Colloid Polym Sci 274:8–13 (1996)

ORIGINAL CONTRIBUTION

J. Sarobe
J. Forcada

Synthesis of core-shell type polystyrene monodisperse particles with chloromethyl groups

Received: 21 March 1995
Accepted: 6 July 1995

J. Sarobe · Dr. J. Forcada (✉)
Grupo de Ingenieria Quimica
Departamento de Quimica Aplicada
Facultad de Ciencias Quimicas
Universidad del Pais Vasco/EHU
Apdo. 1072
20090 Donostia-San Sebastian, Spain

Abstract The synthesis of core-shell type polystyrene monodisperse particles with surface chloromethyl groups was carried out by a two-step emulsion polymerization process at different reaction temperatures. In a first step, the core was synthesized at 90 °C by means of batch emulsion polymerization of styrene (St), and in the second step, the shell was polymerized by batch emulsion copolymerization of St and chloromethylstyrene (CMS) using the seed obtained previously. With the aim of optimizing the production of these core-shell type polystyrene monodisperse particles with surface chloromethyl groups, the reaction temperature in the second step, the purification or not of the functionalized monomer (CMS), the amount and type of the redox initiator system used, and the type of addition of the initiator system to the reactor were studied.

Key words Emulsion polymerization – seeded – redox initiator – chloromethyl group

Introduction

Polymer particles have many potential applications due to such properties as their spherical shape, well characterized surface, accurately determined diameter and high surface area. Applications such as standardizing or calibrating electron microscopes and particle counters [1], affinity chromatography [2], use of particles as model systems for the study of physical properties such as light scattering, electrophoresis, rheology, turbidity [1], etc., have been reported.

One of the most important applications that has been developed with polymeric microspheres is related to the biomedical field, in which the synthesis and use of new polymeric materials with different properties should make polymers valuable tools in this field [1, 3, 4].

Hence, polymer latexes have received much attention as carriers or supports for antibodies and antigens in immunoassays [5–11]. In the first published study, Singer et al. [12] studied the use of monodisperse polystyrene and polyvinyltoluene polymer particles as the support on which the biomolecules were going to adsorb. In this case, however, the applicability of these systems, in which the biomolecules are physically bound, is limited. Although the process is easy to carry out, the possible desorption of the adsorbed species or loss of specific activity of the complex formed could occur. This type of system can be improved by the covalent bonding of the protein to the microsphere surface. Some covalent bonding procedures have been developed using polymer particles with different reactive functional groups on their surfaces. In this way, polymer particles with surface carboxylate [13], amino [14], aldehyde [15], acetal [10], hydroxyl [16], dissaccharide [17] or chloromethyl [18] groups have been synthesized.

The synthesis of polymer particles with surface chloromethyl groups and by different reaction conditions has been investigated previously. Thus, homopolymers or copolymers, even terpolymers of CMS and other monomers (styrene, vinylnaphthalene, acrylic acid, 2-hydroxyethyl acrylate, etc.) were synthesized by emulsion polymerization [5–7, 18–21] or by dispersion polymerization [22–23]. In emulsion polymerization, syntheses have been carried out by a one-step [18–22] or by a two-step [5–7, 19, 23] emulsion polymerization process (in this case, a previously prepared seed was used).

Although little has been published, some authors have investigated the side reactions that the chloromethyl group could undergo in the aqueous phase: hydrolysis of the chloromethyl group into hydroxymethyl group and crosslinking reaction by radical transfer to the polymer chain [20]. Moreover, other parameters such as the use of a redox initiator system [7, 18, 19], the presence or not of divinylbenzene in the recipes to obtain lightly crosslinked polymers [20, 22], the monodispersity of the latexes [19], etc. have been studied.

In this work, the synthesis of core-shell type polystyrene monodisperse particles with surface chloromethyl groups was carried out by a two-step emulsion polymerization process. The influence of the temperature (30°, 45° or 80 °C) on the conversion of the reactions carried out in the second polymerization step and on the monodispersity of latexes, the purification or not of the CMS, the type of redox initiator system used as well as the form of addition of the latter to the reactor were investigated.

Some characterization studies (surface charge density, colloidal stability, electrophoretic mobility, surface chloromethyl group concentration determination) of three latexes obtained in these sets of reactions and the immunoassay results carried out with C-reactive protein covalently bound to one of these latexes, will be reported subsequently.

Experimental

Materials

Styrene (St) was distilled under reduced pressure. Chloromethylstyrene (CMS) was purified by washing it with a 0.1% sodium hydroxide solution or was used as received. Both monomers were stored at −18 °C until used. All the other materials were used as received. Potassium persulfate ($K_2S_2O_8$, Fluka), sodium disulfite (Panreac) and iron (II) sulfate heptahydrate (Merck) were used as the components of the redox initiator system. Aerosol MA80 (sodium dihexyl sulfosuccinate, Cyanamid) and sodium hydrogen carbonate (Merck) were used as surfactant and buffer, respectively. Double deionized water was used throughout the work.

Table 1 Recipe used to obtain the seeds of S1PS and S2PS

Reagents	S1PS*	S2PS
DDI water (g)	1250.0	1250.0
Aerosol MA80 (g)	16.94	22.89
$NaHCO_3$ (g)	2.0	2.0
St (g)	526.0	526.0
$K_2S_2O_8$ (g)	2.0	2.0

Reaction conditions: $T = 90$ °C; rpm = 250; reaction time = 24 h
*: this recipe was also used to synthesize the seeds S3PS and S4PS.

Preparation of latexes

Polymerizations were carried out in a 1 or 2 liter, thermostatted reactor fitted with a reflux condenser, stainless-steel stirrer, sampling device, and nitrogen inlet tube.

All of the core-shell type polymer particles were obtained by a two-step emulsion polymerization process. In the first step, the core of the polymer particles (the seed used in the second step) was prepared at 90 °C by batch emulsion polymerization of St using the reaction conditions and recipe given in Table 1. After polymerization, the seed was kept overnight at 90 °C to decompose the initiator.

The seeded batch emulsion copolymerizations of St and CMS were carried out to put the shell onto the core synthesized in the first step. Three different reaction temperatures (with different recipes) were used for this purpose (30°, 45° and 80 °C). The recipes and reaction conditions used in these runs are given in Tables 2, 3 and 4. DDI water, buffer solution (if used) and seed were added to the reactor and purged with nitrogen for 20 min. Monomers were added and the system was stirred and purged with N_2 for 3 h at 30 °C to swell the seed particles. The aqueous solutions of the initiator system components were then added to the reaction mixture either in a single aliquot or in three aliquots at different times, the first at the beginning of the reaction.

The overall conversion (x_T) of the reactions was determined gravimetrically.

Particle size measurements

The average particle sizes of the latexes were measured by Transmission Electron Microscopy (TEM, H-7000 FA Hitachi). The particle size distributions (PSDs) were obtained by TEM from representative samples of more than 500 particles.

Table 2 Recipes used for the batch emulsion copolymerizations at 30 °C

RUN	S1CS4	S1CS5	S1CS6	S1CS7	S1CS8	S2CS1
Seed (g)	148.42	148.42	148.42	148.42	148.42	149.05
$NaHCO_3$ (g)	0.5	–	–	–	–	–
$K_2S_2O_8$ (g)	0.487	0.487	0.487	0.654	0.758	1.08
$Na_2S_2O_5$ (g)	0.148	0.148	0.148	0.2	0.379	0.541
$FeSO_4 \cdot 7H_2O$ (g)	3.2e-4	3.2e-4	0.050	0.068	0.151	0.217

DDI water = 403.2 g; St = 9.2 g; CMS = 9.2 g.
Reaction conditions: $T = 30\,°C$; rpm = 200; reaction time = 20 h.

Table 3 Recipes used for the batch emulsion copolymerizations at 80 °C

RUN	S3CS2	S3CS3	S3CS4	S3CS5[a]	S3CS6[a]
$K_2S_2O_8$ (g)	0.329	0.165	0.093	0.093	0.093
$Na_2S_2O_5$ (g)	0.224	0.112	0.063	0.063	0.063

DDI water = 403.2 g; Seed = 150.48 g; St = 9.2 g; CMS = 9.2 g.
Reaction conditions: $T = 80\,°C$; rpm = 200; reaction time = 7 h
[a]: reaction carried out without washing the functionalized monomer.

Number ($\bar{d}_n$), weight ($\bar{d}_w$) and volume ($\bar{d}_v$) average diameters were calculated from the PSDs, defined as follows:

$$\bar{d}_n = \frac{\sum n_i d_i}{\sum n_i} \tag{1}$$

$$\bar{d}_w = \frac{\sum n_i d_i^4}{\sum n_i d_i^3} \tag{2}$$

$$\bar{d}_v = \left[\frac{\sum n_i d_i^3}{\sum n_i}\right]^{1/3}, \tag{3}$$

where n_i is the number of particles of diameter d_i.

The polydispersity index (PDI) and the coefficient of variation (CV) are defined as:

$$\mathrm{PDI} = \frac{\bar{d}_w}{\bar{d}_n} \tag{4}$$

$$\mathrm{CV} = \frac{[(\sum_{i=1}^{N}(d_i - \bar{d}_n)^2)/(N-1)]^{1/2}}{\bar{d}_n} \times 100, \tag{5}$$

where N is the total number of particles measured.

Results and discussion

In Tables 5, 6, 7, and 8, the overall conversion at the end of the polymerization reactions, the pH of the final latexes, the volume average diameter (nm), the PDI index, and the CV coefficient are shown. Table 5 shows the results of the reactions carried out to obtain the seeds. In Tables 6, 7, and 8 the results of the reactions in which the shell of the particles was obtained are shown.

The results of the batch copolymerization reactions carried out at 30 °C are shown in Table 6. All reactions in this series were carried out using S1PS seed as the core of the particles, except in the case of run S2CS1, in which S2PS seed was used.

The difference between runs S1CS4 and S1CS5 is that in S1CS4 a small amount of $NaHCO_3$ was added to the system to maintain the pH of the reaction neutral, and, as could be expected [24], the reaction conversion was higher in the case in which reaction medium was acid. In both cases, monodisperse particles were obtained.

In reactions S1CS6, S1CS7, S1CS8, and S2CS1 the amounts of one or all components of the initiator system

Table 4 Recipes used for the batch emulsion copolymerizations at 30° and 45 °C

RUN	S3CS7[a]	S3CS8[a]	S3CS9[a]	S3CS10[a]	S3CS11[a]	S4CS1[a]	S4CS2[b]	S4CS3[b]	S3CS4[b]
Seed (g)	150.48	150.48	150.48	150.48	150.48	149.71	150.21	150.21	150.21
St (g)	9.2	9.2	9.2	9.2	9.2	9.2	9.2	4.6	–
CMS (g)	9.2	9.2	9.2	9.2	9.2	9.2	9.2	13.8	18.4
$K_2S_2O_8$ (g)	0.093	0.093	0.218	0.218	0.218	0.218	0.315	0.210	0.327
$Na_2S_2O_5$ (g)	0.066	0.066	0.150	0.151	0.149	0.150	0.239	0.158	0.226
$FeSO_4 \cdot 7H_2O$ (g)	0.109	0.010	0.109	0.109	0.2	0.110	–	–	0.050

DDI water = 403.2 g.
Reaction conditions: $T = 30$ or $45\,°C$; rpm = 200; reaction time = 20 h.
[a]: reaction carried out 30 °C.
[b]: reactions carried out at 45 °C.

Table 5 Results of the reactions carried out to obtain the seeds*

RUN	S1PS	S2PS	S3PS	S4PS
pH	7.4	7.5	7.5	7.5
$\bar{d}_v$ (nm)	166	104	208	185
PDI	1.0044	1.008	1.0052	1.0064
CV (%)	3.9	5.3	4.1	4.1

* All reactions achieved complete conversion.

Table 6 Results of the batch emulsion copolymerizations carried out at 30 °C

RUN	S1CS4	S1CS5	S1CS6	S1CS7	S1CS8	S2CS1
x_T	0.41	0.56	0.63	0.70	0.64	0.51
pH	7.5	1.9	1.8	1.8	1.8	1.7
$\bar{d}_v$ (nm)	180	182	183	188	183	108
PDI	1.0039	1.0040	1.0043	1.0036	1.0034	1.009
CV (%)	3.7	3.7	3.8	3.5	3.4	5.9

Table 7 Results of the batch emulsion copolymerizations carried out at 80 °C*

RUN	S3CS2	S3CS3	S3CS4	S3CS5	S3CS6
pH	2.0	1.9	1.7	1.7	1.7
$\bar{d}_v$ (nm)	227	228	224	230	225
PDI	1.0044	1.0042	1.0041	1.0038	1.0039
CV (%)	3.8	3.7	3.7	3.6	3.6

* All reactions achieved complete conversion.

were gradually increased (see Table 2), and as can be seen in Table 6, the conversion reaches a maximum as a function of initiator concentration. Although the amounts of the initiator system components in runs S1CS8 and S2CS1 were higher than in the other cases, final conversion values of these reactions were not improved. One characteristic of these redox initiator systems is that due to the quick radical generation that takes place in the reaction mixture, reaction kinetics can be accelerated and final conversions will be achieved more quickly [24]. However, if the amounts of the initiator components were too high, the radical concentration in the aqueous phase could be so high that self-deactivation of part of these radicals could occur, leading to a lower final radical concentration than might be expected (initiator efficiency was reduced due to greater chain termination by initiator). This effect could take place in runs S1CS8 and S2CS1, in which, in spite of the initial higher initiator concentration, final conversions were not improved. In all reactions monodisperse particles were obtained.

Using this type of redox initiator system at low reaction temperature it was seen that, by increasing the amount of the initiator system added, the final conversion was not always higher. Reactions carried out at higher temperatures (i.e. 80 °C) and without adding iron sulfate to the reaction mixture, could be used for optimizing a suitable initiator system concentration for these low temperature reactions. With these runs, suitable persulfate and disulfite concentrations to obtain complete or high conversions at 80 °C were sought (the generation of the radicals takes place by thermal decomposition of persulfate and by redox reaction between persulfate and bisulfite). When this initiator concentration was known, the reaction temperature was decreased to carry out the copolymerization reactions at 30 °C using the persulfate/disulfite/iron initiator system. In this case, the objective was to achieve an effect similar to that which had been obtained at high temperature reactions, by adding iron sulfate to the reactor and working at low temperatures.

The recipes that were used in order to carry out the copolymerization reactions at 80 °C are shown in Table 3. In these copolymerizations, persulfate and bisulfite amounts in the reaction mixture were gradually decreased. In all reactions S3PS seed was used as the core of the particles. Another important parameter studied in this set of reactions was the washing or not of the functional monomer (CMS) by 0.1% sodium hydroxide solution. As Table 7 shows, all reactions achieved complete conversion and in all cases monodisperse particles were obtained (volume average diameter values reveal a good reaction reproducibility). On the other hand, the results in Table 7 suggest that the effects of washing the CMS on the final conversion, particle average diameter and PDI, are negligible.

Table 8 Results of the batch emulsion copolymerizations carried out at 30° and 45 °C

RUN	S3CS7[a]	S3CS8[a]	S3CS9[a]	S3CS10[a]	S3CS11[a]	S4CS1[a]	S4CS2[b]	S4CS3[b]	S4CS4[b]
x	0.39	0.3	0.53	0.54	0.57	0.59	0.66	0.41	0.86
pH	2.0	1.8	2.0	2.3	2.4	2.5	2.0	1.8	1.8
$\bar{d}_v$ (nm)	222	213	*	*	*	*	196	187	200
PDI	1.0046	1.0040	*	*	*	*	1.0037	1.0046	1.0041
CV (%)	3.6	3.7	*	*	*	*	3.5	4.0	3.7

* Reactions in which destabilization of some particles occurred.
[a]: reactions carried out at 30 °C.
[b]: reactions carried out at 45 °C.

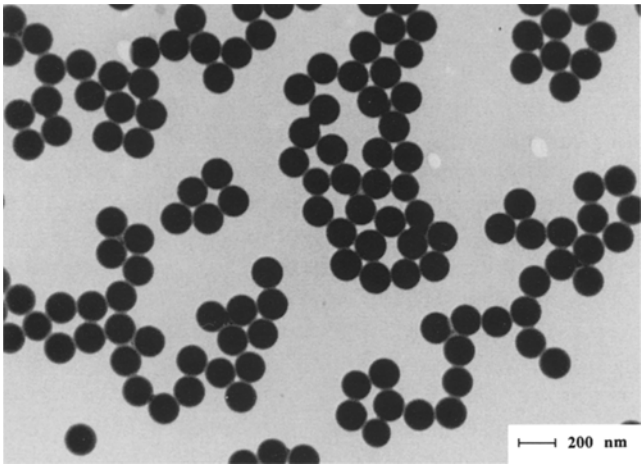

Fig. 1 TEM micrograph of latex S1CS7

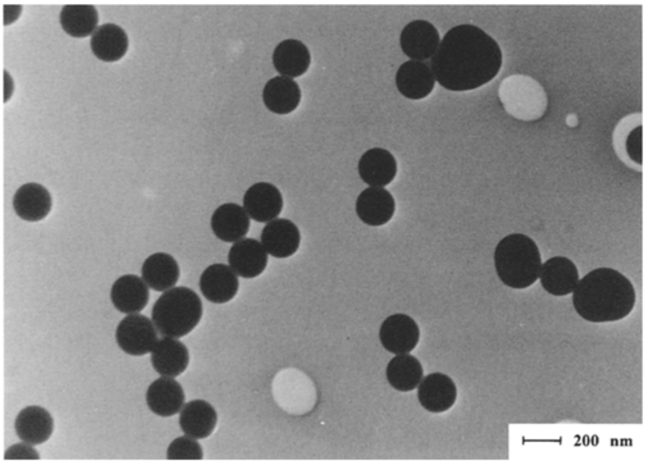

Fig. 2 TEM micrograph of latex S3CS10

Once the set of reactions at 80 °C had been carried out and suitable amounts of persulfate and disulfite optimized, the reaction temperature was again decreased, the third series of copolymerization reactions with the persulfate/disulfite/iron initiator system being carried out at 30 °C (S3PS and S4PS seeds were used as the particles core). In order to avoid the partial radical deactivation that could occur in the reaction mixture due to the high concentration of the latter in the aqueous phase, initiator components were added at three different stages during the polymerization process. In this way, the aqueous solutions of the first third of the initiator system were added after the swelling of the seed particles. The other two-thirds, 3 and 6 h later, respectively.

Table 8 shows the results of the third series of reactions carried out at 30° and 45 °C. In S3CS7 and S3CS8 runs monodisperse particles and low conversions were obtained. In the next four reactions (S3CS9, S3CS10, S3CS11 and S4CS1) a slight change was introduced in the way in which the initiator components were added. Thus, while persulfate and disulfite were added as in the two latter runs, iron sulfate addition was carried out only in the first stage. This slight change, introduced in order to have a higher amount of iron in the early stages of the reactions, led to slightly polydisperse latexes in the four reactions (in some micrographs obtained by transmission electron microscopy some coagulums formed by two or three coagulated particles were seen). In Figs. 1 and 2 TEM micrographs of a monodisperse latex (S1CS7) and a slightly polydisperse latex (S3CS10) are presented, respectively.

An explanation for the few coagulations that took place in the system due to the destabilization of the particles, could be related to the amount of iron in the reaction medium [25, 26]. The stability of the particles comes mainly from the emulsifier molecules adsorbed onto the polymer particles and from particle surface chemically-bound sulfate and sulfonate groups (generated from persulfate and bisulfite decomposition). On the other hand, there are Fe^{2+} or even Fe^{3+} cations in the reaction mixture that will act as counterions to the stabilizing groups, creating a sheilding effect against them. The most important difference between these latter four reactions and the former ones carried out with iron is that, in the latter, this shielding effect is stronger with respect to the stabilization that the addition of a third part of the initiator system could produce. Thus, it appears that the few coagulums formed in the reaction mixture were generated in the first stages of the copolymerization reaction, that is to say, before adding the other two-thirds of the persulfate/disulfite system.

Finally, the last three reactions shown in Table 8 (S4CS2, S4CS3 and S4CS4) were carried out at 45 °C. As can be seen in the first two reactions (see Table 4), simply by increasing the reaction temperature to 45 °C and without adding iron to the medium, final conversions were similar to those obtained in the reactions carried out at 30 °C with the persulfate/disulfite/iron initiator system. In the last reaction (S4CS4), in order to analyze the effect that the addition of a small amount of iron to the system could produce, iron (II) sulfate heptahydrate was added together with similar amounts of persulfate and disulfite to those used in reaction S4CS2, leading to a substantial increment in the final conversion. In all the reactions carried out at 45 °C, monodisperse particles were obtained.

Conclusions

Core-shell-type monodisperse polymer colloids with chloromethyl functionality were synthesized by a two-step emulsion polymerization process at three different reaction temperatures. Once the core was formed by batch emulsion polymerization of St at 90 °C, the shell was added by batch emulsion copolymerization of St and CMS in a second step. In order to optimize the production of these functionalized particles, some reaction parameters, such as the reaction temperature in the second step (30°, 45° and 80 °C), the amount and type of redox initiator system used, the type of addition of the initiator system (at one single step or at some different stages during the polymerization process) and the washing or not of the functional monomer were investigated.

By increasing the reaction temperature in the second step (without adding iron sulfate) final conversions were higher than in those reactions carried out in similar conditions but at lower temperatures.

The effect of washing or not of the functionalized monomer on the final conversion, particle average diameter and PDI was negligible.

The relation between the amount of iron sulfate used and the amount of the persulfate/bisulfite system added should be controlled to obtain monodisperse particles and prevent the premature coagulation of the polymer particles during the polymerization process.

Acknowledgements This work is supported by the Comisión Interministerial de Ciencia y Technología (CICYT), proyect MAT 93-0530-C02-02. J. Sarobe acknowledges the grant from the Ministerio de Educación y Ciencia.

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