Synthesis and Characterization of New Micrometer-Sized Radiopaque Polymeric Particles of Narrow Size Distribution by a Single-Step Swelling of Uniform Polystyrene Template Microspheres for X-ray Imaging Applications

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Radiopaque micron-sized non-cross-linked polystyrene/poly(2-methacryloyloxyethyl(2,3,5-triiodobenzoate)) particles of narrow size distribution were prepared by a single-step swelling of uniform polystyrene template microspheres with emulsion droplets of methylene chloride containing the initiator benzoyl peroxide and the iodinated monomer 2-methacryloyloxyethyl(2,3,5-triiodobenzoate), followed by the polymerization of the monomer within the swollen template particles at 73 °C. Radiopaque micron-sized uniform cross-linked polystyrene/poly-(2-methacryloyloxyethyl(2,3,5-triiodobenzoate)-divinylbenzene) composite particles were prepared similarly with emulsion droplets of methylene chloride containing divinylbenzene, in addition to the initiator and the iodinated monomer. Radiopaque micron-sized uniform cross-linked poly(2-methacryloyloxyethyl(2,3,5-triiodobenzoate)-divinylbenzene) particles were formed by dissolving the template polystyrene polymer belonging to the former cross-linked composite particles. Characterization of these novel radiopaque polymeric particles was performed by methods such as FTIR, TGA, DSC, SEM, XPS, elemental analysis, and light microscopy. The influence of the weight ratio [2-methacryloyloxyethyl(2,3,5-triiodobenzoate)]/[polystyrene] and [2-methacryloyloxyethyl(2,3,5-triiodobenzoate)]/[divinylbenzene] on the bulk and surface properties of the non-cross-linked and cross-linked particles, respectively was elucidated. The radiopacity of these iodinated particles was demonstrated by an imaging technique based on X-ray absorption usually used in hospitals. These novel radiopaque particles may be used for different X-ray imaging needs, e.g., blood pool, body organs, embolization, dental composition, implants, protheses, and nanocomposites.

Introduction

Recent literature concerning novel biomaterials indicates increasing interest in developing radiopaque polymers as contrast agents for X-ray imaging.[1−21] The radiopaque polymeric agents may be used for various applications, e.g., imaging of blood pool[1,2] or certain body organs[3] in order to detect or diagnose various disease states, monitoring embolization processes,[4−10] construction of implants used in surgery to determinate their exact location,[11−16] and dental composition.[16−18]

There are different reported techniques for preparing radiopaque polymers of various types. For example, radiopaque polymer blends have been prepared by incorporating radiopacifying agents such as heavy metal powders, inorganic salts of a heavy element, or organic compounds containing a heavy atom substituent as physical mixtures with an appropriate polymer.[6−8] Radiopaque polymer−salt complexes have been produced by incorporation of radiopaque heavy metal salts into an appropriate polymer ligand via chelation. Radiopaque polymers have also been formed by the polymerization of methyl methacrylate with metal salts of vinyl monomers such as barium or zinc acrylates,[16] or by grafting iodine-containing molecules onto preformed high molecular weight polymers.[5−7,15]

Another approach for preparing radiopaque polymers is based on homo or copolymerization of aromatic iodine containing vinylic monomers with other vinylic monomers such as 2-hydroxyethyl metacrylate (HEMA) or methyl methacrylate (MMA).[4,11−21] One of the first iodinated monomers of that type was triiodophenyl methacrylate.[13,16] This iodinated monomer is highly resistant to both homo and copolymerization, and only low molecular weight polymers (oligomers) could be formed.[13,16] This was attributed to the bulky nature of the iodinated aromatic nucleus sterically hindering the propagation step during attempted polymerization. In the next generation of radiopaque monomers, the steric hindrance was reduced by introducing a spacer arm between the bulky iodinated aromatic nucleus and the vinyl group.[11,12,14,16−21] This change allowed facile homo and copolymerization of monomers such as 2-methacryloyloxyethyl(2,3,5-triiodobenzoate) [MAOETIB], 2-hydroxy-3-methacryloyloxypropyl(2,3,5-triiodobenzoate), and 3-(methacryloylamidoacetamido)-2,4,6-triiodobenzoic acid with HEMA or MMA by dispersion, suspension, and bulk polymerization processes.[11,12,16−19,21]

Radiopaque iodinated copolymeric spherical particles were prepared, according to previous literature, by two major ways: precipitation of iodinated copolymeric chains[19,21] or suspension polymerization of aromatic iodinated vinylic monomers with HEMA or ethylene glycol dimethacrylate.[11] However, these radiopaque particles were formed in sizes of tens of microns, and above, with a broad size distribution.

The present article describes a method to prepare novel radiopaque non-cross-linked and cross-linked micron-sized polymeric spherical composite particles with a narrow size distribution, by a single-step swelling of uniform micron-sized polysrytene (PS) template particles with methylene chloride emulsion droplets containing the initiator benzoyl peroxide (BP)

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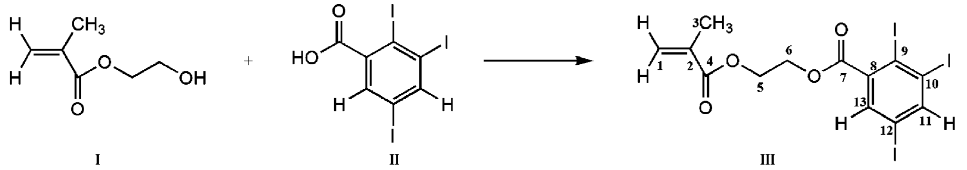
Scheme 1. Synthesis of MAOETIB



and the iodinated monomer MAOETIB in the absence, or presence, of the cross-linker monomer divinylbenzene (DVB), followed by the polymerization of the monomers within the swollen template particles.

Ugelstad and co-workers invented a useful multistep swelling method of uniform template particles with various acrylate monomers and initiators for the production of different uniform-sized particles of controlled desired properties.[22,23] This basic swelling process was then significantly elaborated by Cheng et al.[24] and Hosoya and co-workers.[25−28] The first step of this multistep swelling method is associated with the activation of template uniform particles (usually PS) formed by either emulsion or dispersion polymerization processes. The activation of the template particles is accomplished by swelling the particles dispersed in an aqueous phase with emulsion droplets of a swelling solvent, e.g. dibutyl phthalate or 1-chlorodecane. The first swelling step stimulates the swelling of the template particles in the subsequent steps. When the activation-swelling step is completed, the second swelling step takes place by introducing the slightly enlarged template particles to monomers, initiator, and porogens. This can be done in one step, or through the sequential addition of each component. The initiator can be added in the first or second swelling step. Polymerization of the monomers within the uniformly swollen particles can then be induced by increasing the temperature. An alternative swelling method was invented by Okubo et al. and was named “the dynamic swelling method”.[29,30] According to this method, uniform PS template particles can be swollen enormously, while maintaining their uniformity, by slow, continuous, dropwise addition of water into an ethanol/water medium containing the template particles and hydrophobic monomer/s and initiator (e.g., styrene and BP). Polymerization can then be performed, as previously described, by increasing the temperature. According to the dynamic swelling method there is no need to use a swelling solvent, and the process can be performed in a one-step procedure. A new method for preparing particles of narrow size distribution and controlled properties based on a single-step swelling process of template uniform microspheres was recently published by Margel et al.[31−33] According to this process, the swelling of the template particles with the initiator and monomer/s via a swelling solvent is accomplished in a single step, in contrast to the multi-swelling steps where the swelling with these reagents is accomplished in two or more steps.

The present manuscript describes the synthesis and characterization of radiopaque non-cross-linked (PS/polyMAOETIB) and cross-linked [PS/poly(MAOETIB-DVB)] micron-sized composite particles with narrow size distribution, based on a single-step swelling of uniform micron-sized PS template particles with methylene chloride emulsion droplets containing BP and MAOETIB in the absence, or presence, of DVB, followed by polymerization of the monomer/s within the swollen template particles at 73 °C. Cross-linked micron-sized uniform radiopaque poly(MAOETIB-DVB) particles were formed by dissolving the template PS polymer belonging to the composite cross-linked particles. The effect of various polymerization parameters, e.g., the ratio [MAOETIB]/[PS] and [MAOETIB]/[DVB] on the bulk and surface properties of the particles has been elucidated. The radiopacity of these particles was demonstrated by a computed tomography (CT) scanner.

Experimental Section

Chemicals. The following analytical-grade chemicals were purchased from Aldrich and were used without further purification: 2,3,5-triiodobenzoic acid (98%), HEMA (99%), 1,3-dicyclohexylcarbodiimide (DCC, 99%), 4-pyrrilidinopyridine (98%), anhydrous diethyl ether (99.7%), ethyl acetate (99.5%), DVB (90%),BP (98%), sodium dodecyl sulfate (SDS), poly(vinylpyrrolidone) (PVP, mw 360 000), ethanol (HPLC), 2-methoxy ethanol (HPLC), and methylene chloride (HPLC). Styrene (Aldrich 99%) was passed through activated alumina (ICN) to remove inhibitors before use. Water was purified by passing deionized water through an Elgastat Spectrum reverse osmosis system (Elga Ltd., High Wycombe, U.K.).

Synthesis of MAOETIB. The monomer MAOETIB was synthesized according to the literature[17] (Scheme 1):

Briefly, 2,3,5-triiodobenzoic acid, II, (50 g, 0.10 mol), HEMA, I, (15 g, 0.11 mol), DCC (23 g, 0.11 mol), and 4-pyrrilidinopyridine (1.5 g, 0.010 mol) were dispersed in ether (500 mL) and then stirred at room temperature for 18 h. The solid was then filtered off and the residue washed with fresh ether. The ether solution was then washed with HCl (2 N), saturated $NaHCO_3$, and brine. The organic phase was then dried over $MgSO_4$, filtered, and evaporated to produce an orange solid. Pure white crystals of MAOETIB, III, (mp 95 °C) were obtained by recrystallization of the orange solid twice from ethyl acetate (yield 84%).

^{1}H NMR ($CDCl_3$) δ 1.97 (s, 3H, CH3), 4.57 and 4.48 (m, 4H, OCH2CH2O), 5.61 (s, 1H, olefinic), 6.16 (s, 1H, olefinic), 7.33 (d, 1H, $J = 1.68$ Hz, Ar−H), 8.30 (d, 1H, $J = 1.68$ Hz, Ar−H). ^{13}C NMR ($CDCl_3$) δ 18.33 (C-3), 61.92 (C-5), 63.93 (C-6), 93.64 (C-12), 106.56 (C-9), 113.39 (C-10), 126.41 (C-1), 135.72 (C-2), 137.13 (C-13), 148.86 (C-11), 165.60 (C-4), 166.97 (C-7). MS (ES^+): m/z 635 (MNa^+, 100). Elemental analysis (calculated): C, 25.52; H, 1.81; O, 10.46; I, 62.21. Found: C, 25.65; H, 1.82; O, 10.49; I, 62.04.

Synthesis of PS Template Microspheres. PS template microspheres of narrow size distribution were prepared according to a procedure similar to that described in the literature.[26−28,35] Briefly, these microspheres were synthesized in a three-neck round-bottom flask equipped with a condenser and immersed in a constant temperature silicone oil bath at a preset temperature. In a typical experiment, PS microspheres with an average diameter of 2.6 ± 0.2 μm were formed by introducing into the reaction flask (1 L) a solution containing PVP (3.75 g) dissolved in a mixture of ethanol (150 mL) and 2-methoxy ethanol (62.5 mL). The temperature of the mechanically stirred solution (200 rpm) was then preset to 73 °C. Nitrogen was bubbled through the solution for ca. 15 min to exclude air, after which a blanket of nitrogen was maintained over the solution during the polymerization period. A deairated solution containing the initiator BP (1.5 g, 6.2 mmol) and styrene (37.5 mL, 327.3 mmol) was then added to the reaction flask. The polymerization reaction continued for 24 h and was then stopped by cooling to room temperature. The microspheres formed were washed by extensive centrifugation cycles with ethanol and water and then dried by lyophilization. Uniform PS microspheres of sizes ranging between 0.2 and 5.0 μm were prepared similarly by changing the polymerization parameters, e.g., monomer or initiator concentration.

Synthesis of PolyMAOETIB Powder. PolyMAOETIB powder was prepared by chain growth radical polymerization of MAOETIB in

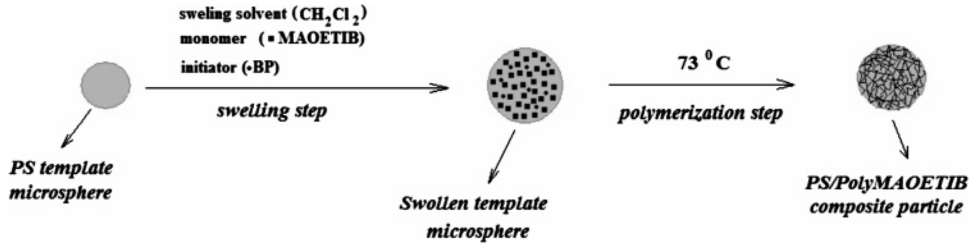


Figure 1. Preparation of the radiopaque non-cross-linked PS/polyMAOETIB composite particles via a single-step swelling process.

2-methoxy ethanol. Briefly, in a 20 mL vial, 0.4 g (0.65 mmol) of MAOETIB, 0.1 g of PVP, and 10 mg (0.04 mmol) of BP were dissolved in 10 mL of 2-methoxy ethanol. The vial with the reagents was then shaken under N_2 at 73 °C for 18 h. The formed polyMAOETIB was then washed by extensive centrifugation cycles with 2-methoxy ethanol and water and then dried by lyophilization.

Single-Step Swelling of the PS Template Microspheres. In a typical experiment, PS template microspheres of 2.6 ± 0.2 μm were swollen up to approximately 6.9 μm by adding to a 20 mL vial 10 mL of an SDS aqueous solution [1.5% (w/v)] and 5 mL of the swelling solvent methylene chloride in the absence, or presence, of 10 mg of BP and 0.32 g (0.52 mmol) of MAOETIB. Emulsion droplets of the swelling solvent were then formed by sonication (Sonics and Materials, model VCX-750, Ti-horn 20 kHz) of the mixture at 4 °C for 60 s. A total of 3.5 mL of an aqueous suspension of the PS template microspheres (7% w/v, 245 mg) was then added to the stirred methylene chloride emulsion. After the swelling of the PS particles was completed, and the mixture did not contain any small emulsion droplets of the swelling solvent, as verified by optical microscopy, the swollen microspheres diameter was measured. Similar trials were also accomplished in the presence of different concentrations of MAOETIB and DVB dissolved in methylene chloride.

Synthesis of Uniform Micrometer-Sized Non-Cross-Linked PS/PolyMAOETIB Composite Particles. In a typical experiment, non-cross-linked PS/polyMAOETIB composite particles with an average diameter of 3.3 ± 0.1 μm were prepared by the polymerization of the MAOETIB within the swollen particles prepared as described in the previous paragraph, by shaking the vial containing the swollen particles at 73 °C for 18 h. The formed composite particles were then washed by extensive centrifugation cycles with 2-methoxy ethanol and water and then dried by lyophilization. PS/polyMAOETIB composite particles of various properties were prepared by changing polymerization parameters, e.g., the weight ratio [MAOETIB]/[PS].

Synthesis of Uniform Micrometer-Sized Cross-Linked PS/Poly(MAOETIB-DVB) Composite Particles. Uniform micrometer-sized cross-linked PS/poly(MAOETIB-DVB) composite particles were prepared via a similar procedure to that described in the previous paragraph for non-cross-linked PS/polyMAOETIB composite particles, except that the swelling of the PS template particles was performed in the presence of DVB, in addition to BP and MAOETIB. For example, in a typical experiment, cross-linked PS/poly(MAOETIB-DVB) composite particles of an average diameter of 3.9 ± 0.2 μm were prepared by swelling the PS template particles according to the former procedure with 5 mL of methylene chloride containing 10 mg of BP, 0.57 g (0.93 mmol) of MAOETIB, and 0.03 g (0.23 mmol) of DVB. Polymerization of the monomers within the swollen particles was then performed at 73 °C for 18 h. The formed cross-linked composite particles were then washed by extensive centrifugation cycles with 2-methoxy ethanol and water and then dried by lyophilization. PS/poly(MAOETIB-DVB) composite particles of various properties were prepared by changing polymerization parameters, e.g., the weight % ratio [MAOETIB]/ [DVB].

Synthesis of Uniform Micrometer-Sized Cross-Linked Poly(MAOETIB-DVB) Particles. Uniform micrometer-sized cross-linked poly(MAOETIB-DVB) particles were prepared by dissolving the PS template polymer of the PS/poly(MAOETIB-DVB) composite particles prepared as described in the previous paragraph. Briefly, PS/poly(MAOETIB-DVB) composite particles dispersed in methylene chloride were shaken at room temperature for 18 h. The soluble PS was then washed from the cross-linked dispersed poly(MAOETIB-DVB) particles by extensive centrifugation cycles with methylene chloride, ethanol, and water and then dried by lyophilization.

Characterization. ^{1}H and ^{13}C NMR spectra were obtained with a Bruker DPX-300 spectrometer. For chloroform-*d*, chemical shifts are expressed in ppm downfield from tetramethylsilane used as internal standard.

Elemental analysis, including iodine, was performed by the Microanalysis Lab., Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem. The reported values are an average of measurements performed on at least three samples of each of the tested particles and have a maximum error of about 2%.

Mass spectra were obtained with Finnigan 4021 spectrometer (ES = Electrospray).

Fourier transform infrared (FTIR) analysis was performed with a Bomem FTIR spectrophotometer, model MB100, Hartman & Braun. The analysis was performed with 13 mm KBr pellets that contained 2 mg of the examined particles and 198 mg KBr. The pellets were scanned over 200 scans at a 4 cm^{-1} resolution.

Optical microscope pictures were obtained with an Olympus microscope, model BX51. The particles average size and size distribution were determined by measuring the diameter of more than 100 particles on optical micrographs with the image analysis software AnalySIS Auto (Soft Imaging System GmbH, Germany).

The size and size distribution of dried particles were measured with a scanning electron microscope (SEM; JEOL JSM-840). For this purpose, a drop of dilute microspheres' dispersion in 2-methoxyethanol was spread on a glass surface and then dried at room temperature. The dried sample was coated with gold in a vacuum before viewing under SEM. The particles' average size and distribution were determined by measuring the diameter of more than 100 particles with the image analysis software AnalySIS Auto (Soft Imaging System GmbH, Germany).

The thermal behavior of the particles was measured by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). The analysis was performed with a TC15 system equipped with TGA, model TG-50, and DSC, model DSC-30, Mettler Toledo. The analysis was performed with approximately 10 mg of dried samples under a dynamic nitrogen atmosphere (200 mL/min) with a heating rate of 10 °C/min.

The surface area of the microspheres was measured by the Brunauer-Emmet-Teller (BET) method [34], Gemini III model 2375, Micrometrics.

Surface elemental analysis was obtained by X-ray photoelectron spectroscopy (XPS), model AXIS−HS, Kratos Analytical, England, using Al Kα lines, at 10^{-9} Torr. The reported values of the XPS are an average of measurements performed on at least three samples of each of the tested particles and have a maximum error of about 10%.

The radiopacity of the various dried iodinated particles was demonstrated by a CT scanner (MARCONI, HeliCAT II).

Results and Discussion

Non-Cross-Linked Radiopaque Micrometer-Sized PS/PolyMAOETIB Composite Particles. Figure 1 describes the fundamental process of the preparation of the radiopaque non-cross-linked PS/polyMAOETIB composite particles via a single-step swelling of the PS template microspheres with methylene chloride containing BP and MAOETIB, followed by the polymerization of the monomer within the swollen particles.

The diameter of the swollen particles is commonly significantly higher than that of the template particles, since the particles are filled with the swelling solvent (methylene chloride containing BP and MAOETIB). Methylene chloride is evaporated before or during the initial stage of the MAOETIB polymerization at 73 °C. As a consequence, the PS/polyMAOETIB composite particles, depending on polymerization conditions, shrink to form composite particles with a diameter higher than that of the original template particles but less than the swollen ones. Figure 2 shows light microscope pictures that allow one to follow the size changes of the PS template microspheres during the swelling and polymerization processes.

The PS template microspheres have a size and size distribution of 2.6 ± 0.2 μm (Figure 2A). As a result of their swelling with 5 mL of methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB, their size distribution is maintained while their diameter increases to 6.9 ± 0.2 μm (Figure 2B). Polymerization of the MAOETIB within the swollen particles at 73 °C leads to the formation of grainy radiopaque non-cross-linked PS/polyMAOETIB composite particles of 3.3 ± 0.1 μm (Figure 2C). The size decrease of the swollen particles due to the polymerization step is probably as a consequence of the evaporation of methylene chloride, as previously explained.

The kinetics study of the swelling of the PS template microspheres by methylene chloride only (●) indicates that under the experimental conditions the swelling rate is relatively fast and completed within ca. 30 min with a final diameter of the swollen particles of 7.5 ± 0.2 μm. On the other hand, the kinetics of the swelling of the PS template microspheres with methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB (○) is significantly slower and is completed after approximately 240 min with a final swollen diameter of 6.9 ± 0.2 μm. The lower swelling capacity of the template particles toward methylene chloride containing BP and MAOETIB compared to methylene chloride only indicates that methylene chloride alone is a better swelling agent of the PS particles than methylene chloride containing the initiator and the monomer. This may indicate that the solubility of MAOETIB within PS is lower than that of methylene chloride and that during the swelling process methylene chloride carries the MAOETIB into the PS particles. Similar conclusions were also currently reported by Galperin et al. in their efforts to prepare radiopaque PS microspheres, by entrapping 2,3,5-triiodobenzoylethyl ester within PS microspheres via a single-step swelling process of the particles with methylene chloride containing the iodo ester.[33]

Figure 4 depicts FTIR spectra of the PS template microspheres (A), polyMAOETIB powder (B), and the radiopaque PS/polyMAOETIB composite particles prepared by the single-step swelling of the template microspheres with methylene chloride containing BP and MAOETIB (C).

Figure 4A shows a typical IR spectrum of PS: the transition frequencies 1492 and 3000−3100 cm^{-1} correspond to the aromatic CH stretching bands, 2849 and 2922 cm^{-1} correspond to the CH$_2$ stretching bands, and 700 cm^{-1} corresponds to vibrational band of C−C. Figure 4B shows an IR spectrum of polyMAOETIB powder: the transition frequencies at 2930 and 2847 cm^{-1} correspond to the aliphatic CH$_2$ stretching bands and the transition frequencies at 1732 and 1265 cm^{-1} correspond to carbonyl CO and ester C−O stretching bands, respectively. Figure 4C shows the IR spectrum of the radiopaque PS/polyMAOETIB composite particles. This spectrum is composed of peaks belonging both to PS (700, 1492, 3000 cm^{-1}, etc.) and to polyMAOETIB (1265 and 1732 cm^{-1}) and thus demonstrates the presence of the radiopaque polyMAOETIB in combination with PS.

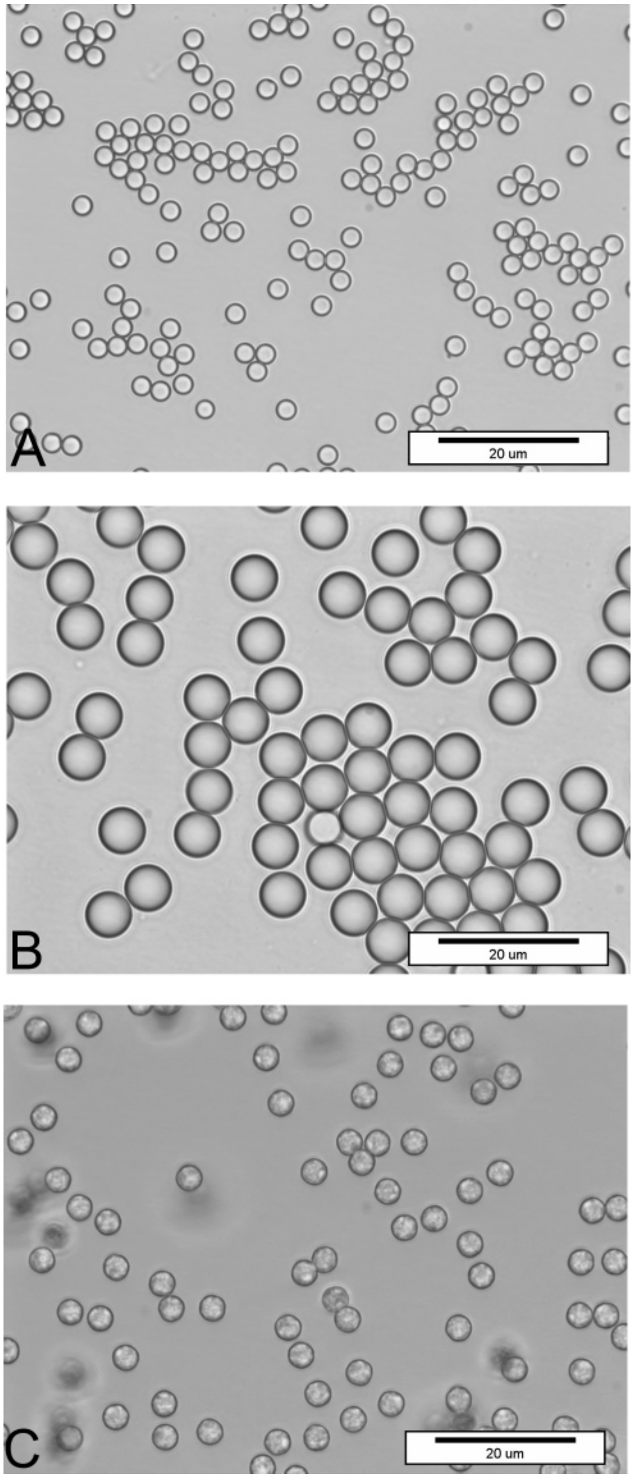


Figure 2. Light microscope pictures of the template PS microspheres before (A) and after swelling with methylene chloride containing BP and MAOETIB (B), followed by the polymerization of MAOETIB within the swollen particles (C). The swelling and polymerization processes were accomplished according to the Experimental Section with 5 mL of methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB.

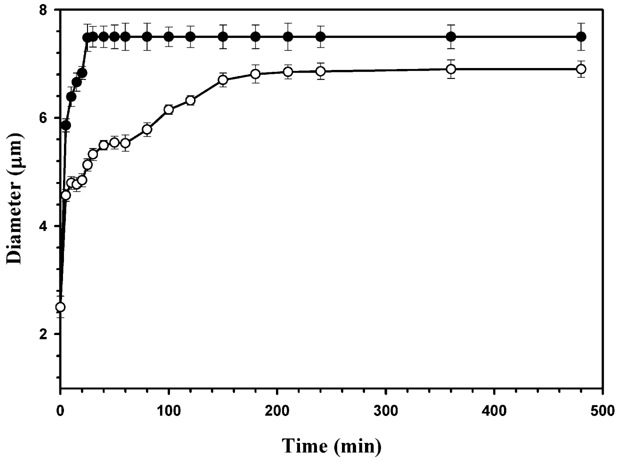


Figure 3. Kinetics' study of the swelling of the PS template microspheres with methylene chloride only (●) and with methylene chloride containing BP and MAOETIB (○). The swelling of the template microspheres was performed according to the experimental part with 5 mL of methylene chloride in the absence or presence of 10 mg of BP and 0.32 g of MAOETIB.

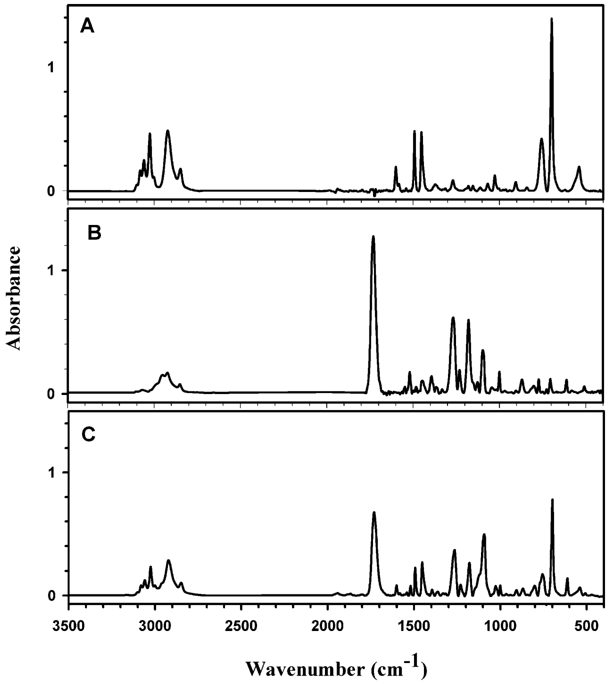


Figure 4. FTIR spectra of the PS template microspheres (A), polyMAOETIB powder (B), and the radiopaque PS/polyMAOETIB composite particles (C). The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 5 mL of methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB.

Figure 5 illustrates TGA (A) and DSC (B) thermograms of the PS template microspheres (curve 1), polyMAOETIB powder (curve 2), and the radiopaque non-cross-linked PS/polyMAOETIB composite particles (curve 3). The TGA thermogram of the PS template microspheres (Figure 5A-1) indicates almost 100% weight loss at temperatures between 350 and 450 °C. This weight loss is due to the decomposition of the PS polymer, as indicated by the broad endothermic DSC peak at ca. 425 °C (Figure 5B-1). The TGA thermogram of the polyMAOETIB powder (Figure 5A-2) indicates almost 100% weight loss at temperatures between 280 and 370 °C. This weight loss is due to the decomposition of the polyMAOETIB, as supported by the endothermic DSC peak at ca. 350 °C (Figure 5B-2). The dominant exothermic peak at ca. 355 °C, followed the endothermic peak, of the polyMAOETIB (Figure 5B-2) is due to the reaction between two iodine atoms (formed during the decomposition of the polyMAOETIB) to produce I_2, as was confirmed by mass spectrometry (by decreasing and then increasing of the parent peak of iodine atom and I_2, respectively). The TGA (Figure 5A-3) and DSC (Figure 5B-3) thermograms of the radiopaque non-cross-linked composite PS/polyMAOETIB particles represent the thermal behavior of the combination of the polyMAOETIB and the PS template microspheres.

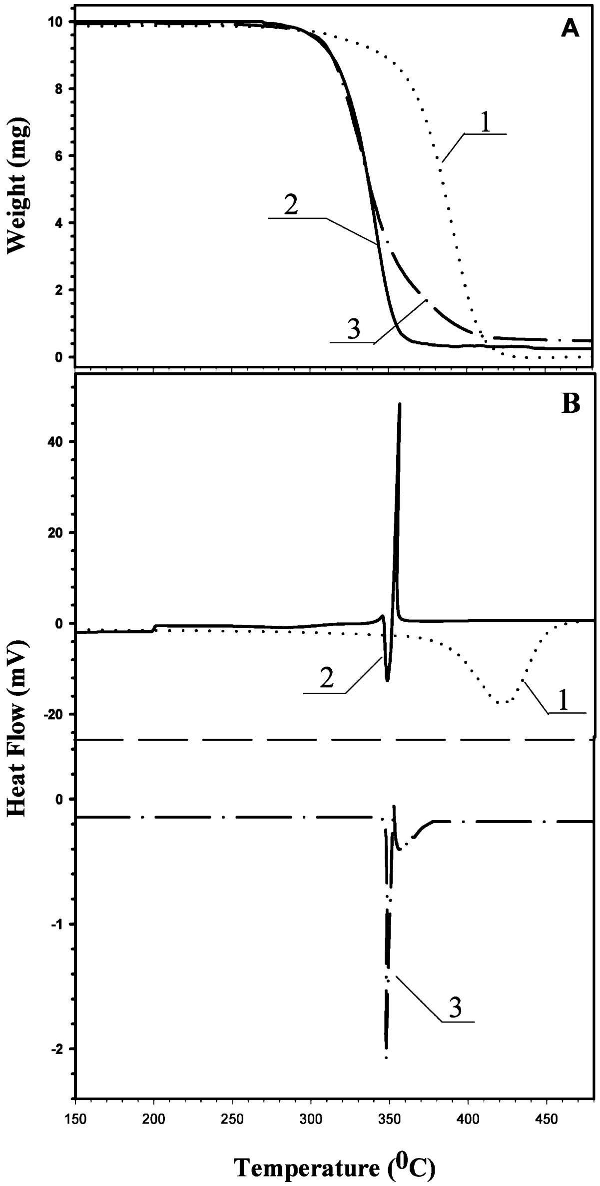


Figure 5. TGA (A) and DSC (B) thermograms of the PS template microspheres (curve 1), polyMAOETIB powder (curve 2), and the radiopaque non-cross-linked PS/polyMAOETIB composite particles (curve 3). The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 5 mL of methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB.

The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 5 mL of methylene chloride containing 10 mg of BP and 0.32 g of MAOETIB.

This figure also indicates a significant shift toward lower temperature in the decomposition temperature of the PS part of

Table 1. Influence of the Weight Ratio [MAOETIB]/[PS] on the % Iodine and Composition of the Radiopaque PS/PolyMAOETIB Composite Particles[a]

	PS/polyMAOETIB composite particles		
[MAOETIB]/[PS] (w/w)	% I	% polyMAOETIB[b]	% PS[c]
PS only	0	0	100
0.33	16.5	26.5	73.5
1.30	38.4	61.7	38.3
2.45	44.2	71.1	28.9

[a] The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 0.245 g of PS template particles swollen by 5 mL of methylene chloride containing 10 mg of BP and different amounts of MAOETIB. [b] %polyMAOETIB = (%I × 100)/62.2, where %Iodine is obtained from the elemental iodine analysis; 62.2 is the % iodine in pure polyMAOETIB. [c] %PS = 100 − %polyMAOETIB.

the composite particles compared to that of the PS template particles, e.g., the endotherm DSC decomposition peak of the PS template microspheres (Figure 5B-1) shifts from ca. 425 to ca. 360 °C in the PS/polyMAOETIB composite particles (Figure 5B-3). Also, the intensity of the DSC endothermic peaks of both the polyMAOETIB and the PS parts of the PS/polyMAOETIB composite particles (Figure 5B-3) is lower than that measured for the polyMAOETIB powder (Figure 5B-2) and the PS template microspheres (Figure 5B-1). This difference is obvious since each of the DSC measurements was performed with a 10 mg sample. However, the 10 mg of the composite particles was composed of two components (PS and polyMAOETIB), so each component contains much less than 10 mg. It should also be noted that the DSC curve of the PS/polyMAOETIB composite particles (Figure 5B-3) indicates an overlapping between the endothermic peak of the PS part and the exothermic peak of the polyMAOETIB part. This overlapping may explain the contradiction between the ratio of the endothermic peak to the exothermic peak of the polyMAOETIB part of the composite particles relative to that shown for the polyMAOETIB powder (Figure 5B-2).

Table 1 demonstrates the influence of the weight ratio [MAOETIB]/[PS] on the % iodine and the composition of the PS/polyMAOETIB composite particles, as calculated from elemental iodine analysis. This weight ratio was changed by using for the swelling process 0.245 g of PS template particles and various amounts of MAOETIB: 0.08, 0.32, and 0.6 g, respectively. Table 1 indicates that increasing the weight ratio [MAOETIB]/[PS] from 0.33 (0.08/0.245 = 0.33) to 1.30 and 2.45 leads to the increase in the weight % iodine of the radiopaque PS/polyMAOETIB composite particles from 16.5% to 38.4% and 44.2%, respectively. The increasing % iodine indicates the increase in the polyMAOETIB part relative to the PS part of the PS/polyMAOETIB composite particles. For example, increasing % iodine from 16.5% to 38.4% and 44.2% increased the polyMAOETIB part of the composite microspheres from 26.5% to 61.7% and 71.1%, respectively. It should be noted that elemental analysis of the PS/polyMAOETIB composite particles did not indicate the presence of N, which means that the PVP content in the PS fraction of the composite particles is less than 0.3% (the sensitivity of N elemental analysis). Oxygen analysis cannot distinguish between oxygen belonging to the polyMAOETIB and that belonging to the BP fraction. However, it can be assumed that the BP weight fraction in the composite particles is neglected. For example, when the weight ratio of [MAOETIB]/[PS] is 0.33, the calculated weight % BP in the composite particles is 1.8% (assuming that all of the initiator and monomer were used for the polymerization): [0.01 g of BP/(0.32 g o MAOETIB + 0.245 g of PS particles)] × 100 = 1.8%.

Elemental analysis is often an excellent tool for studying the bulk composition of particles. For example, in the present studies, iodine analysis has been used, as shown in Table 1, to study the bulk composition of the PS/polyMAOETIB composite particles. However, elemental analysis cannot be used for measuring surface compositions of micron-sized particles, which are frequently different from that of the bulk.

XPS, on the other hand, is a common tool for studying the elemental surface composition (except hydrogen) of materials.[35,36] The sampling depth of XPS is limited by the effective mean free path of electrons escaping from the surface. At a take off angle normal to the surface, the effective sampling depth is approximately 2.5λ, where λ is the mean free path. For organic substances, $\lambda \approx 20$ Å, so XPS may provide the composition of ca. 50 Å of the outermost surface of these substances. The typical XPS survey spectrum obtained for the PS template particles shows a carbon peak (C_{1s}) at ca. 283 eV, a nitrogen peak (N_{1s}) at ca. 398 eV, and an oxygen (O_{1s}) peak at ca. 530 eV. The XPS curves belonging to the radiopaque non-cross-linked PS/polyMAOETIB composite particles are similar, except for the presence of an iodine peak (I_{3d}) at ca. 619 eV. The intensity ratio of the different peaks changes according to the weight ratio between the PS fraction and the polyMAOETIB fraction of the PS/polyMAOETIB composite particles. The nitrogen peak of the microspheres belongs to the stabilizer (PVP) fraction of the particles surface. The oxygen peak of the various particles (PS, PS/polyMAOETIB) belongs to the surface initiator fraction ($PhCO_2-$ the active species of BP), surface stabilizer (PVP), and surface polyMAOETIB. The carbon peak of the various particles belongs to the PS, polyMAOETIB, initiator, and stabilizer fractions of the surface. The iodine peak of the radiopaque non-cross-linked PS/polyMAOETIB composite particles belongs to the polyMAOETIB fraction of the surface. Table 2 summarizes the XPS characterization data of the PS template microspheres and the radiopaque non-cross-linked PS/polyMAOETIB composite particles prepared at different weight ratios [MAOETIB]/[PS], thereby containing a different percentage of surface polyMAOETIB fraction (see Table 1). The weight % of the elements N, O, C, and I was calculated from their XPS binding energy peaks.

The % surface fraction of the PS, the stabilizer PVP and the initiator BP of the PS template microspheres was calculated from the following equations:

1. The whole surface (100%) of PS template microspheres composed of the surface fraction of following components:

% surface PS + % surface PVP + % surface BP = 100

2. % surface PVP = [(% surface N_{PVP}) × 100]/12.60

where % surface N_{PVP} is the XPS data of % (wt) surface N (Table 2); 12.60 is the % nitrogen in pure PVP.

3. % surface BP = [(% surface O_{BP}) × 100]/26.42

where % surface O_{BP} is the % surface O of $PhCO_2$ (calculated below); 26.42 is the % oxygen in pure BP.

% surface O_{BP} = % surface O − % surface O_{PVP}

where % surface O is the XPS data of % (wt) surface O of all fractions (Table 2); % surface O_{PVP} is the % surface O of PVP, as calculated below:

% surface O_{PVP} = [(% surface N_{PVP}) × 14.40]/12.60

where % surface N_{PVP} is the XPS data of % (wt) surface N (Table 2); 14.40 and 12.60 are the % oxygen and nitrogen in pure PVP, respectively.

4. % surface PS = 100 − % surface PVP − % surface BP

Table 2. XPS Elemental Data Illustrating the Influence of the Weight Ratio [MAOETIB]/[PS] on the % Surface Iodine and Composition of the PS Template Particles and the Radiopaque PS/PolyMAOETIB Composite Particles[a]

		XPS weight (%)				% surface fraction			
[MAOETIB]/[PS]	% polyMAOETIB	N	O	C	I	polyMAOETIB	PS	BP[b]	PVP
PS only	0	3.5	10.1	86.4	0	0	49.1	23.1	27.8
0.33	26.5	1.1	10.4	73.2	15.3	24.6	42.2	24.9	8.3
1.30	61.7	0.8	13.6	57.3	28.2	45.3	18.3	30.1	6.3
2.45	71.1	0.6	13.6	57.1	28.7	46.1	18.5	30.6	4.8

[a] The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 0.245 g of PS template particles swollen by 5 mL of methylene chloride containing 10 mg of BP and different amounts of MAOETIB. [b] The % surface initiator fraction is related to the active species of BP ($PhCO_2$).

The solution of the above equations, as shown in Table 2, suggests that the % surface fractions of PS, BP, and PVP of the template particles are 49.1, 23.1, and 27.8%, respectively. The presence of a relatively high % of surface initiator fraction on the PS template microspheres was discussed previously.[35,37] Briefly, it was demonstrated that the true stabilizer in PVP-stabilized dispersion polymerization of styrene in polar solvents is PVP grafted by PS chains. This PVP−PS grafted stabilizer is relatively rich in the initiator fraction and may be a major reason for the unexpected high % initiator fraction on the PS template microspheres. An additional explanation for the relatively high surface % of the initiator is the relative higher polar nature (ester group) of the BP fraction compared to PS, which therefore tends more to be exposed at the interface between the particles and the continuous phase.

The surface composition of the radiopaque non-cross-linked PS/polyMAOETIB composite particles was calculated similarly, taking into account that these composite particles contain in addition to surface PS, PVP, and BP also surface polyMAOETIB, according to eqs 5−9:

5. The whole surface (100%) of PS/polyMAOETIB composite particles composed of the following components:

% surface PS + % surface PVP + % surface BP + % surface polyMAOETIB = 100

6. % surface polyMAOETIB = [(% surface $I_{\text{polyMAOETIB}}$) × 100]/62.20

where % surface $I_{\text{polyMAOETIB}}$ is the XPS data of % (wt) surface I (Table 2); 62.20 is the % iodine in pure polyMAOETIB.

7. % surface PVP = [(% surface N_{PVP}) × 100]/12.60

where % surface N_{PVP} is the XPS data of % (wt) surface N (Table 2); 12.60 is the % nitrogen in pure PVP.

8. % surface BP = [(% surface O_{BP}) × 100]/26.42

where % surface O_{BP} is the % surface O of $PhCO_2$ (calculated below); 26.42 is the % oxygen in pure BP.

% surface O_{BP} = % surface O − % surface O_{PVP} − % surface $O_{\text{polyMAOETIB}}$

where % surface O is the XPS data of % (wt) surface O of all fractions (Table 2); % surface O_{PVP} and % surface $O_{\text{polyMAOETIB}}$ are the % surface O of PVP and polyMAOETIB, respectively, as calculated below.

% surface O_{PVP} = [(% surface N_{PVP}) × 14.40]/12.60

where % surface N_{PVP} is the XPS data of % (wt) surface N (Table 2); 14.40 and 12.60 are the % oxygen and nitrogen in pure PVP, respectively.

% surface $O_{\text{polyMAOETIB}}$ = [(% surface $I_{\text{polyMAOETIB}}$) × 10.46]/62.20

where % surface $I_{\text{polyMAOETIB}}$ is the XPS data of % (wt) surface I (Table 2); 10.46 and 62.20 are the % oxygen and iodine in pure polyMAOETIB, respectively.

9. % surface PS = 100 − % surface polyMAOETIB − % surface PVP − % surface BP

Table 2 demonstrates the surface composition of the non-cross-linked PS/polyMAOETIB composite particles. These composite particles were prepared at weight ratio [MAOETIB]/[PS] of 0.33, 1.3, and 2.45 and composed of 26.5, 61.7, and 71.1% polyMAOETIB fraction, respectively, as shown in Table 1. Table 2 shows that the surface of the PS/polyMAOETIB composite particles prepared at a weight ratio [MAOETIB]/[PS] of 0.33 is composed of 24.6% polyMAOETIB, 42.2% PS, 24.9% BP, and 8.3% PVP. The presence of polyMAOETIB surface fraction is probably due to the polymerization of MAOETIB on the surface of the template microspheres. The presence of surface polyMAOETIB leads to the decrease in the % surfaces of PS and PVP. A major drop was noted for the PVP surface fraction, from 27.8% belonging to the surface of the PS template particles to 8.3% of the composite particles. The % surface BP fraction of the composite particles (24.9%) is similar to that of the template particles (23.1%). Table 2 also demonstrates that the PS/polyMAOETIB composite particles prepared at a weight ratio [MAOETIB]/[PS] of 1.30 compared to that prepared at a weight ratio of 0.33 is composed of significantly higher surface fractions of polyMAOETIB (45.3 and 24.6%, respectively) and BP (30.1 and 24.9%, respectively) and lower surface PS (18.3 and 42.2%, respectively) and PVP (6.3 and 8.3%, respectively). Table 2 also shows that the surface compositions of the PS/polyMAOETIB composite particles prepared at a weight ratio [MAOETIB]/[PS] of 2.45 is similar to that prepared at a weight ratio of 1.30, e.g., surface polyMAOETIB: 46.1 and 45.3%, respectively; PS: 18.5 and 18.3%, respectively; BP: 30.6 and 30.1%, respectively; and PVP: 4.8 and 6.3%, respectively. A comparison between the XPS measurements (Table 2) and the iodine elemental analysis (Table 1) indicates that at the weight ratio [MAOETIB]/[PS] of 0.33 the % surface polyMAOETIB is similar to that of the bulk (24.6 and 26.5%, respectively). On the other hand, at higher weight ratios (1.30 and 2.45) the % surface polyMAOETIB concentration is significantly lower than that of the bulk. For example, at a weight ratio [MAOETIB]/[PS] of 2.45, the % surface polyMAOETIB concentration is 46.1%, whereas that of the bulk is 71.1%. Similar differences between the I content and Fe content of the most outer surface and the bulk of PS particles entrapped with 2,3,5-triiodobenzoylethyl ester or $Fe(CO)_5$, prepared by a single-step swelling process of the PS particles with the iodo ester or $Fe(CO)_5$, respectively, have already been reported by Galperin et al. and Shpaisman et al.[33] The fact that the most outer surface composition of the particles is different than that of the bulk is not surprising and dependent to a large extent on the environment of the particles. The most outer surface of the PS particles is relatively polar due to the presence of PVP and BP fraction, whereas the interior part of the particles is relatively hydrophobic.[35,37] These may explain why the hydrophobic monomer MAOETIB in spite its relatively large dimension is

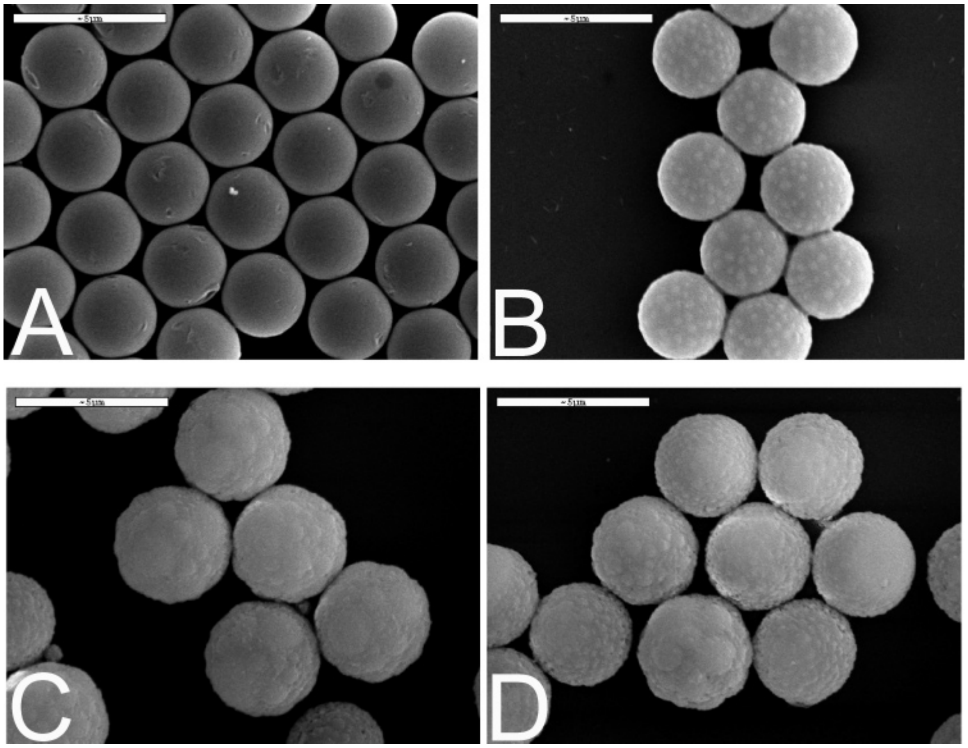


Figure 6. SEM pictures of the PS template microspheres (A) and the radiopaque PS/polyMAOETIB composite particles formed at weight ratios [MAOETIB]/[PS] of 0.33, 1.30, and 2.45 (B, C, and D, respectively). The radiopaque PS/polyMAOETIB composite particles were prepared according to the Experimental Section with 0.245 g of PS template particles swollen by 5 mL of methylene chloride containing 10 mg of BP and different amounts of MAOETIB.

carried by methylene chloride and concentrated in the bulk of the particles.

Figure 6 illustrates SEM pictures of the PS template particles (A) and the radiopaque PS/polyMAOETIB composite particles prepared at a weight ratio [MAOETIB]/[PS] of 0.33, 1.30, and 2.45 (B, C, and D, respectively). These pictures clearly show the smooth surface of the PS template particles compared to the rough surfaces of the PS/polyMAOETIB composite particles. These bumpy dotted surfaces of the composite particles are probably due to the polymerization of MAOETIB on the surface of the PS template particles. Size measurements of the template and the composite particles indicate a slight increase in the diameter of the particles as long as the ratio [MAOETIB]/[PS] increases: 2.6 ± 0.2, 2.8 ± 0.1, 3.3 ± 0.1, and 3.7 ± 0.3, respectively. Despite the increase in the diameter, BET measurements did not indicate a meaningful decrease, as expected, in the surface area of the various particles: between 2 and 2.2 m^2/g. This contradiction can be explained by the bumpy surfaces of the PS/polyMAOETIB composite particles which slightly increase their surface area and compensate for the expected decreased surface area due to their slight diameter increase.

Cross-Linked Radiopaque Micrometer-Sized PS/Poly(MAOETIB-DVB) and Poly(MAOETIB-DVB) Particles. In attempts to prepare micron-sized radiopaque polyMAOETIB particles with a higher surface area and iodine content, trials to dissolve the PS part of the PS/polyMAOETIB composite particles with different organic solvents have been accomplished. However, it soon became very clear that during the dissolution of the PS part with solvents such as methylene chloride and toluene at least part, if not all, of the polyMAOETIB is also dissolved. The solution to this was to prepare cross-linked PS/poly(MAOETIB-DVB) composite particles by a single-step swelling of the PS template particles with emulsion droplets of methylene chloride containing in addition to the iodinated monomer MAOETIB the cross-linker monomer DVB. To form stable spherical particles with a higher iodine content, the effect of the weight % ratio of [MAOETIB]/[DVB] on the properties of the cross-linked PS/poly(MAOETIB-DVB) composite particles has been studied. For this purpose, 0.245 g of PS template particles were swollen with 10 mg of BP and 0.6 g of monomers with different weight % ratios of [MAOETIB]/[DVB]: 99:1, 95:5, 80:20, and 60:40. The monomers within the swollen template particles were then polymerized at 73 °C. Table 3 demonstrates that, as expected, by decreasing the weight % ratio [MAOETIB]/[DVB] lower % iodine and polyMAOETIB in the cross-linked composite particles are obtained. For example, by decreasing the weight % ratio [MAOETIB]/[DVB] from 99:1 to 95:5, 80:20 and 60:40 the weight % polyMAOETIB of the composite particles decreased from 70.4% to 67.8, 56.1 and 35.7%, respectively. Table 3 also illustrates that, as expected, by dissolving the PS part of the cross-linked PS/poly-

Table 3. Influence of the Weight % Ratio [MAOETIB]/[DVB] on the % of Iodine and the Composition of the Radiopaque Cross-Linked PS/Poly(MAOETIB-DVB) and Poly(MAOETIB-DVB) Particles[a]

[MAOETIB]/	PS/poly(MAOETIB-DVB)		poly(MAOETIB-DVB)	
[DVB], (w/w)	% I	% polyMAOETIB[b]	% I	% polyMAOETIB[b]
99:1	43.8	70.4	59.1	95.0
95:5	42.2	67.8	56.8	91.3
80:20	34.9	56.1	45.6	73.3
60:40	22.2	35.7	34.1	54.8

[a] The radiopaque cross-linked PS/poly(MAOETIB-DVB) composite particles were prepared according to the Experimental Section with 0.245 g of PS template particles swollen by 5 mL of methylene chloride containing 10 mg of BP and 0.6 g of monomers with different weight % ratios of [MAOETIB]/[DVB]. The radiopaque cross-linked poly(MAOETIB-DVB) particles were prepared by dissolution of the PS template polymer of the cross-linked composite particles with methylene chloride, according to Experimental Section. [b] PolyMAOETIB = (%I × 100)/62.2, where %Iodine is obtained from the elemental iodine analysis; 62.2 is the % iodine in pure polyMAOETIB.

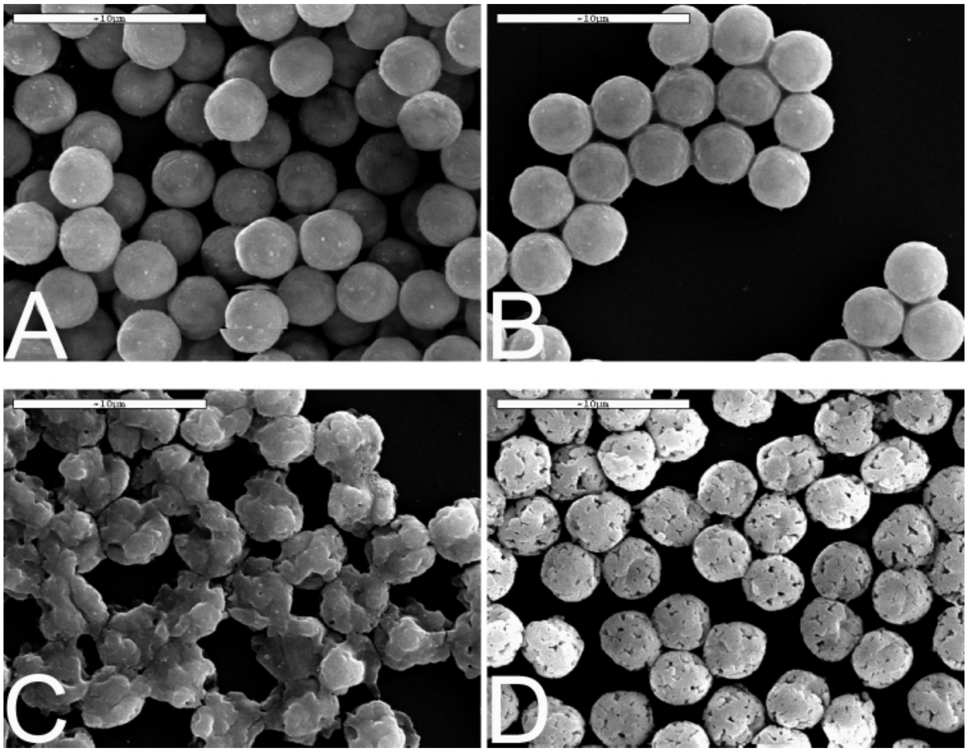


Figure 7. SEM pictures of the cross-linked PS/poly(MAOETIB-DVB) composite particles prepared in the presence of 0.6 g of monomers at weight % ratios [MAOETIB]/[DVB] of 99:1 and 95:5, before (A and B, respectively) and after (C and D, respectively) dissolution of the PS part of the composite particles. The radiopaque cross-linked PS/poly(MAOETIB-DVB) composite particles were prepared according to the Experimental Section with 0.245 g of PS template particles swollen by 5 mL of methylene chloride containing 10 mg of BP and 0.6 g of monomers with different weight % ratios of [MAOETIB]/[DVB]. The radiopaque cross-linked poly(MAOETIB-DVB) particles were prepared by dissolution of the PS template polymer of the cross-linked composite particles with methylene chloride, according to Experimental Section.

(MAOETIB-DVB) composite particles the % iodine and polyMAOETIB fraction significantly increased. For example, the % polyMAOETIB of the PS/poly(MAOETIB-DVB) and poly(MAOETIB-DVB) particles prepared at a weight ratio [MAOETIB]/[DVB] of 99:1 and 80:20, according to Table 3, is 70.4 compared to 95.0% and 56.1 compared to 73.3%, respectively. It should also be noted, according to Table 3, that the dissolution of the PS part of the composite particles did not provide the expected % of polyMAOETIB. For example, dissolution of the PS part of the composite particles prepared at a weight % ratio [MAOETIB]/[DVB] of 99:1 provided cross-linked particles containing 95% polyMAOETIB, and not 99%, as expected. It is possible that the remaining 4% fraction is due to minor residuals of PS chains grafted to PDVB or polyMAOETIB.

Figure 7 shows SEM pictures of the cross-linked PS/poly(MAOETIB-DVB) composite particles prepared at weight % ratios [MAOETIB]/[DVB] of 99:1 and 95:5 before (A and B, respectively) and after (C and D, respectively) the dissolution of the PS part of the composite particles.

These figures illustrate the relatively smooth surface of the cross-linked PS/poly(MAOETIB-DVB) composite particles compared to rougher surface of the cross-linked poly(MAOETIB-DVB) particles. Figure 7 also indicates that the dissolution of the PS part of the cross-linked PS/poly(MAOETIB-DVB) harms significantly the spherical shape of the composite particles prepared at a weight % ratio [MAOETIB]/[DVB] of 99:1 (Figure 7C), whereas the spherical shape of the particles prepared at ratio of 95:5 more or less remained (Figure 7D). It should be noted that the cross-linked poly(MAOETIB-DVB) particles prepared at weight % ratios [MAOETIB]/[DVB] of 80:20 and 60:40 had similar SEM pictures to that prepared at the ratio [MAOETIB]/[DVB] of 95:5 (Figure 7D).

SEM measurements of the diameter and size distribution of the cross-linked PS/poly(MAOETIB-DVB) and poly(MAOETIB-DVB) particles prepared at the different weight % ratios of [MAOETIB]/[DVB] indicate a similar diameter for all the particles: between 3.7 ± 0.3 to 3.9 ± 0.2 μm. A similar diameter and size distribution was also measured for the non-cross-linked PS/polyMAOETIB composite particles prepared under the same conditions (0.6 g of total monomer amount, MAOETIB or [MAOETIB + DVB]). BET measurements indicate for all the cross-linked PS/poly(MAOETIB-DVB) composite particles a similar surface area to that of the non-cross-linked PS/polyMAOETIB composite particles prepared under the same conditions: 2.0−2.2 m^2/g. On the other hand, the surface area of the cross-linked poly(MAOETIB-DVB) particles obtained after dissolution of the PS part of the cross-linked PS/poly(MAOETIB-DVB) composite particles was higher than that of the composite particles and increased as the weight ratio [MAOETIB]/[DVB] decreased. For example, at weight % ratios [MAOETIB]/[DVB] of 99:1, 95:5, 80:20, and 60:40, surface areas of 3.0, 4.5, 9.7, and 11.6 m^2/g have been measured for the cross-linked poly(MAOETIB-DVB) particles. It is indeed expected that the removal of the PS template part from the cross-linked composite particles will produce particles of significantly higher porosity and surface area. Previous studies by Kedem et al. concerning the preparation of cross-linked PS/polychloromethylstyrene composite particles by a single-step swelling process, followed by the dissolution of the PS part of these composite particles, demonstrated also an increased surface area as the weight % ratio [chloromethylstyrene]/[DVB] decreased.[31]

Table 4 demonstrates the surface composition of the radiopaque cross-linked PS/poly(MAOETIB-DVB) and poly(MAOETIB-DVB) particles, prepared at a weight % ratio [MAOETIB]/[DVB] of 95:5. The surface composition was

Table 4. XPS Elemental Data Illustrating the % Surface Composition of the Radiopaque Cross-Linked PS/Poly(MAOETIB-DVB) and Poly(MAOETIB-DVB) Particles[a]

	XPS weight %				% surface fraction			
particles type	N	O	C	I	polyMAOETIB	PS−PDVB	BP[b]	PVP
PS/poly(MAOETIB-DVB)	1.1	14.2	59.6	25.1	40.3	18.0	33.0	8.7
poly(MAOETIB-DVB)	0.2	12.0	47.0	40.8	65.6	14.2	18.6	1.6

[a] The radiopaque cross-linked PS/poly(MAOETIB-DVB) composite microspheres were prepared according to the Experimental Section with 5 mL of methylene chloride containing containing 0.6 g of monomers at a weight ratio [MAOETIB]/[DVB] of 95:5. The radiopaque cross-linked poly(MAOETIB-DVB) particles were prepared by dissolving the PS template polymer with methylene chloride, according to Experimental Section. [b] The % surface initiator fraction is related to the active species ($PhCO_2$) of BP.

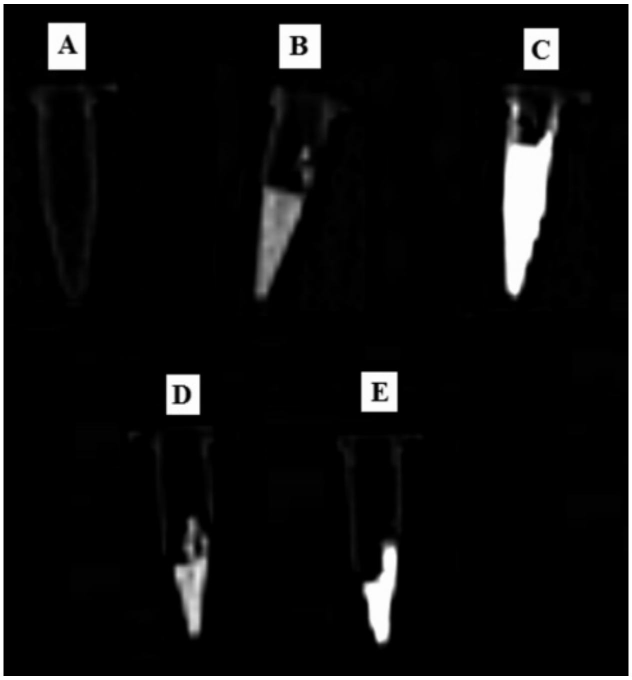


Figure 8. X-ray opacity of the PS template microspheres (A), the non-cross-linked PS/polyMAOETIB particles containing 26.5% (B) and 71.1% (C) polyMAOETIB, and the cross-linked poly(MAOETIB-DVB) particles containing 56.8% (D) and 91.3% (E) polyMAOETIB. The radiopaque non-cross-linked PS/polyMAOETIB and the cross-linked poly(MAOETIB-DVB particles were prepared according to the Experimental Section. The X-ray images were obtained with a CT scanner.

calculated from the XPS data of these particles, according to eqs 5−9, which were previously used for calculating the surface composition of the non-cross-linked PS/polyMAOETIB composite particles. The only difference is that the PS surface fraction could not be calculated separately from the PDVB surface fraction, so that they were calculated together as % surface (PS + PDVB). Table 4 illustrates that the surface of the PS/poly(MAOETIB-DVB) composite particles is composed of 40.3% surface polyMAOETIB, 18.0% surface PS−PDVB, 33% surface BP fraction, and 8.7% surface PVP. The dissolution of the PS part of the former composite particles results in cross-linked poly(MAOETIB-DVB) particles composed of a significantly higher % of surface polyMAOETIB: 65.6%, and a lower % surface PS−PDVB (14.2%), BP fraction (18.6%), and PVP (1.6%). A comparison between the XPS measurements (Table 4) and the iodine elemental analysis (Table 3) of these particles demonstrated that under the experimental conditions the % surface polyMAOETIB of both the cross-linked PS/poly(MAOETIB-DVB) and the poly(MAOETIB-DVB) is significantly lower than that of the bulk. For example, the % surface and bulk polyMAOETIB are 40.3 and 67.8%, respectively, for the cross-linked PS/poly(MAOETIB-DVB) composite particles and 60.6 and 91.3%, respectively, for the cross-linked poly(MAOETIB-DVB) particles.

X-ray Opacity of the Particles. Figure 8 illustrates the X-ray visibility of the dried PS template microspheres (A), the non-cross-linked PS/polyMAOETIB particles containing 26.5 (B) and 71.1% (C) polyMAOETIB, and the cross-linked poly(MAOETIB-DVB) particles containing 54.8 (D) and 91.3% (E) polyMAOETIB.

The PS template microspheres (A) are transparent to the X-ray irradiation, whereas the non-cross-linked and cross-linked composite particles (B−E) due to their iodine content show an excellent radiopaque nature. Figures 8B,C and 9D,E, as expected, clearly demonstrate that the X-ray visibility increases as the % of the polyMAOETIB fraction in the composite particles increases.

Summary

This article describes a new method for preparing novel uniform radiopaque non-cross-linked and cross-linked micrometer-sized composite particles based on a single-step swelling of polystyrene template microspheres of narrow size distribution with methylene chloride containing BP and MAOETIB in the absence or presence of DVB, followed by the polymerization of the monomer/s within the swollen particles. Porous uniform particles with a higher surface area were formed by the dissolution of the PS part of the cross-linked composite particles. Future studies concerning the effect of various parameters, e.g., swelling solvent type, initiator concentration and type, and cross-linking monomer type and concentration, on the bulk and surface properties of non-cross-linked and cross-linked particles, are ongoing in our laboratory. The optimal radiopaque particles will then be investigated in vitro and then in vivo as new potential polymeric contrast agents for different X-ray imaging needs, e.g., blood pool, body organs, embolization, dental composition, implants, protheses, and nanocomposites.

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