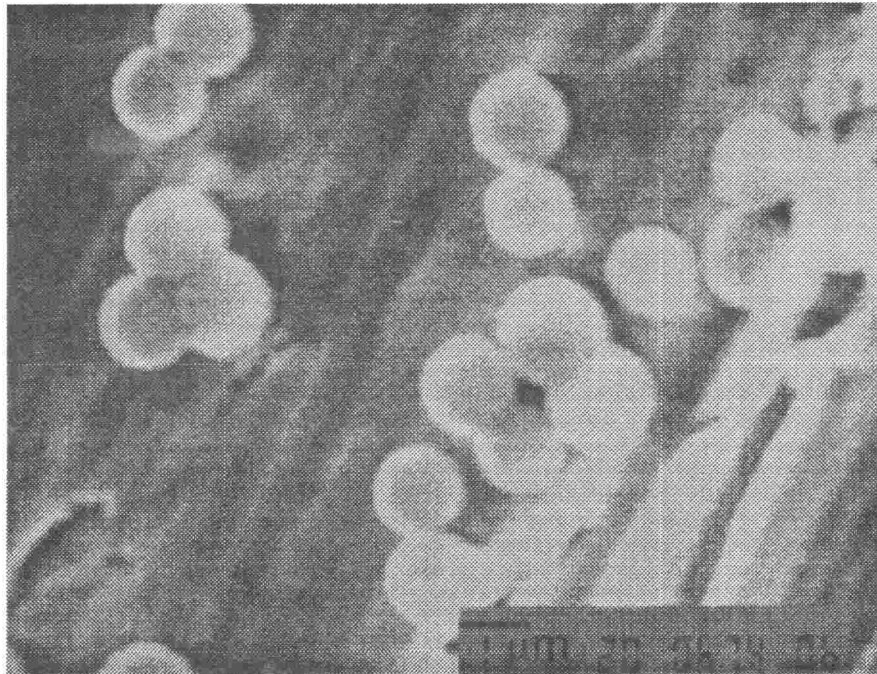
(d)

(e)

Figure 5..   (Continued from the previous page)

Their shapes are like gourd, cocoon, or pear, suggesting that the particles are generated by joining two particles. The whole shape is a partial penetration of two spheres. The size of sphere part is the same as that of the complete spherical particle. Polymerization with the ultrasonic vibration from 40 to 50 min and from 60 to 70 min also gave non-spherical particles as shown in Figs. 5.2(c) and 5.2(d). Non-spherical particles were not obtained in the polymerization with the ultrasonic vibration from 80 to 90 min during the polymerization as shown in Fig. 5.2(e).

Figure 5.3(a) shows the SEM photograph obtained from the polymerization with the ultrasonic vibration given for 10 min from 40 to 50 min of the polymerization time. Polymerization with ultrasonic vibration from 40 to 50 min and from 60 to 70 min gave non-spherical particles as shown in Figs. 5.3(a) and 5.3(b). Non-spherical particles were not obtained in the polymerization with ultrasonic vibration from 80 to 90 min .

Figures 5.4(a) and 5.4(b) show the non-spherical particles obtained by the polymerization with the ultrasonic vibration from 40 to 50 min and from 60 to 70 min for the sample containing 15 vol % 2EGDM monomer. Figures 5.5(a) and 5.5(b) show the non-spherical particles obtained by the polymerization with the ultrasonic vibration from 40 to 50 min and from 60 to 70 min for the sample containing 20 vol % of 2EGDM monomer. Non-spherical particles are obtained from the 15 vol % solution with somewhat distortion. There are lots of nonspherical particles obtained from the 20 vol % solution without smoothness. The polymerization without ultrasonic vibration gives particles with rough surface. The effect of the ultrasonic vibration is not clear on the 20 vol % solution.

The yield of the doublet particle is lower for the 10 % solution than for the 5 vol % solution, although their sizes are almost the same. The doublet nonspherical particles obtained from the 15 vol % solution show somewhat distortion. The ratio of nonspherical particles is high in the case of the 20 vol % solution. Originally,
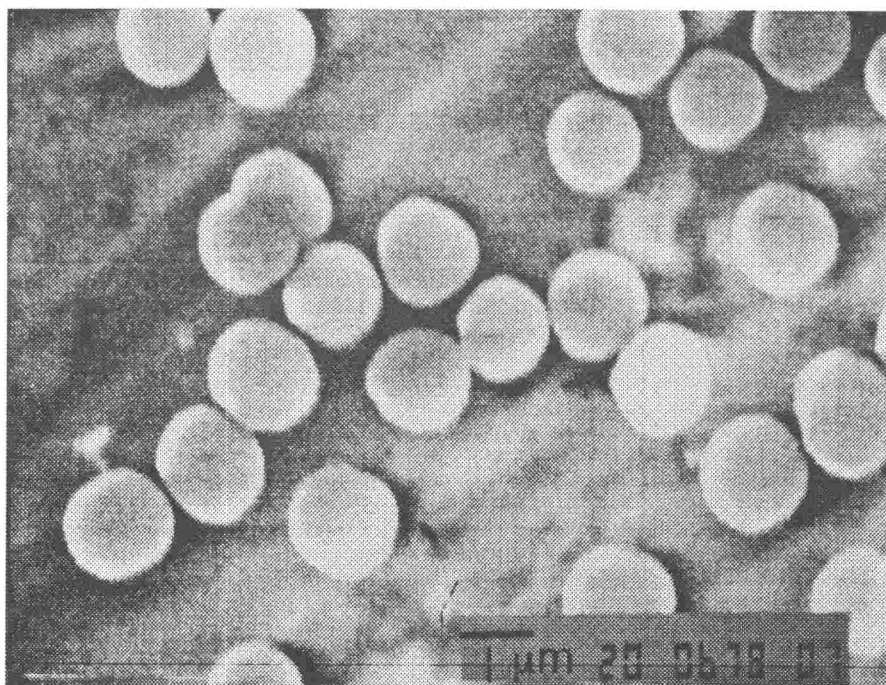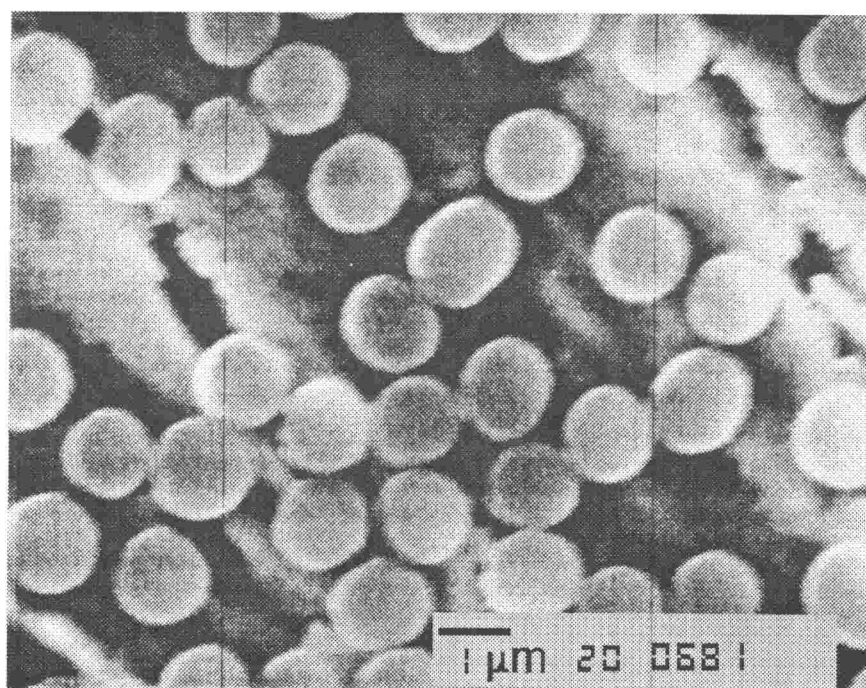
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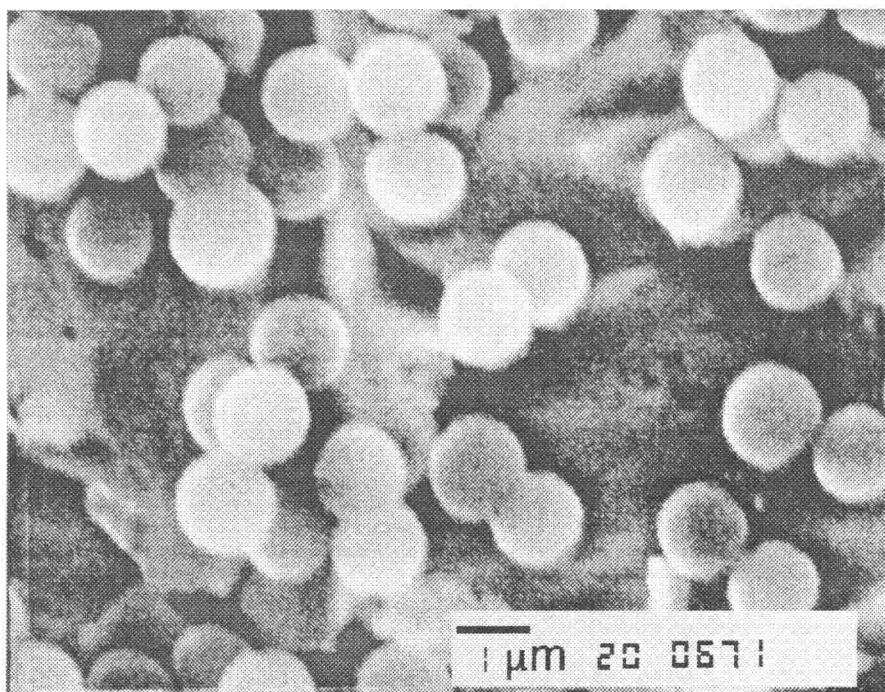
(a)
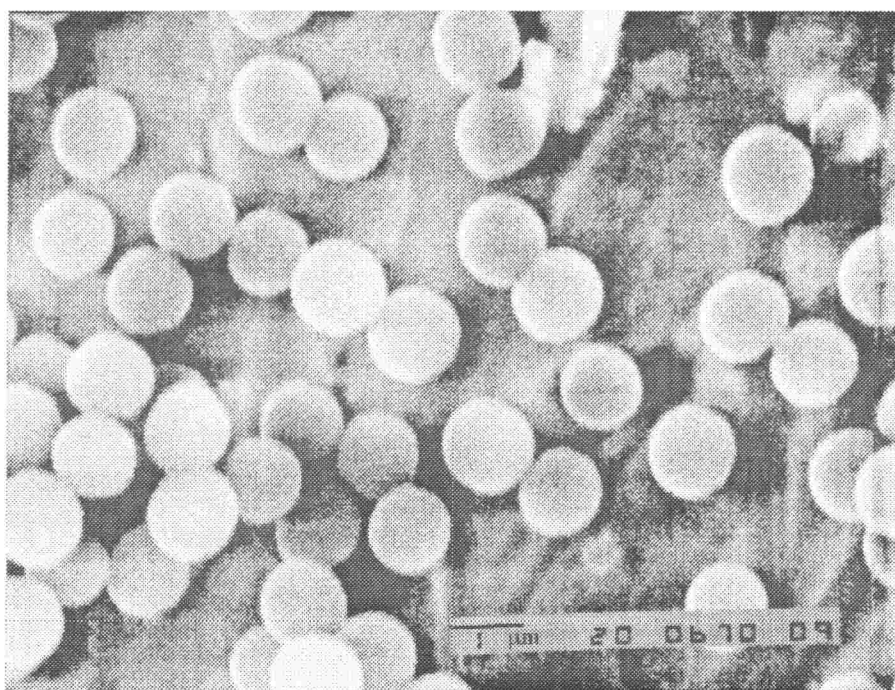
(b)

Figure 5.3.   SEM photograph of particles obtained from the solution of 10 vol % monomer. Ultrasonic vibration was applied for the duration of the polymerization time (a) 40-50 min and (b) 60-70 min.
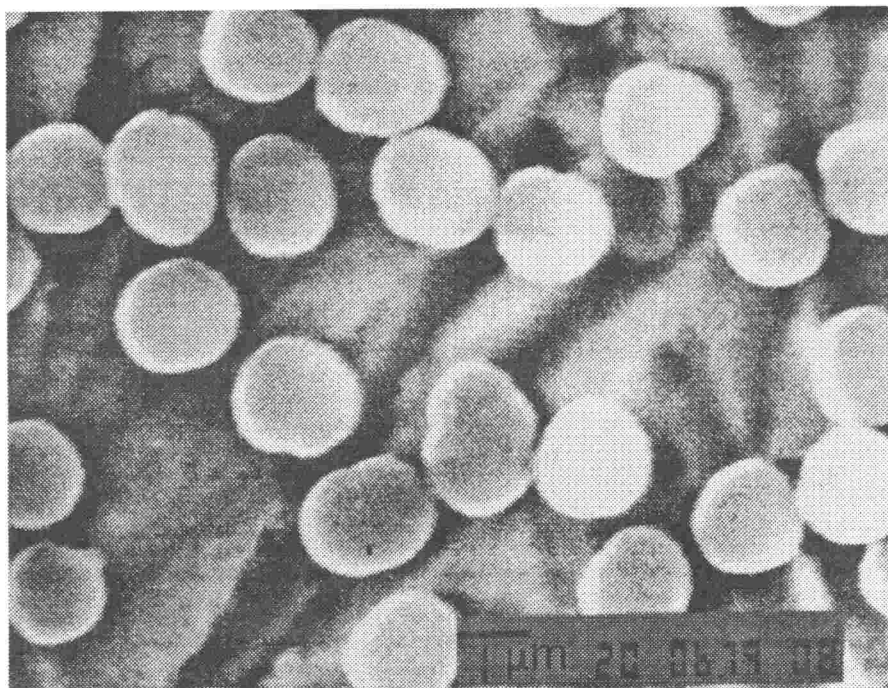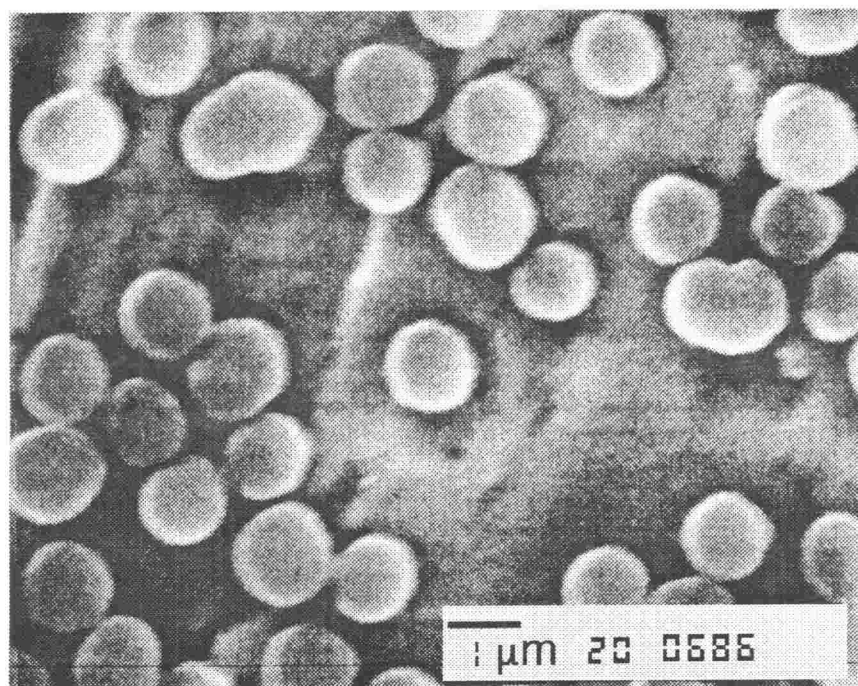
(a)

(b)

Figure 5.4.   SEM photograph of particles obtained from the solution of 15 vol % monomer. Ultrasonic vibration was applied for the duration of the polymerization time (a) 40-50 min and (b) 60-70 min.

(a)

(b)

Figure 5.5.   SEM photograph of particles obtained from the solution
of 20 vol % monomer. Ultrasonic vibration was applied for the duration
of the polymerization time (a) 40-50 min and (b) 60-70 min.

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the shape of particles obtained from the 20 vol % solution is not spherical and has rough surfaces. It is difficult to distinguish whether the high concentration or ultrasonic vibration is responsible for the result. The effective concentration giving nonspherical particle with smooth surface is around 10 vol %.

5.3.2   Time Dependence of the Application of Ultrasonic Vibration

The yield and the size of the microspheres are 80 to 90 % and around 1.2 μm, respectively, when the polymerization is carried out without ultrasonic vibration at the polymerization time of 2h. The doublet nonspherical particles are obtained effectively from the polymerization with ultrasonic vibration for 10 min at 40 and 60 min from the beginning of the polymerization. These periods are the time that 50 % of the monomer is consumed. Although the space of particle contacting each other is not clear, the remaining monomer polymerizes on the contacted microspheres and surrounds the surface to give doublet nonspherical particles. Giving ultrasonic vibration at the beginning of the polymerization is not effective to get doublet nonspherical particles. The nuclei may be too small to come into contact by the ultrasonic vibration. With ultrasonic vibration for the period from 80 to 90 min no doublet nonspherical particle is observed. This period is almost the end of the polymerization and the remaining monomer concentration is too low to help the connection of the particles. Even if the particles contacted, it may be too late for growing to the doublet particles. It is difficult to distinguish whether the joining of microspheres is taken place or not. The middle of the polymerization period is effective to obtain doublet nonspherical particles by giving ultrasonic vibration.

5.3.3   Shape of the Particle

Figures 5.6(a)-5.6(d) show the growing scheme of the doublet nonspherical particles. Under the normal conditions, without ultrasonic vibration, each microsphere grows independently as shown in figure 5.6(a). Ultrasonic vibration causes a contact of the neighboring two microspheres during the growth of the microspheres shown as Fig. 5.6(b). The growth keeping contact gives joined particles shown as Fig. 5.6(c) and 5.6(d). If the border of the microspheres is completely stable, a contact does not give joined particle. On the other hand, if the border of the microspheres during the polymerization is not stable, no microspheres is obtained. The border between microspheres is considered as meta-stable during the polymerization.

The shape of nonspherical particles is the penetration of two spheres as shown in Fig. 5.7(a), not cocoon shaped as shown in Fig. 5.7(b). The boundary line of two parts of spheres remains clearly. The doublet particle does not have smooth surface at the border as shown Fig. 5.7(b). The half of the doublet particle
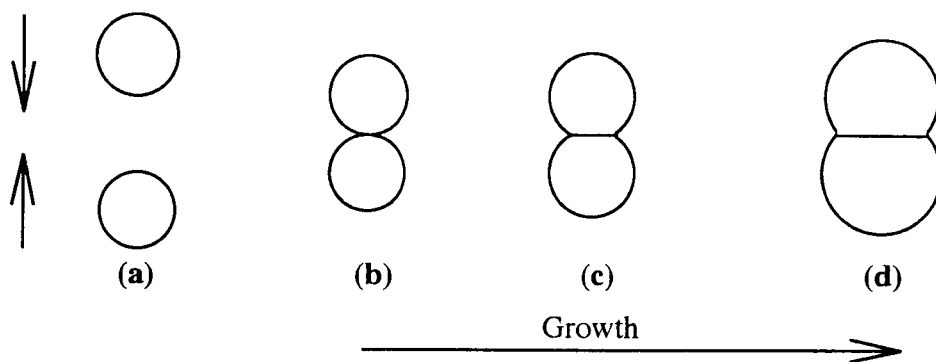

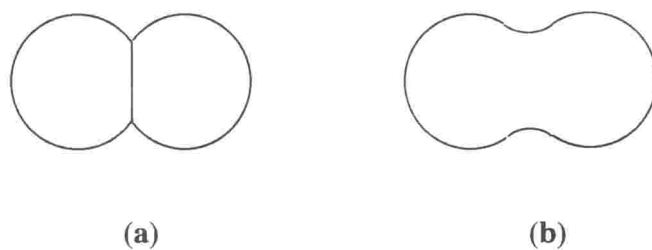Figure 5.6.   Formation process of the nonspherical particles by ultrasonic vibration.

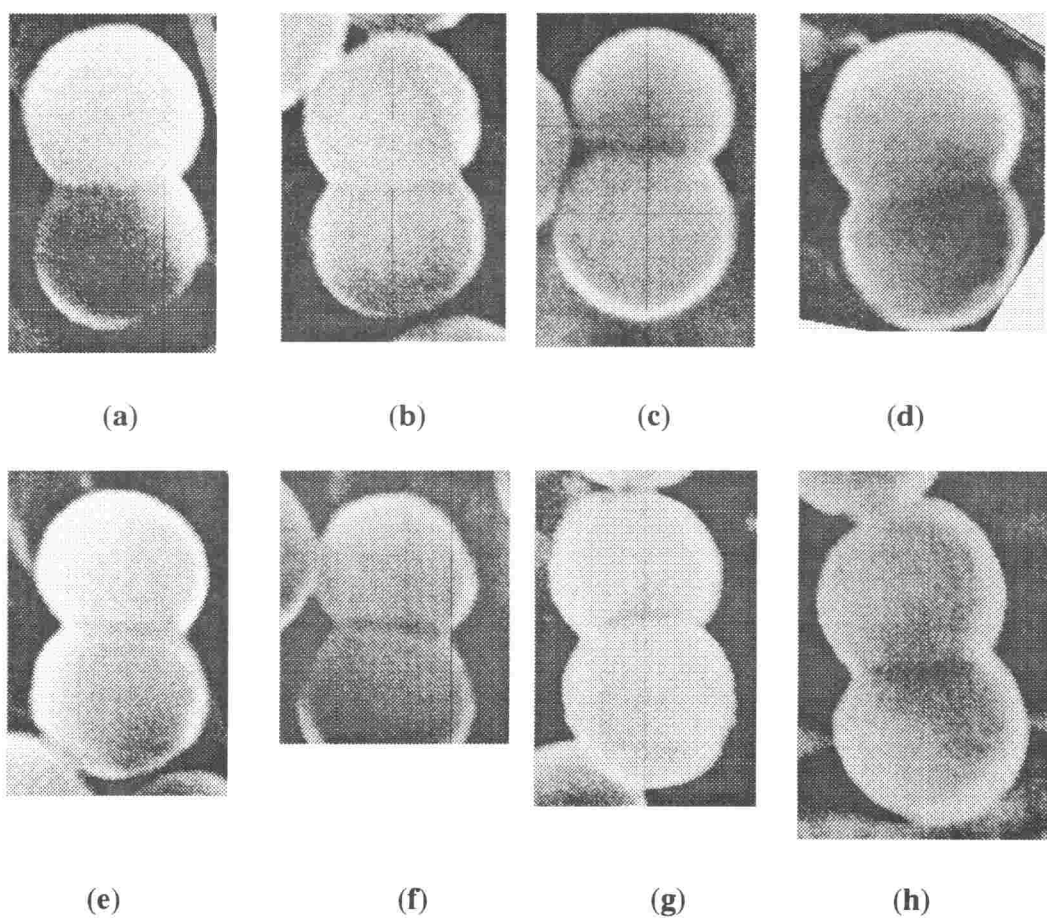Figure 5.7   Two models of nonspherical doublet particles.

Figure 5.8.   The picked up SEM photograph of nonspherical doublet particles from the same polymerization condition. The ultrasonic vibration was applied from 20 to 30 min to the 5 vol % solution.

keeps a part of the sphere even at the end of the polymerization. This can be explained as follows: (1) the structure of the microspheres is rigid when two microspheres come into contact which is kept until end of the polymerization, (2) the growth of the polymerization proceeds on the surface of the particle. The deposition of polymer contributing to the growth of the particle does not make hole under the surface.

Figures 5.8(a)-5.8(h) are the SEM photographs of nonspherical doublet particles obtained from 5 vol % solution with the ultrasonic vibration from 20 to 30 min. Their shapes are almost the same. The center to center distance (between one center to another center of spherical parts of a doublet nonspherical particle on the SEM photograph) are almost the same. The average of the half distance is 0.5 μm and it means the size of the microspheres when contacted by the ultrasonic vibration. The doublet nonspherical particles have the almost same shapes. The contact is supposed to be happened on the surface of each microspheres. That is to say, in order to form the complete connection between two microspheres the microspheres must to move to close and come into contact on their surface. The stirring or the vibration disturbs the formation of microspheres. The ratio of nonspherical particles is rather low, less than 5 % observation from the SEM photograph. These facts suggest that the region of a microsphere is rather stable.

Conclusion

The appearance of the nonspherical particle by the ultrasonic vibration supports the cross-linking proceeding polymerization mechanism. The microspheres are growing independently and stable under stationary polymerization.

Summary

This study seals with the preparation, mechanism and application of microspheres. This study is summerized as follows:

Chapter 1. Polymerization of some bi- and tri- vinyl monomers in several organic solvents by the radiation induced polymerization are investigated. Diethylene glycol dimethacrylate (2EGDM) is the unique monomer that gives microspheres. The number of the nuclei, produced in the early stage of the polymerization, is found to be constant during the polymerization. This lead to monodisparse microspheres. The nuclei grow to be monodisperse polymer particles without aggregation. Preparation of fine particles of poly (N,N'-methylenebisacrylamide) is one of examples for the particle formation promoted by crosslinking polymerization. The cross-linking reaction is suposed to have an important role for the formation of the microspheres.

Chapter 2. Effects of solvent viscosity and monomer solubility were investigated for various kinds of solvents. The comparison of the solvent properties for the preparation of microspheres suggests the good solvents for 2EGDM monomer are favorable to prepare microspheres. The forms of the monomer molecules in the solutions are also important, that is, the stretched form is favorable. Alcohols except *tert* -butanol are not favorable as the solvents for the preparation of microspheres because of not only solubility but also an occurrence of the chain transfer reaction. The chain transfer reactions to the solvents and additives interfere the formation of microspheres.

Chapter 3. The effects of the monomer concentration were investigated on the preparation of 2EGDM microspheres by radiation-induced polymerization. The monomer concentration strongly affected the conversion and the shape of the microspheres. The particles were obtained in the range from 2 to 24 vol% of 2EGDM monomer. Higher monomer concentrations up to 24 vol% gave rough surface particles. Considering the effects on the number of microspheres in the solution, the formation of microsphere consists of two process. This is confirmed by the gel permiation chromatgram of the hydrolized 2EGDM microsphere that prepared in the range of 3 to 22 vol % of 2EGDM monomer. The competition between the propagation and cross-linking reactions is balanced to give the microspheres. The uses of the bi-functional monomer, such as 2EGDM, make it possible to prepare microspheres by this method.

Chapter 4. Copolymerization of 2EGDM with several co-monomers, such as ethyl methacrylate, acrylamide, maleic anhydride and styrene by radiation-induced radical polymerization give microspheres successively. The copolymerization resulted in gelation more easily than the 2EGDM homopolymerization. The allowed ratio of copolymerization is up to about 0.4 as the mole fraction of comonomer for the solution containing 10 vol % 2EGDM monomer. Copolymerization affected the size of microspheres with keeping its narrow distribution. The size of microspheres is increased by the copolymerization with EMA and styrene, and is decreased with acrylamide. The results also suport that the formation of microsphere strongly depends on the cross-linking ability of monomers.

Chapter 5. Radiation-induced polymerization with the ultrasonic vibration of 2EGDM in ethyl acetate gives doublet nonspherical particles. The effective condition is giving 10 min of ultrasonic vibration at the middle of 2h of the polymerization priod by the γ ray irradiation . The shape of the obtained particles is the partial penetrating of two spheres. The contact of two spheres by the

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ultrasonic vibration and the following accumulation of polymer chains on the particle give them. Their nonspherical shape suports the proposed mechanism for the microsphere growth.

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List of Publications

(1) Preparation of Microspheres by Radiation-Induced Polymerization. 1. Mechanism for the Formation of Monodisperse Poly(diethylene glycol dimethacrylate) Microspheres.
Y. Naka, I. Kaetsu, Y. Yamamoto, and K. Hayashi, *J. Polym. Sci., Part A, Polym. Chem.*, **29**, 1197-1202 (1991).

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(3) Preparation of Copolymer Microspheres of Diethylene Glycol Dimethacrylate.
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(4) Solvent Effects on the Formation of Cross-Linking Microspheres in γ Irradiated Solutions.
Y. Naka, Y. Yamamoto, and K. Hayashi, *Radiat. Phys. Chem.*, **40**, 83-88 (1992).

(5) Preparation of Poly (N,N' -Methylenebisacrylamide) Fine Particles by Radiation-Induced Polymerization
Y. Naka and Y. Yamamoto, *Chem. Lett.*, 2263-64 (1992)

(6) Preparation of Nonspherical Fine Particles by Ultrasonic Vibration during Radiation-Induced Polymerization.
Y. Naka and Y. Yamamoto, *Koubunshironbunshyu*, **50**, 287-93 (1993)

(7) GPC Analysis of Highly Cross-linked Polymer Microspheres.
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