Macromolecules

ARTICLE

pubs.acs.org/Macromolecules

Nitroxide-Mediated Copolymerization of Methacrylic Acid and Sodium 4-Styrenesulfonate in Water Solution and One-Pot Synthesis of Amphiphilic Block Copolymer Nanoparticles

Ségolène Brusseau,[†,‡] Franck D'Agosto,[‡] Stéphanie Magnet,[§] Laurence Couvreur,[⊥] Cécile Chamignon,[∥] and Bernadette Charleux*[,‡]

[†]Laboratoire de Chimie des Polymères, UPMC Université de Paris 6, CNRS, UMR 7610, 3, rue Galilée, 94200 Ivry, France

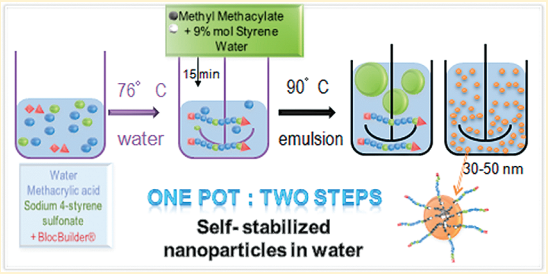
[‡]Laboratoire de Chimie Catalyse Polymères et Procédés (C2P2), Université de Lyon 1, CPE Lyon, CNRS UMR 5265, Equipe LCPP Bat 308F, 43 Bd du 11 Novembre 1918, 69616 Villeurbanne, France

[§]ARKEMA, Groupement de Recherches de Lacq, RN 117, B.P. n°34, 64170, Lacq, France

[⊥]ARKEMA, 420, rue d'Estienne d'Orves, 92705, Colombes, France

[∥]Centre de RMN des Polymères, Institut de Chimie de Lyon, INSA de Lyon, Bât Jules Verne, 17 avenue Jean Capelle, 69621 Villeurbanne, France

ABSTRACT: The SG1-mediated copolymerization of methacrylic acid and a small percentage of sodium 4-styrenesulfonate was performed in water solution at 76 °C, using BlocBuilder as an alkoxyamine initiator under acidic conditions. Unexpectedly, these conditions, which could be considered as rather unfavorable due to the instability of SG1 in acidic water, led to very good results in term of polymerization kinetics and control over polymer chain growth. It appeared that low temperature and short reaction time were the key parameters to maintain a good living character to the chains as evaluated by in situ ^{31}P NMR. The aqueous system was then used directly as the polymerization medium for the emulsion copolymerization of methyl methacrylate and styrene performed at 90 °C. This one-pot procedure led to the synthesis of amphiphilic block copolymers that self-assembled into stable core−shell nanoparticles.



INTRODUCTION

The development of controlled/living free radical polymerization (CRP)[1−3] methods based on the reversible deactivation of the propagating radicals[4] allowed a broad variety of polymer architectures to be created, on the basis of a multitude of monomers able to react via a radical polymerization mechanism. Among them, block copolymers represent an important class of materials, especially those exhibiting incompatible polymer blocks.[5,6] In particular, the amphiphilic block copolymers composed of hydrophilic and hydrophobic segments present a great interest for the development of self-assembled nanostructures in water.[7,8] Such suspensions of self-stabilized particles may find applications in several domains, such as drug delivery.[8] The preparation procedure relies on several steps including, first, the synthesis of the amphiphilic block copolymer, generally in an organic nonselective solvent, followed, after purification, by the self-assembly in water.[9] Differently from these usual methodologies, a few teams (including ours) developed a new strategy that intends to avoid the use of organic solvents as much as possible and save time and materials by reducing the number of steps. Our technique is to use surfactant-free emulsion polymerization in the presence of a hydrophilic, living, polymer precursor prepared via CRP in the first step.[10−33] In these conditions, chain extension of the water-soluble, end-functionalized polymer takes place in the monomer/water biphasic system: it starts with the formation of amphiphilic block copolymer chains in water, which spontaneously self-assemble when the hydrophobic block reaches a critical length. Then, the polymerization resumes in the monomer-swollen core of the so-formed nanoparticles until high conversion. This leads to kinetically frozen objects that are stabilized by a hydrophilic polymer shell composed of the starting hydrophilic precursor. High solids contents can be attained in batch conditions. For this purpose, we used nitroxide-mediated polymerization (NMP)[15−18,21−23] as well as reversible addition−fragmentation chain transfer (RAFT),[13,20,25−28,30] and the method allowed us to achieve not only core−shell spherical nanoparticles or nanogels but also fibers and vesicle-like objects dispersed in water. In all cases, however, the hydrophilic polymer precursor was synthesized in a preliminary step by solution polymerization in an organic solvent such as dioxane, dimethyl sulfoxide or ethanol, and further purified by precipitation before being used in emulsion polymerization. Such a multistep

Received: April 12, 2011
Revised: June 2, 2011
Published: June 22, 2011

Table 1. Experimental Conditions for the SG1-Mediated Copolymerizations of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) Initiated by the BlocBuilder Alkoxyamine in Water in Acidic Condition (pH = 3.5)

expt	$[MAA]_0$ (mol L^{-1})	$[SS]_0$ (mol L^{-1})	$f_{SS,0}$[a]	$[DMF]_0$ (mol L^{-1})	$[BlocBuilder]_0$ (mol L^{-1})	r[b] (%)	T (°C)	target M_n[c] at full conv. (g mol^{-1})	polym time (min)
1/blue ■	2.00	0.172	0.079	0.23	2.13×10^{-2}	12.0	76	10 250	120
2/●	1.96	0.168	0.079	0.21	2.06×10^{-2}	11.5	70	10 250	195
3/green ▲	1.91	0.170	0.081	0.27	1.91×10^{-2}	0	76	10 950	95
4/orange ♦	1.96	0.171	0.080	0.23	1.08×10^{-2}	12.0	76	19 500	120
5/purple •	1.90	0.166	0.080	0.35	4.52×10^{-3}	14.5	76	44 600	150

[a] Initial molar fraction of sodium 4-styrenesulfonate. [b] $r = 100 \times [SG1]_0/[BlocBuilder]_0$ [c] Theoretical number-average molar mass, calculated according to M_n = MM(BlocBuilder) + conversion × initial weight of monomers/initial mol number of BlocBuilder, with conversion =1 and molar mass of the initiator, MM(BlocBuilder) = 381 g·mol^{-1}.

procedure was important for model systems, allowing a better understanding of polymerization-induced micellization technique but cannot be considered as satisfactory for further applications. We have thus decided to develop a one-pot strategy applicable to both RAFT[34] and NMP. This requires to perform and control the synthesis of the hydrophilic polymer precursor in water.

In the present article, we will focus on NMP and on the use of poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) SG1-based macroalkoxyamines in the emulsion copolymerization of methyl methacrylate and styrene. Synthesis of the macroinitiator with complete kinetic study was reported recently using SG1-mediated polymerization in DMSO with the BlocBuilder alkoxyamine as an initiator.[22] Our aim now is to prepare it in aqueous solution and to further use the polymerization medium as the starting aqueous phase for the subsequent emulsion polymerization step.

NMP of hydrophilic monomers has been very seldom performed in aqueous solution. A few examples are available in the literature[35−40] and only four articles[36−39] described it using SG1 as the nitroxide. The considered monomers were either the neutral acrylamide,[37,38] *N*,*N*-dimethylacrylamide,[36] and poly(ethylene glycol) methyl ether methacrylate[39] or the anionic salt, sodium 4-styrenesulfonate.[36] Methacrylic acid has never been tested and the choice of the experimental conditions for NMP in aqueous solution may not be straightforward, due to potential effect of the pH on the polymerization outcome. In addition, the SG1-mediated homopolymerization of methacrylate monomers is not a living/controlled system due to poor stability of the derived macroalkoxyamines, favoring high radical concentration and hence side reactions, such as extensive termination of the propagating radicals and hydrogen transfer from the propagating radical to the nitroxide.[41,42] To favor the formation of stable terminal alkoxyamine, the copolymerization of methacrylic esters or methacrylic acid with a small amount of styrene was particularly efficient.[43−45] The method led to alkoxyamine end-group based on a terminal isolated styrene unit, in which the methacrylic penultimate unit induced a decrease in the C-ON bond dissociation energy and hence a lower dissociation temperature. This was advantageously used to decrease the NMP temperature below 100 °C. More recently, styrene was replaced by sodium 4-styrenesulfonate in the case of hydrophilic monomer such as methacrylic acid, but the polymerization was exclusively performed in organic solvent.[22]

In this article we will first describe the aqueous SG1-mediated copolymerization of methacrylic acid and a small percentage of sodium 4-styrenesulfonate initiated by BlocBuilder at low temperature with the objective of determining the most appropriate experimental conditions for a good living character of the polymer. Then, we will examine the subsequent emulsion copolymerization of methyl methacrylate and styrene performed in the same reactor, without purification of the macroinitiator.

EXPERIMENTAL PART

1. Materials. The monomers, methacrylic acid (MAA, purest grade, Acros, stabilized with 250 ppm of methylethylhydroquinone), sodium 4-styrenesulfonate (SS, purity ≥90%, Fluka), methyl methacrylate (MMA, purest grade, Acros, stabilized with 250 ppm of methylethylhydroquinone) and styrene (S, 99%, Acros stabilized with 10−20 ppm of *p*-*tert*-butylcatechol) were used without further purification. The *N*-(2-methylpropyl)-*N*-(1-diethylphosphono-2,2-dimethyl propyl)-*O*-(2-carboxyl prop-2-yl) hydroxylamine initiator (the so-called BlocBuilder-MA, pure) and the *N*-*tert*-butyl-*N*-(1-diethyl phosphono-2,2-dimethylpropyl) nitroxide (SG1, 85%) were kindly supplied by Arkema. Dimethyl sulfoxide-d_6 (DMSO-d_6, Euriso-top), deuterium oxide (D_2O extra, Aldrich 99.99% deuterium atom), dimethylformamide (DMF, Prolabo, pure), trimethylsilyldiazomethane (2.0 M in diethyl ether, Aldrich), tetrahydrofuran (THF, GPR rectapur stabilized with 0.025−0.04% BHT), and sodium carbonate (Na_2CO_3, Aldrich, pure) were used without purification. Deionized water (system purelab classic UV, Elga LabWater) was used for all reactions.

2. Copolymerization of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) in Water. The copolymerization reactions were carried out in deionized water at various temperatures (Table 1). In a typical experiment (experiment **1** in Table 1), a mixture of SG1 (22.1 mg, 2.57×10^{-3} mol L^{-1}), DMF (0.5 g, 0.24 mol·L^{-1}), MAA (5.05 g, 2.0 mol·L^{-1}) and SS (1.15 g, 1.72×10^{-1} mol L^{-1}, initial molar fraction of SS in the comonomer mixture: $f_{SS,0} = 0.079$) in water (23.8 g) was deoxygenated with a nitrogen stream for 20 min at room temperature. An internal reference, dimethylformamide was used in order to determine the monomers conversions via ^1H NMR. The BlocBuilder initiator (0.235 g, 2.13×10^{-2} mol L^{-1}) was then added and nitrogen bubbling was carried out for 10 more minutes. The final solution was slightly turbid for all experiments due to poor solubility of BlocBuilder at room temperature, which improved upon heating. The mixture was then transferred into a 50 mL three-neck round-bottom flask, immersed in an oil bath heated at 76 °C. Time zero of the polymerization was taken when the reaction temperature reached 50 °C. Samples were withdrawn at regular time intervals and quenched by cooling the flask in an iced-water bath. For each sample, the monomers overall molar conversions (x_{mol}) were determined by ^1H NMR analysis. The copolymers were analyzed by size exclusion chromatography (SEC) in DMF (with 0.01 mol of LiBr). Before injecting in SEC, the samples were dried and treated under stirring during 3 h with a solution of trimethylsilyldiazomethane (THF/water, 90/10, v/v) to turn the acid

dx.doi.org/10.1021/ma2008282 |*Macromolecules* 2011, 44, 5590–5598

Table 2. Experimental Conditions for the SG1-Mediated Copolymerizations of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) Initiated by the BlocBuilder Alkoxyamine at 75°C in Deuterated Solvent, in the Absence of Added Free SG1

expt	$[MAA]_0$ (mol L^{-1})	$[SS]_0$ (mol L^{-1})	$f_{SS,0}$[a]	$[BlocBuilder]_0$ (mol L^{-1})	solvent	target M_n[b] at full conv (g mol^{-1})	polym time (min)
6	3.39	0.38	0.090	2.85×10^{-2}	D_2O	13 200	105
7	2.73	0.29	0.087	2.17×10^{-2}	DMSO-d_6	13 700	73

[a] Initial molar fraction of sodium 4-styrenesulfonate. [b] Theoretical number-average molar mass, calculated according to M_n = MM(BlocBuilder) + conversion × initial weight of monomers/initial mol number of BlocBuilder, with conversion =1 and molar mass of the initiator, MM(BlocBuilder) = 381 g·mol^{-1}.

Table 3. Experimental Conditions for the One-Pot, Surfactant-Free, ab Initio, Batch Emulsion Polymerizations of Methyl Methacrylate (MMA) with 9.0 mol % of Styrene (S) at 90 °C Initiated by a Poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) Macroinitiator Synthetized in Situ in Water in a First Step Conducted at 76 °C

	first step: 15 min at 76 °C								second step: 90 °C				
expt	$[MAA]_0$ (mol L^{-1})	$[SS]_0$ (mol L^{-1})	$f_{SS,0}$[a]	$[BlocBuilder]_0$ (mol L^{-1})	water in the 1st step (g)	r[b] (%)	target M_n[c] at full conv (g mol^{-1})	M_n[d] (g mol^{-1})	$[MMA]_0$[e] (mol L^{-1}_{aq})	$[S]_0$[e] (mol L^{-1}_{aq})	water added in the 2nd step (g)	overall polymer content (wt %)	target M_n[f] at full conv. (g mol^{-1})
8/blue ●	2.06	0.15	0.070	1.1×10^{-2}	38.8	9.8	19950	12800	2.32	0.22	40.3	27.2	59920
9/×	2.15	0.16	0.069	2.3×10^{-2}	37.0	9.3	10000	8750	2.27	0.22	42.5	26.9	27900
10/orange ■	2.06	0.15	0.070	4.0×10^{-2}	38.9	9.9	5570	6800	2.38	0.22	40.2	27.1	16450

[a] Initial molar fraction of sodium 4-styrenesulfonate. [b] $r = 100 \times [SG1]_0/[BlocBuilder]_0$ [c] Theoretical number-average molar mass, calculated according to M_n = MM(BlocBuilder) + conversion × initial weight of hydrophilic monomers/initial mol number of BlocBuilder, with conversion =1 and molar mass of the initiator, MM(BlocBuilder) = 381 g·mol^{-1}. [d] Experimental number-average molar mass of the in situ synthesized macroinitiator obtained via SEC in DMF with 0.01 mol·L^{-1} LiBr using a PMMA calibration after methylation. [e] All concentrations are calculated on the basis of the overall volume of aqueous phase in the latex. [f] Theoretical number-average molar mass of the formed block copolymer, calculated according to M_n = MM(BlocBuilder) + conversion × (initial overall weight of hydrophilic and hydrophobic monomers/initial mol number of the initiator), with conversion =1 and molar mass of the initiator, MM(BlocBuilder) = 381 g·mol^{-1}.

groups into methyl esters.[46,47] The dried methylated copolymers were then dissolved in the SEC solvent.

In order to calculate the monomer conversions, one resonance peak of dimethylformamide (DMF, δ = 7.95 ppm) was used as an internal reference (peak integral: I_{DMF}). The conversion of SS (x_{SS}) was calculated on the basis of the 3 vinylic protons of SS (δ = 6.75 ppm, δ = 5.80 ppm and δ = 5.25 ppm). The corresponding integral I_{ss} for one proton was the average of the 3 integrals. For MAA (x_{MAA}), the integral I_{MAA} for one proton was the average of those of the two $=CH_2$ protons at δ = 6.00 ppm and δ = 5.56 ppm. For kinetic analysis, the overall conversion considered was the molar conversion directly accessible via the NMR analysis or calculated from the individual monomer conversions according to the relationship $x_{mol} = x_{SS} \times f_{SS,0} + x_{MAA} \times f_{MAA,0}$ ($f_{SS,0}$ and $f_{MAA,0}$ are the initial molar fractions of SS and MAA, respectively, in the monomer mixture). For the plots representing M_n as a function of the overall conversion, one used the weight conversion, that can be calculated according to $x_w = x_{SS} \times w_{SS,0} + x_{MAA} \times w_{MAA,0}$ ($w_{SS,0}$ and $w_{MAA,0}$ are the initial weight fractions of SS and MAA, respectively, in the monomer mixture) or that can be determined directly via gravimetric analysis.

3. Copolymerization of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) Monitored by ^{31}P NMR. The copolymerization reactions were carried out at 75 °C in Young tubes of 5 mm in diameter directly in the NMR spectrometer. In a typical experiment (Table 2, experiment 7), the monomers SS (0.067 g, 2.9×10^{-1} mol L^{-1}, initial molar fraction of SS in the comonomer mixture: $f_{SS,0}$ = 0.087) and MAA (0.29 g, 2.7 mol·L^{-1}) were mixed in DMSO-d_6 (1.14 g) and deoxygenated with a nitrogen stream for 30 min at room temperature. During this time, the BlocBuilder initiator (0.0104 g, 2.17×10^{-2} mol L^{-1}) was introduced into the NMR tube under a nitrogen flow. With a syringe, the prepared monomer solution was introduced in the NMR tube; the latter was sealed under nitrogen and maintained in an ice bath before starting the experiment. The tube was then introduced into the spectrometer at 25 °C and the first spectrum was recorded. Then the temperature was set at 75 °C marking the time 0 of the polymerization and a second spectrum was recorded after 15 min. The spectra (32 scans during 3 min 38s with a delay of 5 s between each) were recorded every 10 min during an overall polymerization time of 1−2 h.

4. One-Pot Emulsion Copolymerization of Methyl Methacrylate with a Low Percentage of Styrene Initiated by the Water-Soluble Poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) Macroinitiator Formed in Situ. The emulsion copolymerizations were performed in two different steps, both performed consecutively in the same 300 mL thermostated glass Parr reactor.

For the first step, the copolymerization of methacrylic acid and sodium 4-styrenesulfonate was carried out at 76 °C in deionized water. In a typical experiment (experiment **10** in Table 3), a mixture of SG1 (5.5 mg, 4.03×10^{-3} mol L^{-1}), MAA (8.38 g, 2.06 mol·L^{-1}), and SS (1.5 g, 1.55 $\times 10^{-1}$ mol L^{-1}, initial molar fraction of SS in the comonomer mixture: $f_{SS,0}$ = 0.070) in water (38.9 g) was deoxygenated with a nitrogen stream for 20 min at room temperature. The BlocBuilder initiator (0.7254 g, 4.04×10^{-2} mol L^{-1}) was added in the mixture and nitrogen bubbling was maintained for 10 more minutes. The mixture was introduced into the preheated (76 °C) and stirred (250 rpm) reactor under 1.1 bar of nitrogen. At 15 min reaction time, the mixture of hydrophobic monomers and water (prepared as described below) for the second step, i.e., the emulsion polymerization of MMA with a small percentage of S, was injected into the reactor stirred at 250 rpm, and immediately heated to 90 °C, under a 3 bar pressure of nitrogen. For preparation of this second step mixture, methyl methacrylate (18.83 g) and styrene (1.85 g; initial molar fraction of S in the comonomer mixture: $f_{S,0}$ = 0.089) were mixed with a water solution (40.2 g) of Na_2CO_3 (0.325 g). The hydrophobic monomers content was 18.6 wt % based on the overall mass of the

dx.doi.org/10.1021/ma2008282 |*Macromolecules* 2011, 44, 5590–5598

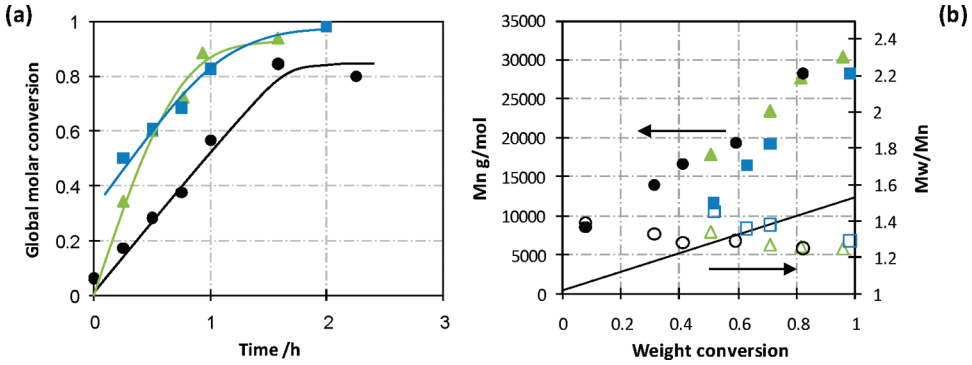


Figure 1. Effect of the temperature and of the free SG1 initial concentration for the copolymerizations of methacrylic acid with 8 mol % of sodium 4-styrenesulfonate in water: experiments **1** (blue ■, T = 76 °C and 12 mol % of free SG1), **2** (●, T = 70 °C and 11.5 mol % of free SG1) and **3** (green ▲, T = 76 °C and no free SG1). (a) Overall molar conversion vs time and (b) M_n (full symbols) and M_w/M_n (corresponding empty symbols; SEC in DMF with 0.01 mol·L^{-1} of LiBr, methylated copolymers, PMMA calibration) versus weight conversion.

reaction medium. The biphasic mixture was stirred under nitrogen at room temperature during 20 min before being injected into the reactor. The polymerization was allowed to proceed for 5 h more. Samples were periodically withdrawn to follow monomer conversion by gravimetry and to analyze the copolymers by SEC in DMF after methylation as described in a previous section, and the particle size and size distribution by dynamic light scattering (DLS) and transmission electron microscopy (TEM).

5. Analytical Techniques. ^{1}H NMR spectroscopy for kinetic analysis (i.e., monomer conversion) was performed in 5 mm diameter tubes in DMSO-d_6 at 25 °C using a Bruker Avance 300 (300 MHz) spectrometer. The chemical shift scale was calibrated on the basis of the solvent peak (δ = 2.50 ppm).

The SEC analyses were performed in DMF at 70 °C with 0.01 mol·L^{-1} of LiBr, at a flow rate of 1 mL·min^{-1}, using toluene as a flow rate marker. All polymers were analyzed at a concentration of 5 mg·mL^{-1} after filtration through a 0.45 μm pore-size membrane. The separation was carried out on two Agilent technologies columns (two columns PolarGet-M 8 μm, MIXED, 300 × 7.5 mm). The setup was equipped with a refractive index (RI) detector (Waters 410 differential refractometer at λ = 930 nm). The average molar masses (number-average molar mass, M_n, and weight-average molar mass, M_w) and the polydispersity index (PDI = M_w/M_n) were derived from the RI signal by a calibration curve based on poly(methyl methacrylate) (PMMA) standards. The software used for data collection and calculation was Empower Pro version 5.0 from Waters.

^{31}P NMR spectroscopy for in situ kinetic analysis was performed in 5 mm diameter Young tube in DMSO-d_6 or D_2O solution at 75 °C, using a Bruker Avance III 400 NMR spectrometer (9,4 T; 161,97 MHz for 31P). The spectra were acquired with power gate proton decoupling using an acquisition time of 1 s, a 30° pulse angle, and a relaxation delay of 5 s. Chemical shifts were measured relative to external diethyl phosphite (δ = 7.1 ppm) in $CDCl_3$. Spectra were recorded with a line-broadening of 2 Hz.

The intensity-average diameters (D_i) of the latex particles and the dispersity factor (σ) were measured by dynamic light scattering (DLS) at a temperature of 25 °C using a Zetasizer Nano Series (Nano ZS) from Malvern Instrument using the Zetasizer 6.2 software. The instrument was calibrated with a standard polystyrene latex in water exhibiting a particle size of 220 nm ±6 nm. Before measurements, the latex samples were diluted in deionized water. The particles were also visualized by transmission electron microscopy (TEM, Philips CM 120 at 80 keV equipped with a high resolution CCD camera).

■ RESULTS AND DISCUSSION

1. Copolymerization of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) in Water Solution. Before performing the one-pot emulsion polymerizations, the SG1-mediated copolymerization of MAA with a small percentage of SS in water was studied under conditions very similar to those previously reported for the polymerization in DMSO (see Table 1).[22] The aim was to follow the polymerization kinetics and to determine the most appropriate duration for achieving high conversion together with good living character of the formed macroalkoxyamines. The reactions were performed without any pH control, which means under acidic conditions (pH = 3.5). This option was tested because neutralization of methacrylic acid in water with a sodium hydroxide solution led to solubility problems (formation of insoluble salt). Because of the previously reported difficulties of performing SG1-mediated polymerizations at low pH,[48−50] these new experimental conditions were examined with great care.

When targeting a final M_n of 10 000 g·mol^{-1} at full conversion, which is the appropriate molar mass range for the macroalkoxyamines used in emulsion polymerization, we observed that the reactions performed at 76 °C were particularly fast under the conditions employed. Indeed, conversions close to 100% were reached within 2 h. This can be seen in Figure 1a for experiment 1 detailed in Table 1. The number-average molar masses (Figure 1b) increased linearly with mononomer conversion and the molar mass distributions were narrow as attested by the low polydispersity index values. Like for the polymerizations performed in DMSO and discussed in our previous article,[22] the experimental M_n values were above the expected data, showing a possible effect of a fast incorporation of SS in the chains. This would lead to the formation of SS dyad-based alkoxyamines in the early stage of the polymerization, that do not dissociate efficiently at low temperature. Indeed, the individual monomer conversions were followed by ^{1}H NMR and showed a faster conversion rate for SS than for MAA (Figure 2). The controlled character of the polymerization (i.e., the fast initiation and simultaneous growth of all chains) was further attested by the complete shift of the SEC peaks with monomer conversion (Figure 3). Interestingly, SS was not completely converted at 68.5% overall monomer conversions, which is an important condition for maintaining a good control in this type of system.[22,43,44]

dx.doi.org/10.1021/ma2008282 |Macromolecules 2011, 44, 5590–5598

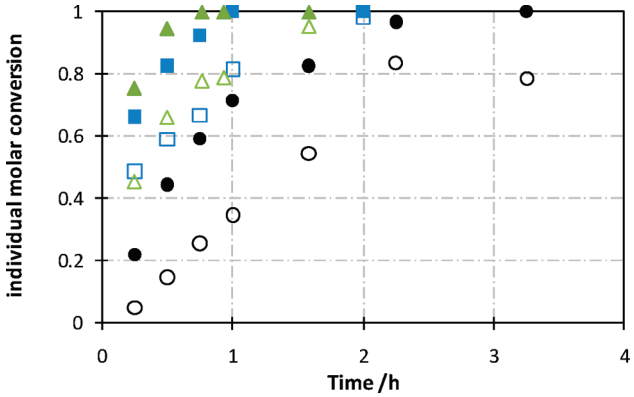


Figure 2. Individual molar conversion of monomers vs time for the copolymerizations of methacrylic acid (MAA) (empty symbols) with 8 mol % of sodium 4-styrenesulfonate (SS) (full symbols) in water: experiments **1** (blue ■, T = 76 °C and 12 mol % of free SG1), **2** (●, T = 70 °C and 11.5 mol % of free SG1) and **3** (green ▲, T = 76 °C and no free SG1).

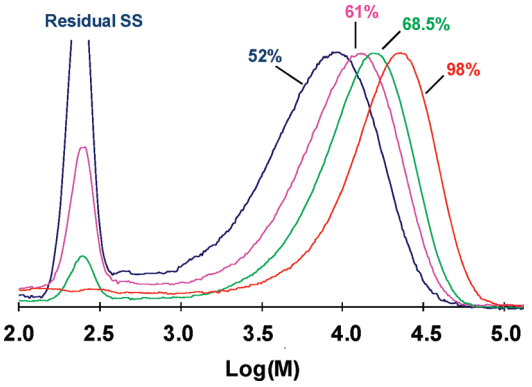


Figure 3. Size exclusion chromatograms (DMF solution with 0.01 mol·L^{-1} of LiBr) at various monomer weight conversions for the copolymer of methacrylic acid and sodium 4-styrenesulfonate (SS) synthesized in water at 76 °C with $f_{SS,0}$ = 0.088 and 12 mol % of free SG1 (experiment 1 in Table 1).

In the experiment 1, 12 mol % of free SG1 (based on the BlocBuilder initiator) were added in the reaction medium, but its effect appeared to be rather negligible when experiment 1 was compared with experiment 3, performed in the absence of free nitroxide (Figure 1). Differently, a decrease in temperature to 70 °C contributed to decrease the polymerization rate (experiment 2, Table 1 and Figure 1) without affecting the evolutions of M_n and M_w/M_n with monomer conversion.

By comparison with the same series of experiments performed in DMSO,[22] the most important outcome was the larger polymerization rate and higher final conversions reached within 2 h. This result might be ascribed to the instability of SG1 in aqueous acidic condition.[47] Additionally, the propagation rate constant, k_p, of MAA as determined by pulsed laser photopolymerization experiments[51] is high and close to 8000−9000 L·mol^{-1}·s^{-1} in water at 80 °C for an initial concentration in the 2.3−1.7 mol·L^{-1} range. It is significantly lower in DMSO i.e., 2000−3000 L.mol^{-1}.s^{-1} in the 71 °C - 88 °C temperature range for a concentration of 3.42 mol·L^{-1}.[52]

A change in the BlocBuilder initial concentration, so as to target higher molar masses (experiments 4 and 5, compared with experiment 1 in Table 1) was also studied and the results are displayed in Figure 4. It appears that the polymerization rate decreased significantly when the initiator concentration was decreased. In particular, the lowest value (4.52×10^{-3} mol L^{-1}) led to rather slow polymerization and low conversion in the time frame of the polymerization, due to the release of a large proportion of free SG1 explained by the pronounced persistent radical effect in diluted conditions.[53] The initiator efficiency (estimated by the theoretical M_n vs conversion slope over the experimental one) was rather low and increased from 25%, to 30%, and then to 40% approximately when the initial concentration of BlocBuilder was increased. Again, this may be explained by the formation of short chains with inactive terminal SG1-capped SS dyads, favored at low initiator concentration.

To further assess the living character of the formed polymer chains, ^{31}P NMR was used for in situ monitoring (i.e., identification of the presence of an alkoxyamine end-group bearing a P atom in the SG1 structure). The corresponding experiments are described in the following section.

2. Copolymerization of Methacrylic Acid (MAA) with Sodium 4-Styrenesulfonate (SS) in Solution Monitored by ^{31}P NMR. Experiments with conditions close to those of experiment 1 (Table 1) were performed in deuterated solvent, i.e., D_2O for the experiment 6 and DMSO-d_6 for the experiment 7 and were monitored by ^{31}P NMR directly in the spectrometer at 75 °C. The conditions are detailed in the Experimental Part and in Table 2. The spectra at various reaction times are shown in Figures 5a (D_2O) and 5b (DMSO-d_6). The ^{1}H NMR conversions could not be followed simultaneously due to too short time interval between the spectra. The time−conversion correspondence in water solution has thus to be evaluated via the plot shown in Figure 1 for experiment 1 performed in water and via experiment 3 reported in the ref 22 (around 50% overall conversion within 1 h and 75% within 2 h), for the experiment performed in DMSO.

The resonances corresponding to the alkoxyamine can be seen in the 24−25 ppm region and are consistent with the peaks already observed for poly(methyl methacrylate-*co*-styrene) SG1-based alkoxyamine.[43] In water, the intensity of the peak decreased after ca. 30 min polymerization time (close to 60% conversion from experiment 1), whereas there was no change during the first 73 min in DMSO (also ca. 60% conversion due to slower polymerization[22]). Simultaneously a peak close to 0 ppm appeared with time in both solvent systems, and was assigned to a side product based on SG1, confirming degradation of the nitroxide. This means that polymerizations performed in water should not be conducted for times longer than 30 min, i.e., too high overall conversions. This would avoid the complete consumption of sodium 4-styrenesulfonate and would maintain an alkoxyamine group at the chain end of the formed polymer, as shown in the next section. This information is of high significance to design the experimental conditions for a one-pot emulsion polymerization.

3. One-Pot Emulsion Copolymerization of Methyl Methacrylate with a Low Percentage of Styrene Initiated by the Water-Soluble Poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) Macroinitiator Formed in Situ. As described in the experimental part, the emulsion polymerizations were performed in one pot, via a two step procedure (see Table 3 for the experimental conditions and Table 4 for the results). The first step corresponded to the synthesis of the water-soluble

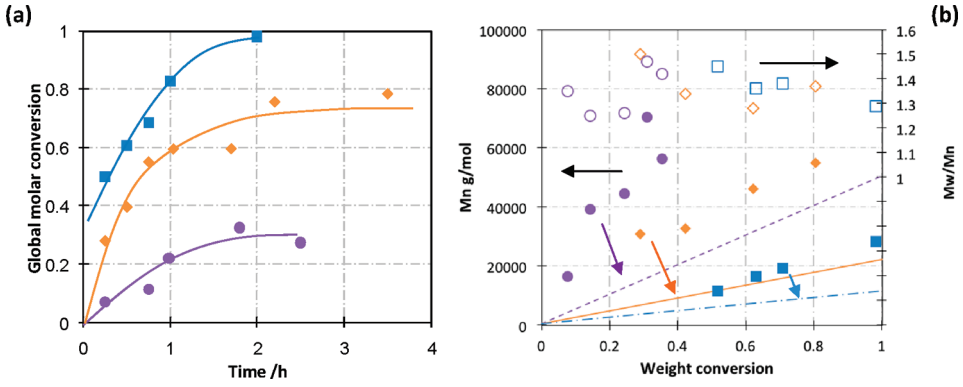


Figure 4. Effect of the initial concentration of BlocBuilder for the copolymerizations of methacrylic acid with 8 mol % of sodium 4-styrenesulfonate in water in the presence of 12 mol % of free SG1 at 76 °C: experiments 1 (blue ■, $[BlocBuilder]_0 = 21.3$ mmol L^{-1}), **4** (orange ◆, $[BlocBuilder]_0 = 10.8$ mmol L^{-1},) and 5 (purple ●, $[BlocBuilder]_0 = 4.52$ mmol L^{-1}). (a) Overall molar conversion vs time and (b) M_n and M_w/M_n (SEC in DMF with 0.01 mol·L^{-1} LiBr, methylated copolymers, PMMA calibration) versus weight conversion.

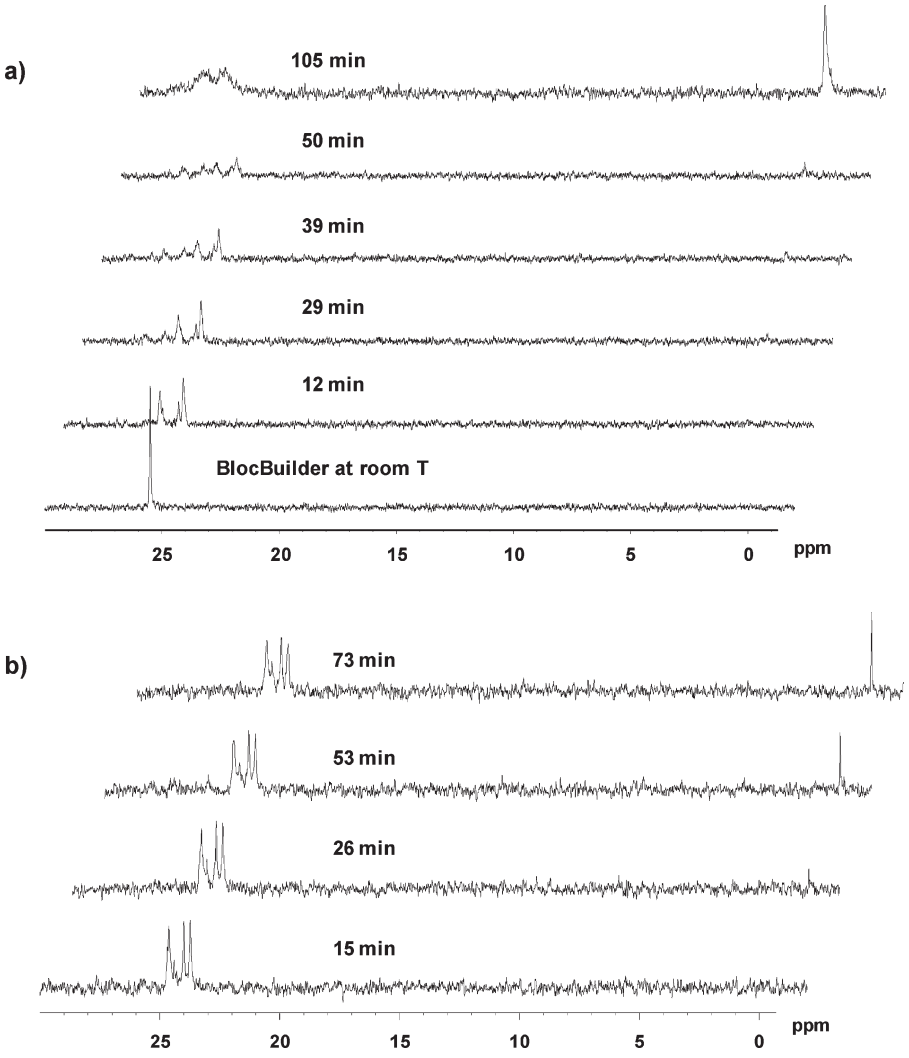


Figure 5. Evolution of the ^{31}P NMR spectra with polymerization time for the copolymerization of methacrylic acid with sodium 4-styrenesulfonate performed at 75 °C (a) in D_2O (experiment **6** in Table 2; upper spectra offset 0.8 ppm) and (b) in DMSO-d_6 (experiment **7** in Table 2; upper spectra offset 1.3 ppm).

poly(methacrylic acid-*co*-sodium 4-styrenesulfonate)−SG1 macroalkoxyamine initiator during a period of 15 min so as to ensure high chain-end functionality. As studied in the previous sections, the reaction was performed in acidic

dx.doi.org/10.1021/ma2008282 |*Macromolecules* 2011, 44, 5590–5598

Table 4. Experimental Results for the One-Pot, Surfactant-Free, ab Initio, Batch Emulsion Polymerizations of Methyl Methacrylate with 9.0 mol % of Styrene at 90 °C

expt	time[a] (h)	overall conv[b] (%)	$M_{n,th}$[c] (g mol^{-1})	$M_{n,SEC}$[d] (g mol^{-1})	M_w/M_n	D_i[e] (nm)	σ	final pH
8	2.3	24	14 450	28 150	1.5	57	0.60	4.2
9	5.1	78	21 850	37 100	1.3	50	0.09	4.3
10	5.3	87	14 300	19 650	1.3	23	0.27	4.1

[a] Overall time of both steps. [b] Overall conversion including all hydrophilic and hydrophobic monomers. [c] Theoretical M_n calculated at the final experimental conversion of hydrophobic and hydrophilic monomers. [d] Experimental M_n determined by size exclusion chromatography in DMF with LiBr on raw polymer after methylation (conventional PMMA calibration). [e] Intensity-average diameter of the final latex from DLS (average over three measurements). In experiments 8 and 10, aggregates larger than 700 nm in diameter were present in very small amount.

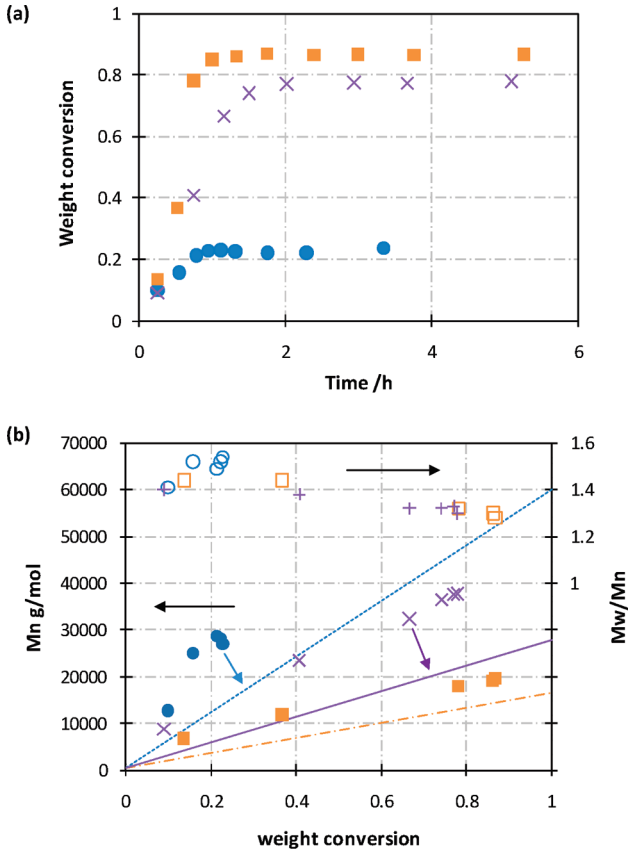


Figure 6. Surfactant-free, ab initio, batch emulsion polymerizations of methyl methacrylate with 9.0 mol % of styrene at 90 °C initiated by the poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) macroinitiator synthesized in situ during 15 min at 76 °C: effect of the initial concentration of BlocBuilder in the first step for the experiments 8 (blue ●, $[BlocBuilder]_0 = 1.1 \times 10^{-2}$ mol L^{-1}), 9 (×, $[BlocBuilder]_0 = 2.3 \times 10^{-2}$ mol L^{-1}), and 10 (orange ■, $[BlocBuilder]_0 = 4.0 \times 10^{-2}$ mol L^{-1}). (a) Overall weight conversion determined by gravimetry vs overall polymerization time; (b) M_n and M_w/M_n (SEC in DMF + LiBr, methylated copolymers, PMMA calibration) versus weight conversion (overall hydrophilic and hydrophobic monomers). The straight lines correspond the theoretical evolutions.

conditions and the macroinitiator was indeed shown to remain living within the first 30 min of the reaction. It has to be mentioned that the experimental conversions of the hydrophilic comonomers in the first step were not determined, to avoid sampling, and the modification of the amount of macroinitiator before the second step. One has to refer to experiment 1, performed under similar conditions with approximately 50% conversion of MAA and 65% conversion of SS within 15 min. It is however clear from the experimental M_n values found for the macroinitiators at the beginning of the second step, (withdrawn under stirring just after the addition of the hydrophobic comonomers; see Table 3) that a conversion difference may exist between the samples in such a short time, considering the high conversion rate of the copolymerization reaction in water. In this situation, the BlocBuilder macroinitiator (with a rate constant of dissociation of 0.004 s^{-1} at 70 °C,[54] i.e., a half-lifetime of 3 min) may have reached close to 100% conversion at the end of the first step, but it remains possible that the presence of SS-SS-SG1 terminal dyads hampers complete reinitiation by the formed macroalkoxyamines.

In the second step, methyl methacrylate with ca. 8−9 mol % of styrene were introduced in the reaction medium together with additional water. The effect of the amount of BlocBuilder initiator was studied so as to target different molar masses at the end of the polymerization (experiments 8, 9, and 10). In all cases, the amount of polymer was around 25−27 wt % (∼18 wt % considering only the hydrophobic polymer). The overall weight conversion of the hydrophilic and hydrophobic monomers was followed via gravimetric analysis as a function of time and the graphs are represented in the Figure 6a. In the same figure (Figure 6b), the M_n values of the copolymers are displayed as a function of the overall comonomer weight conversions to give a general overview of the chain growth control over the whole process. Because of their high water solubility, the hydrophilic monomers remaining at the end of the first step were certainly consumed very quickly at the beginning of the emulsion polymerization step, possibly affording an intermediate amphiphilic block by copolymerization with the hydrophobic monomers.

From the kinetic results (Figure 6a), it appeared that the higher the initiator concentration, the higher the final conversion, which reached a plateau within approximately 1 h. In parallel, the control over chain growth was very good since the M_n values increased linearly with monomer conversion, although they appeared to be slightly higher than the calculated ones, as discussed above. The polydispersity index was 1.3 at full conversion. At the lowest initiator concentration, the polymerization remained very slow and the overall conversion reached not more than 24%, while the quality of control was not as good either, as when lower molar masses were targeted. Interestingly, the SEC peaks were completely shifted toward higher molar masses with increasing conversion (Figure 7). The shift was clearly visible at conversion as low as 9%, which indicates a very fast reinitiation step in all cases.

From the chain growth process and the size exclusion chromatograms, it is clear that the system led to the formation of

dx.doi.org/10.1021/ma2008282 |*Macromolecules* 2011, 44, 5590–5598

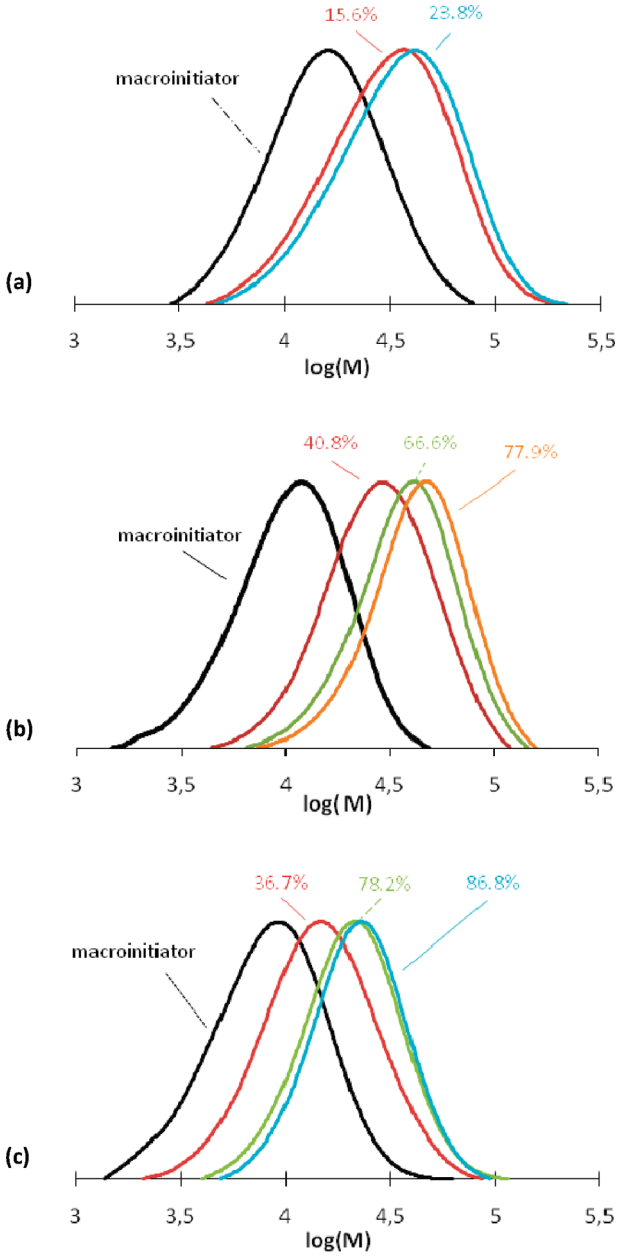


Figure 7. Size exclusion chromatograms (in DMF with 0.01 mol·L^{-1} of LiBr) as a function of the overall weight conversion for the block copolymers resulting from the emulsion polymerization of methyl methacrylate with 9.0 mol % of styrene at 90 °C initiated by the poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) macroinitiator synthesized in situ during 15 min at 76 °C: effect of the initial concentration of BlocBuilder in the first step for the experiments 8 ((a), $[BlocBuilder]_0 = 1.1 \times 10^{-2}$ mol L^{-1}), 9 ((b), $[BlocBuilder]_0 = 2.3 \times 10^{-2}$ mol L^{-1}), and 10 ((c), $[BlocBuilder]_0 = 4.0 \times 10^{-2}$ mol L^{-1}).

amphiphilic block copolymers that self-assembled during the chain extension process to form stable particles even under acidic conditions. The charges from the surface 4-styrenesulfonate units appear to impart efficient colloidal stability to the system.[22] The average diameters measured by dynamic light scattering were below 100 nm and increased with the decreased concentration in BlocBuilder (experiments 8−10), i.e. with the decreased concentration of stabilizing chains. TEM analysis—not shown here—revealed that the particles were spherical.

CONCLUSION

The emulsion polymerization of methyl methacrylate with less than 10 mol % of styrene was performed in the presence of a poly(methacrylic acid-*co*-sodium 4-styrenesulfonate) SG1-based macroalkoxyamine synthesized in situ at low temperature. The novelty of the procedure is the one-pot process that limits the number of synthesis and purification steps and allows to work in water instead of using organic solvents. So far, there was no example in the literature mentioning the aqueous NMP of acidic monomers such as methacrylic acid. The second, unexpected, outcome is the possibility to work under acidic conditions without killing the system due to the instability of SG1: short reaction times and low temperature appeared to be key parameters to reduce the degradation rate of the free nitroxide. The emulsion polymerization led to the formation of amphiphilic block copolymers entirely synthesized in situ, in an aqueous system. This work is the first step toward simplified procedures leading to self-stabilized polymer particles composed of assembled amphiphilic block copolymers and improvement will be needed to reach high conversions in all cases along with high molar masses.

AUTHOR INFORMATION

Corresponding Author

*E-mail: bernadette.charleux@lcpp.cpe.fr.

ACKNOWLEDGMENT

The authors wish to thank Arkema for the financial support of S.B.'s Ph.D. thesis and for kindly providing the BlocBuilder initiator and the nitroxide SG1. They are grateful to Fernande Boisson and Christine Lucas for their help in NMR analyses, and to Olivier Boyron for his invaluable advices concerning SEC. TEM analyses wer performed at the CTμ (Centre Technologique des Microstructures) at the University Claude Bernard, Lyon 1. B.C. acknowledges the IUF (Institut Universitaire de France) for her nomination as a senior member.

REFERENCES

(1) Matyjaszewski, K.; Davis, T. P. In *Handbook of Radical Polymerization*; Wiley-Interscience: Hoboken, NJ, 2002.
(2) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci.* **2007**, *32*, 93–146.
(3) Matyjaszewski, K.; Gnanou, Y.; Leibler, L.; Eds. *Macromolecular Engineering: Precise Synthesis, Materials Properties, Applications - Vol. 1. Synthetic Techniques*; Wiley-VCH: Weinheim, Germany, 2007.
(4) Jenkins, A. D.; Jones, R. G.; Moad, G. *Pure Appl. Chem.* **2010**, *82*, 483–491.
(5) Darling, S. B. *Prog. Polym. Sci.* **2007**, *32*, 1152–1204.
(6) Kim, J. K.; Yang, S. Y.; Lee, Y.; Kim, Y. *Prog. Polym. Sci.* **2010**, *35*, 1325–1349.
(7) Riess, G. *Prog. Polym. Sci.* **2003**, *28*, 1107–1170.
(8) Blanazs, A.; Armes, S. P.; Ryan, A. J. *Macromol. Rapid Commun.* **2009**, *30*, 267–277.
(9) Zhang, L.; Eisenberg, A. *Science* **1995**, *268*, 1728–1731.
(10) Charleux, B.; D'Agosto, F.; Delaittre, G. *Adv. Polym. Sci.* **2010**, *233*, 125–183.
(11) Ferguson, C. J.; Hughes, R. J.; Pham, B. T. T.; Hawkett, B. S.; Gilbert, R. G.; Serelis, A. K.; Such, C. H. *Macromolecules* **2002**, *25*, 9243–9245.
(12) Ferguson, C. J.; Hughes, R. J.; Nguyen, D.; Pham, B. T. T.; Gilbert, R. G.; Serelis, A. K.; Such, C. H.; Hawkett, B. S. *Macromolecules* **2005**, *38*, 2191–2204.

(13) Manguian, M.; Save, M.; Charleux, B. *Macromol. Rapid Commun.* **2006**, *27*, 399–404.
(14) Sprong, E.; Leswin, J. S. K.; Lamb, D. J.; Ferguson, C. J.; Hawkett, B. S.; Pham, B. T. T.; Nguyen, D.; Such, C. H.; Serelis, A. K.; Gilbert, R. G. *Macromol. Symp.* **2006**, *231*, 84–93.
(15) Delaittre, G.; Nicolas, J.; Lefay, C.; Save, M.; Charleux, B. *Chem. Commun.* **2005**, 615–616.
(16) Delaittre, G.; Nicolas, J.; Lefay, C.; Save, M.; Charleux, B. *Soft Matter* **2006**, *2*, 223–231.
(17) Delaittre, G.; Save, M.; Charleux, B. *Macromol. Rapid Commun.* **2007**, *28*, 1528–1533.
(18) Delaittre, G.; Charleux, B. *Macromolecules* **2008**, *41*, 2361–2367.
(19) Božović-Vukić, J.; Mañon, H. T.; Meuldijk, J.; Koning, C.; Klumperman, B. *Macromolecules* **2007**, *40*, 7132–7139.
(20) Bathfield, M.; D'Agosto, F.; Spitz, R.; Charreyre, M. T.; Pichot, C.; Delair, T. *Macromol. Rapid Commun.* **2007**, *28*, 1540–1545.
(21) Dire, C.; Magnet, S.; Couvreur, L.; Charleux, B. *Macromolecules* **2009**, *42*, 95–103.
(22) Brusseau, S.; Belleney, J.; Magnet, S.; Couvreur, L.; Charleux, B. *Polym. Chem.* **2010**, *1*, 720–729.
(23) Delaittre, G.; Dire, C.; Rieger, J.; Putaux, J.-L.; Charleux, B. *Chem. Commun.* **2009**, 2887–2889.
(24) Li, Y.; Armes, S. P. *Angew. Chem., Int. Ed.* **2010**, *49*, 4042–4046.
(25) Rieger, J.; Stoffelbach, F.; Bui, C.; Alaimo, D.; Jérôme, C.; Charleux, B. *Macromolecules* **2008**, *41*, 4065–4068.
(26) Rieger, J.; Osterwinter, G.; Bui, C.; Stoffelbach, F.; Charleux, B. *Macromolecules* **2009**, *42*, 5518–5525.
(27) Rieger, J.; Zhang, W.; Stoffelbach, F.; Charleux, B. *Macromolecules* **2010**, *43*, 6302–6310.
(28) Boissé, S.; Rieger, J.; Belal, K.; Di-Cicco, A.; Beaunier, P.; Li, M.-H.; Charleux, B. *Chem. Commun.* **2010**, *46*, 1950–1952.
(29) Yeole, N.; Hundiwale, D.; Jana, T. *J. Colloid Interface Sci.* **2011**, *354*, 506–510.
(30) Zhang, X.; Boissé, S.; Zhang, W.; Beaunier, P.; D'Agosto, F.; Rieger, J.; Charleux, B. *Macromolecules* **2011**10.1021/ma2005926.
(31) Rieger, J.; Grazon, C.; Charleux, B.; Alaimo, D.; Jérome, C. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 2373–2390.
(32) An, Z.; Shi, Q.; Tang, W.; Tsung, C. K.; Hawker, C. J.; Stucky, G. D. *J. Am. Chem. Soc.* **2007**, *129*, 14493–14499.
(33) Simon, S. R.; Eun Hee Min, T.; Zetterlund, P. B.; Stenzel, M. H. *Macromolecules* **2010**, *43*, 5211–5221.
(34) Chaduc, I.; Zhang, W.; Rieger, J.; Lansalot, M.; D'Agosto, F.; Charleux, B. *Macromol. Rapid Commun.* 2011, DOI: 10.1002/marc.201100240.
(35) Huang, W. L.; Charleux, B.; Chiarelli, R.; Marx, L.; Rassat, A.; Vairon, J. P. *Macromol. Chem. Phys.* **2002**, *203*, 1715–1723.
(36) Nicolay, R.; Marx, L.; Hemery, P.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 6067–6075.
(37) Phan, T. N. T.; Bertin, D. *Macromolecules* **2008**, *41*, 1886–1895.
(38) Grassl, B.; Clisson, G.; Khoukh, A.; Billon, L. *Eur. Polym. J.* **2007**, *44*, 50–58.
(39) Rigolini, J.; Grassl, B.; Billon, L.; Reynaud, S.; Donard, O. F. X. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 6919–6931.
(40) Chenal, M.; Mura, S.; Marchal, C.; Gigmes, D.; Charleux, B.; Fattal, E.; Couvreur, P.; Nicolas, J. *Macromolecules* **2010**, *43*, 9291–9303.
(41) McHale, R.; Aldabbagh, F.; Zetterlund, P. B. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2194–2203.
(42) Dire, C.; Belleney, J.; Nicolas, J.; Bertin, D.; Magnet, S.; Charleux, B. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6333–6345.
(43) Charleux, B.; Nicolas, J.; Guerret, O. *Macromolecules* **2005**, *38*, 5485–5492.
(44) Nicolas, J.; Dire, C.; Mueller, L.; Belleney, J.; Charleux, B.; Marque, S R. A.; Bertin, S.; Magnet, S.; Couvreur, L. *Macromolecules* **2006**, *39*, 8274–8282.
(45) Nicolas, J.; Mueller, L.; Dire, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules* **2009**, *42*, 4470–4478.
(46) Couvreur, L.; Lefay, C.; Belleney, J.; Charleux, B.; Guerret, O.; Magnet, S. *Macromolecules* **2003**, *36*, 8260–8267.
(47) Lefay, C.; Belleney, J.; Charleux, B.; Guerret, O.; Magnet, S. *Macromol. Rapid Commun.* **2004**, *25*, 1215–1220.
(48) Farcet, C.; Lansalot, M.; Charleux, B.; Pirri, R.; Vairon, J. P. *Macromolecules* **2000**, *33*, 8559–8570.
(49) Nicolas, J.; Charleux, B.; Guerret, O.; Magnet, S. *Macromolecules* **2004**, *37*, 4453–4463.
(50) Charleux, B.; Nicolas, J. *Polymer* **2007**, *48*, 5813–5833.
(51) Beuermann, S.; Buback, M.; Hesse, P.; Lacik, I. *Macromolecules* **2006**, *39*, 184–193.
(52) Kuchta, F. D.; van Herk, A.; German, A. L. *Macromolecules* **2000**, *33*, 3641–3649.
(53) Fischer, H. *Chem. Rev.* **2001**, *101*, 3581–3610.
(54) Beaudoin, E.; Bertin, D.; Gigmes, D.; Marque, S. R. A.; Tordo, P. *Eur. J. Org. Chem.* **2006**, *7*, 1755–1768.