Notes

Synthesis of Water-Soluble Homopolymers and Block Copolymers in Homogeneous Aqueous Solution via Nitroxide-Mediated Polymerization

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1. Introduction

The discovery and development of controlled radical polymerization (CRP) techniques enable the synthesis of new homopolymeres and block copolymers with a level of control approaching that of traditional techniques, such as anionic or group transfer polymerization; furthermore, CRP is more tolerant to polar functions on the monomers and can be run in many conventional solvents over a wide range of temperatures.[1] The most common CRP methods are atom transfer radical polymerization ATRP),[2−4] nitroxide-mediated polymerization (NMP),[5−7] and more recently reversible addition−fragmentation chain transfer polymerization (RAFT).[8−10] The success of these techniques in synthesizing complex polymer architectures in organic solvents has been illustrated through numerous articles in the literature. However, CRP is still a challenge in aqueous solution because of a number of practical problems (e.g., compatibility of the radical mediators with water and stability of the dormant species in the presence of water).

Among the various CRP methods, RAFT has emerged as the most powerful technique for the synthesis of hydrophilic (co)-polymers directly in water under homogeneous conditions,[11] although with certain limitations, especially for nonionic monomers with certain dithioester RAFT agents, polymerization often requires extremely long polymerization times (>24 h) to reach appreciable conversion.[12] Additionally, hydrolysis and aminolysis reactions may interfere with the aqueous RAFT polymerization process.[13] ATRP is a reasonably successful strategy for preparing well-defined (co)polymers under homogeneous aqueous conditions,[14,15] although several side reactions such as nucleophilic substitution of the end functionality of the initiator by water and strong coordination between ATRP catalysts and typical hydrophilic groups in the monomers and polymers are difficulties.[16]

In the case of NMP, the process often needs relatively high temperatures to efficiently the control of polymerization because the majority of available alkoxyamines are based on five- or six-membered-ring nitroxides, such as 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO. As a result, polymerization in pressure vessels[17] or addition of a high boiling point solvent, such as ethylene glycol,[18,19] was necessary for aqueous polymerization via NMP.

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With the discovery of the second-generation nitroxides, namely *N-tert*-butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (named SG1, Scheme 1) which displays a higher activation/deactivation equilibrium constant than TEMPO and exhibits a solubility in water of 10^{-2} mol L^{-1} (internal laboratory source), polymerization in "purely" homogeneous aqueous solution should be possible below water's boiling point. However, very few water-soluble alkoxyamines have been described, and most of NMP has been studied in dispersed aqueous media using bicomponent or monocomponent initiating systems.[20−22] There are still relatively few studies that have exploited NMP for the synthesis of water-soluble (co)polymers in homogeneous aqueous solution compared to ATRP or RAFT techniques. Indeed, we are only aware of one report in which Nicolay et al.[23] described the synthesis of a new carboxy functional water- and organo-soluble nitroxide and utilization of the latter in the polymerization of sodium 4-styrenesulfonate. The polymerization was successfully achieved at temperature below 100 °C in homogeneous aqueous solution and led to well-defined polymer, although the blocking ability of the obtained poly(sodium 4-styrenesulfonate) macroinitiator was not tested.

With the growing interest in water as a solvent for controlled radical polymerization and the desire to learn more about the feasibility of the NMP process for successful synthesis of water-soluble (co)polymer with controlled molar mass and structure, we studied the polymerization of several typical water-soluble monomers, such as nonionic (*N*,*N*-dimethylacrylamide), anionic (sodium 4-styrenesulfonate), and cationic (2-(acryloyloxy)ethyl benzyldimethylammonium chloride) ones (Scheme 1) under mild conditions. For this purpose, we used an SG1-based alkoxyamine, which bears a carboxylic acid function (so-called MAMA-SG1, Scheme 1). In its basic form, the carboxylic acid function confers water solubility to the alkoxyamine and thus allows various water-soluble monomers to be polymerized by NMP in homogeneous aqueous solution. In this work, we also demonstrate the living character of the polymer chains produced with the studied water-soluble alkoxyamine system by chain extension polymerization using a second addition of either the same or another monomer.

2. Experimental Section

2.1. Materials. The monomers *N*,*N*-dimethylacrylamide (DMA, 99%) and sodium 4-styrenesulfonate (SSNa, >99%) from Aldrich and 2-(acryloyloxy)ethyl benzyldimethylammonium chloride (ABC, 80 wt % solution in water, trade name ADAMQUAT BZ 80) from Arkema were used as received. SG1 (85%) and alkoxyamine based on SG1 derived from methacrylic acid (MAMA-SG1, >99%, trade name BlocBuilder) were kindly supplied by Arkema. Alkoxyamine was deprotonated by mixing equimolar amounts of MAMA-SG1 (6.00 g, 15.7×10^{-3} mol) and sodium hydroxide (0.63 g, 15.7×10^{-3} mol) in 20 mL of a mixture of water/methanol (50/50, v/v). The mixture was agitated until getting a limpid solution, the solvent was then evaporated under vacuum at room temperature, and the sodium MAMA-SG1 was stored at 4 °C. D_2O (Eurisotop Laboratories) and all other solvents (acetone, diethyl ether, ethanol)

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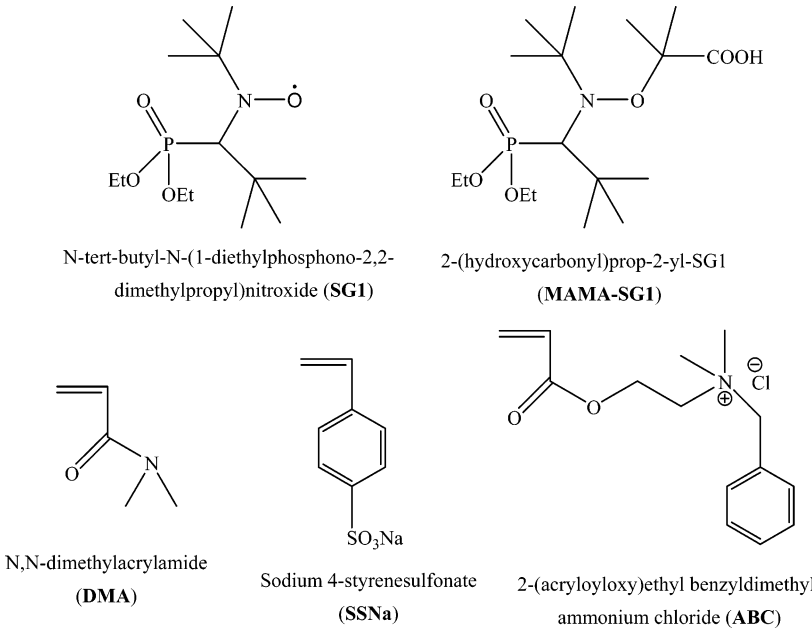
Table 1. Experimental Conditions for the Chain Extension Polymerization in Aqueous Solution

macroalkoxyamine sample	M_n,[a] g mol^{-1}	macroalkoxyamine, g (mol)	DMA, g (mol)	SG1, mg (mol)	target M_n,[e] g mol^{-1}	conv, %, after 2 h[f]
poly(dimethylacrylamide)	24 500[b]	5.00 (2.04×10^{-4})	15.0 (1.50×10^{-1})	7.1 (2.1×10^{-5})	73 500	46
poly(sodium 4-styrenesulfonate)	21 300[c]	6.00 (2.82×10^{-4})	16.9 (1.69×10^{-1})	9.7 (2.8×10^{-5})	60 000	83
poly(2-(acryloyloxy)ethylbenzyl-dimethylammonium chloride)	22 000[d]	8.25 (3.75×10^{-4})	15.0 (1.50×10^{-1})	13.0 (3.7×10^{-5})	40 000	33

[a] As determined by aqueous size exclusion chromatography. [b] Calibrated with poly(ethylene oxide) standards with a mobile phase of 0.1 M $NaNO_3$ using the Mark−Houwink coefficients: $k_{PEO} = 12.5 \times 10^{-3}$ dL g^{-1} and $\alpha_{PEO} = 0.78$; $k_{PDMA} = 23.2 \times 10^{-3}$ dL g^{-1} and $\alpha_{PDMA} = 0.81$.[24] [c] Calibrated with poly(sodium 4-styrenesulfonate) standards with a mobile phase of 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$. [d] Calibrated with poly(ethylene oxide) standards with a mobile phase of 0.5 M acetic acid + 0.3 M Na_2SO_4. [e] Expected molar mass of poly(dimethylacrylamide) part at 100% conversion. [f] Conversion of dimethylacrylamide as determined by ^{1}H NMR spectroscopy in D_2O.

Scheme 1. Chemical Formulas of Nitroxide, Alkoxyamine, and Water-Soluble Monomers



were purchased from commercial sources and used without any further purification.

2.2. Analytical Techniques. Monomer conversion and copolymer composition were determined by ^{1}H NMR spectroscopy using a Brüker AV300 MHz spectrometer. Heavy water (D_2O) was used as solvent.

Number-average molecular weights (M_n) and molecular weights distribution (M_w/M_n, PDI) of resulting water-soluble polymers were determined by aqueous size exclusion chromatography (SEC) operated at 30 °C. The chromatographic device was equipped with a Waters 515 liquid chromatograph pump, a differential refractive index detector (Waters model 410), a PW_{XL} guard column, and TSKgel G3000PWXL (operating range $M_p < 50\,000$) from TOSOH Bioscience. All analysis was performed with the same columns in different eluents according to obtained polymers. For example, aqueous SEC of poly(*N*,*N*-dimethylacrylamide) (PDMA) was performed using aqueous solution of 0.1 M $NaNO_3$ at a flow rate of 0.8 mL min^{-1}. The M_n values are related to the universal calibration referenced against a linear poly(ethylene oxide) (PEO) standards calibration with the following Mark−Houwink coefficients: $k_{PEO} = 12.5 \times 10^{-3}$ dL g^{-1} and $\alpha_{PEO} = 0.78$; $k_{PDMA} = 23.2 \times 10^{-3}$ dL g^{-1} and $\alpha_{PDMA} = 0.81$.[24] For poly(sodium 4-styrenesulfonate), evaluation of M_n was done with a mobile phase of 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$ at a flow rate of 1 mL min^{-1} and by calibration with poly(sodium 4-styrenesulfonate) standards from PSS GmbH. Aqueous SEC of poly(2-(acryloyloxy)-ethyl benzyldimethylammonium chloride) was performed using aqueous solution of 0.5 M acetic acid and 0.3 M Na_2SO_4 at a flow rate of 1 mL min^{-1}. The M_n values and molar mass distribution were derived from a conventional calibration based on the narrow poly(ethylene oxide) standards. In all the figures representing the experimental M_n as a function of monomer conversion, the display dotted line corresponds to the theoretical evolution of M_n calculated by the equation

$$M_n = \mathrm{MW}_{\text{sodium MAMA-SG1}} + \frac{\text{initial mass of monomer}}{\text{initial mol number of alkoxyamine}} \times \text{conversion}$$

2.3. Procedure for the NMP of *N*,*N*-Dimethylacrylamide. Dimethylacrylamide (27.0 g, 0.27 mol), sodium MAMA-SG1 (275 mg, 6.74×10^{-4} mol), SG1 (34.6 mg, 10^{-4} mol), ([SG1]/[alkoxyamine] ratio = 0.15), and distilled water (40.4 g) were weighed and mixed to generate a solution that contained 40 wt % of monomer. This solution was added to a pressure metal reactor (Parr Instrument Co.) equipped with a mechanic stirrer. The mixture was degassed by bubbling argon through the gas inlet valve for 40 min at room temperature. After that, argon gas was charged into the reactor at 2 bar, and the reactor was heated to 110 °C. In kinetic studies, samples were collected from the reaction mixture at given time intervals by opening the liquid sampling valve. Conversion and molecular weights were determined by ^{1}H NMR spectroscopy and aqueous SEC, respectively. The polymerization was stopped by quenching the reactor in an ice bath. The polymer was purified by precipitation in diethyl ether, filtered to remove the volatiles, and dried under high vacuum at room temperature to a constant weight.

2.4. Procedure for the NMP of Sodium 4-Styrenesulfonate. Sodium 4-styrenesulfonate (15 g, 7.2×10^{-2} mol), SG1 (7 mg, 2×10^{-5} mol), and distilled water (42 g) (Table 3, entry 6) were placed in a three-neck flask equipped with a reflux condenser and a magnetic stir bar. The mixture was purged for 40 min with argon

Table 2. Composition and Molar Mass Data of the Synthesized Hydrophilic Block Copolymers

block copolymer	amount of added PDMA block (wt %)	M_n, g mol^{-1}	M_w/M_n
PDMA-*b*-PDMA		58 300[c]	
		60 000[d]	1.45
PSSNa-*b*-PDMA	73[a]	71 200[c]	
	74.5[b]	50 200[e]	1.3
		78 900[f]	
PABC-*b*-PDMA	48[a]	35 300[c]	
		37 900[g]	1.35

[a] Determined by ^{1}H NMR spectroscopy. [b] Determined by microanalysis. [c] Theoretical values calculated based on monomer conversion. [d] Determined by aqueous SEC in 0.1 M $NaNO_3$ basing on the universal calibration curve established with poly(ethylene oxide) standards. [e] Determined by aqueous SEC in 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$ based on the relative calibration curve established with poly(sodium 4-styrenesulfonate) standards. [f] Calculated via ^{1}H NMR spectrum of diblock copolymer and basing on the $M_{n,aq\ SEC}$ of used macroalkoxyamine. [g] Determined by aqueous SEC in 0.5 M acetic acid and 0.3 M Na_2SO_4 based on the relative calibration curve established with poly(ethylene oxide) standards.

at 50 °C to remove oxygen. The water-soluble alkoxyamine, sodium MAMA-SG1 (151 mg, 3.75×10^{-4} mol), was dissolved in 3 g of distilled water and degassed by bubbling argon for 30 min at room temperature. This alkoxyamine solution was transferred, via cannula, to monomer solution that was prepurged with argon. These were heated to 85 °C. The [SG1]/[alkoxyamine] ratio was 0.05, and the monomer concentration in this mixture was 25 wt %.

Samples were removed at different time intervals during polymerization, cooled in ice water, and analyzed in D_2O by ^{1}H NMR spectroscopy to determine conversion. A portion of each sample was diluted and analyzed by aqueous SEC. The resulting homopolymer was precipitated by pouring the reaction solution into a mixture of H_2O/acetone (10/90, v/v), rinsed with acetone, and isolated by filtration. Polymer was then dried under high vacuum at room temperature to a constant weight. The conditions and results of other experiments are presented in Tables 3 and 4.

2.5. Procedure for the NMP of 2-(Acryloyloxy)ethylbenzyldimethylammonium Chloride. Monomer (33.0 g, 13.6×10^{-2} mol), sodium MAMA-SG1 (307 mg, 7.55×10^{-4} mol), SG1 (26.2 mg, 7.57×10^{-4} mol), thus the [SG1]/[alkoxyamine] ratio was 0.10, and distilled water (33 g) were weigheded and mixed to generate a solution that contained 40 wt % of monomer. This solution was placed in a three-neck flask equipped with a reflux condenser and a magnetic stir bar. The mixture was purged for 40 min with argon at room temperature to remove oxygen. In kinetic studies, samples were collected from the reaction mixture at given time intervals by a syringe through a septum. Conversion of monomer was determined by ^{1}H NMR in D_2O with added 1,3,5-trioxane as an internal reference at 5.26 ppm. Average molar mass and molecular weight distribution were determined by aqueous SEC. The polymerization was stopped by quenching the reactor in an ice bath. The polymer was purified by precipitation in acetone, filtered to remove the volatiles, and dried under high vacuum at room temperature to a constant weight.

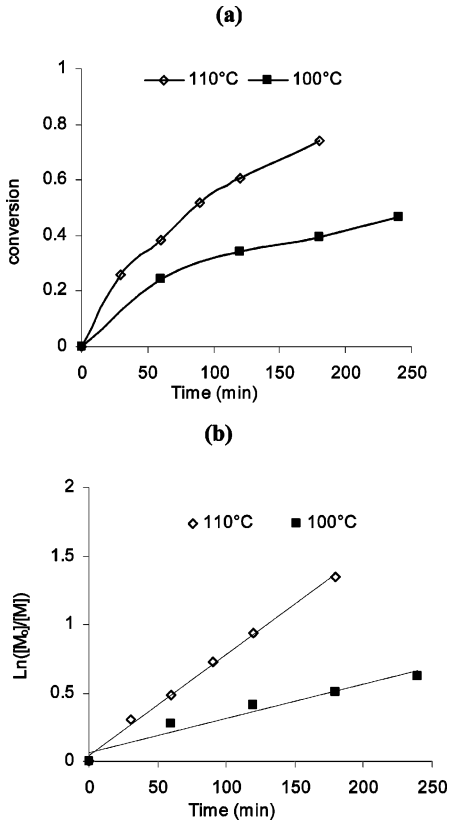


Figure 1. Polymerization of *N*,*N*-dimethyacrylamide (DMA) in water using sodium MAMA-SG1 (Scheme 1) at 110 and 100 °C under a pressure of 2 bar and a targeted molar mass at 100% conversion, M_n = 40 000 g mol^{-1}. Evolution of (a) conversion determined by ^{1}H NMR in D_2O and (b) ln([M_0]/[M]) vs time data. Experimental conditions: [DMA]/[sodium MAMA-SG1] = 400; [SG1]/[sodium MAMA-SG1] = 0.15; [monomer + initiator] in water = 40 wt %; T = 100 and 110 °C; P = 2 bar.

2.6. Chain Extension Polymerization. The purified poly(*N*,*N*-dimethylacrylamide) (PDMA), poly(sodium 4-styrenesulfonate)

Table 3. Experimental Conditions for the Aqueous Polymerization of Sodium 4-Styrenesulfonate

entry	SSNa, g (mol)	MAMA-SG1, mg (mol)	SG1, mg (mol)	target M_n,[a] g mol^{-1}	temp, °C	overall time, min
1	5.00 (2.40×10^{-2})	7.69 (1.91×10^{-4})	0	26 600	75	200
2	5.15 (2.47×10^{-2})	7.17 (1.78×10^{-4})	0	29 400	80	180
3	5.01 (2.41×10^{-2})	7.82 (1.94×10^{-4})	0	26 200	85	200
4	5.00 (2.40×10^{-2})	4.04 (1.00×10^{-4})	0	50 800	85	180
5	5.00 (2.40×10^{-2})	4.02 (9.98×10^{-5})	1.8 (5.2×10^{-6})	50 600	85	210
6	15.00 (7.20×10^{-2})	151 (3.75×10^{-4})	7.0 (2.0×10^{-5})	40 400	85	200

[a] Expected polymer molar mass at 100% conversion. Monomer concentration in water was fixed at 25 wt % for all experiments.

Table 4. Conversion and Macromolecular Characteristics of Poly(sodium 4-styrenesulfonate)

entry	polymer sample	polym time, min	conv,[a] %	theor M_n, g mol^{-1}	exptl M_n,[b] g mol^{-1}	M_w/M_n
1	PSSNa-1	200	47.2	12 600	10 300	1.69
2	PSSNa-2	180	63.6	18 700	17 100	1.93
3	PSSNa-3	200	89.0	23 300	23 500	1.82
4	PSSNa-4	180	81.6	41 500	43 100	1.75
5	PSSNa-5	210	62.9	31 800	31 900	1.31
6	PSSNa-6	200	56.7	22 900	21 300	1.27

[a] Determined by ^{1}H NMR spectroscopy in D_2O. [b] Determined by aqueous SEC in a mobile phase containing 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$ based on the calibration curve established with poly(sodium 4-styrenesulfonate) standards.

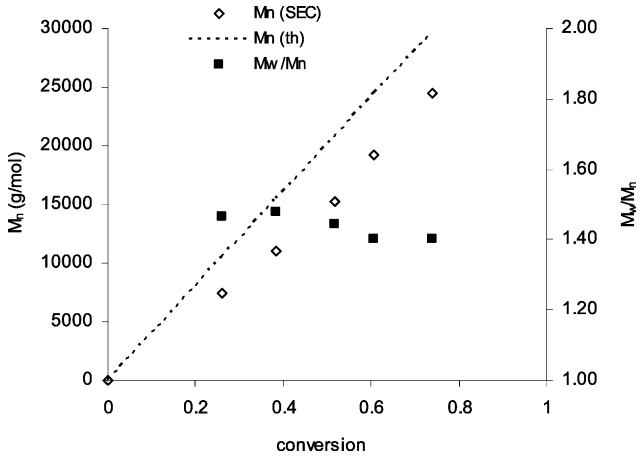


Figure 2. Evolution of molar masses (M_n) and molecular weights distribution (M_w/M_n) vs conversion for homogeneous aqueous polymerization of *N*,*N*-dimethylacrylamide (DMA) at 110 °C with sodium MAMA-SG1 (Scheme 1). M_n according to the universal calibration of linear poly(ethylene oxide) standards with the Mark−Houwink coefficients: $k_{PEO} = 12.5 \times 10^{-3}$ dL g^{-1} and $\alpha_{PEO} = 0.78$; $k_{PDMA} = 23.2 \times 10^{-3}$ dL g^{-1} and $\alpha_{PDMA} = 0.81$.[24] Experimental conditions: [DMA]/[sodium MAMA-SG1] = 400; [SG1]/[sodium MAMA-SG1] = 0.15; [monomer + initiator] in water = 40 wt %; T = 110 °C; P = 2 bar.

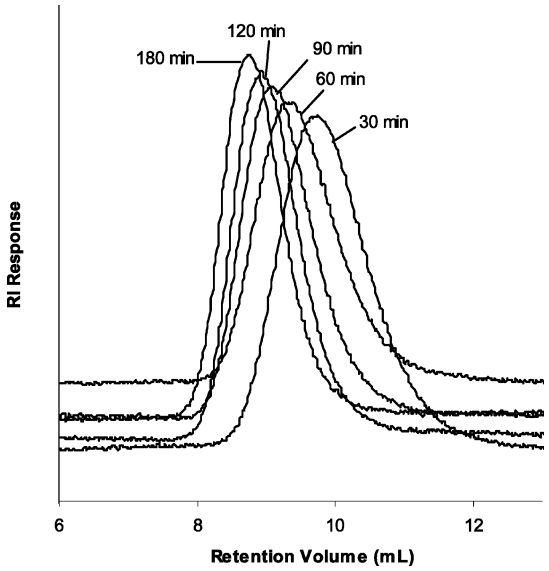


Figure 3. Evolution of aqueous size exclusion chromatograms with polymerization time (eluent: 0.1 M of aqueous $NaNO_3$ at a flow rate of 0.8 mL min^{-1}; detector: differential refractive index) of poly(*N*,*N*-dimethylacrylamide) homopolymer synthesized in water at 110 °C by using sodium MAMA-SG1 (Scheme 1) as initiator. Experimental conditions: [DMA]/[sodium MAMA-SG1] = 400; [SG1]/[sodium MAMA-SG1] = 0.15; [monomer + initiator] in water = 40 wt %; T = 110 °C; P = 2 bar.

(PSSNa), and poly(2-(acryloyloxy)ethyl benzyldimethylammonium chloride) (PABC) polymers formed from aqueous NMP were used as macroinitiator for further chain extension. The chain extension polymerization was carried out by a second addition of *N*,*N*-dimethyacrylamide. An excess of SG1 ([SG1]/[macroinitiator] ratio = 0.1) was introduced in the reaction medium along with DMA. Typically, PSSNa macroinitiator (M_n = 21 300 g mol^{-1}, PDI = 1.27) (6.0 g, 2.8 × 10^{-4} mol), DMA (16.9 g, 16.9 × 10^{-2} mol), SG1 (9.7 mg, 2.8 × 10^{-5} mol), and distilled water (34 g) (Table 1) were charged in the pressure metal reactor. The concentration of monomer plus macroinitiator in the mixture was 40 wt %. Targeted molar mass of PDMA part was 60 000 g mol^{-1}. Reaction mixtures were deoxygenated by bubbling argon for 40 min. The polymerization was carried out at 110 °C for 120 min. All other parameters and procedures were the same as in procedure for the NMP of

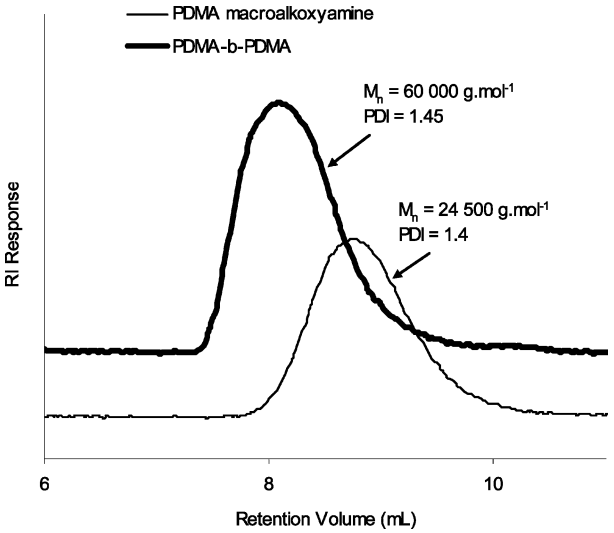


Figure 4. Aqueous size exclusion chromatograms of poly(*N*,*N*-dimethylacrylamide) (PDMA) macroalkoxyamine (sample from kinetic study 180 min at 110 °C) and its subsequent chain-extended product (PDMA-*b*-PDMA) (eluent: 0.1 M of aqueous $NaNO_3$ at a flow rate of 0.8 mL min^{-1}; detector: differential refractive index). M_n estimated according to the universal calibration of linear poly(ethylene oxide) standards with the Mark−Houwink coefficients: $k_{PEO} = 12.5 \times 10^{-3}$ dL g^{-1} and $\alpha_{PEO} = 0.78$; $k_{PDMA} = 23.2 \times 10^{-3}$ dL g^{-1} and $\alpha_{PDMA} = 0.81$.[24] Experimental conditions: [DMA]/[PDMA macroalkoxyamine] = 400; [SG1]/[PDMA macroalkoxyamine] = 0.1; [monomer + macroinitiator] in water = 40 wt %; T = 110 °C; P = 2 bar; t = 120 min.

dimethylacrylamide above (section 2.3). The block copolymer was isolated by precipitattion into a mixture of acetone/diethyl ether (40/60, v/v), collected by filtration, and dried under vacuum at 50 °C for 6 h. The results of this experiment are tabulated in Tables 1 and 2 and also presented in Figures 8 and 9.

The preparation of PDMA-*b*-PDMA and PABC-*b*-PDMA was performed in the same way than that of PSSNa-*b*-PDMA. Details of the reagent amounts, targeted molar mass of PDMA part, and conversion of these experiments are given in Table 1.

3. Results and Discussion

3.1. Aqueous NMP of *N*,*N*-Dimethylacrylamide. *N*,*N*-Dimethylacrylamide is a water-soluble monomer, as are the resulting homopolymers, which have found wide use in the pharmaceutical/personal care laboratories owing to their water solubility and biocompatibility.[25−27] Additionally, DMA can be easily polymerized in both water and organic media. The polymerization of dimethylacrylamide in bulk or in organic solvents such as toluene, *N*,*N*-dimethylformamide, 1,4-dioxane, and benzene by different controlled/living radical polymerization methods was reported in the literature.[28−33] However, its polymerization in aqueous media was mainly performed by using the RAFT method.[34−36]

For monomer with large propagating rate constant, such as DMA,[37] it is essential that the growing radicals could be efficiently scavenged by the nitroxide present in the medium or self-terminated to counterbalance their fast propagation. The strategy to prevent the loss of control of the polymerization and its lack of reproducibility already experimented by several authors[38−40] is to add an excess of scavenging nitroxide before triggering polymerization. The excess of nitroxide that is necessary to control polymerization must be larger than (3 ln $10Kk_t/([P\text{-}SG1]_0k_p))^{1/2}$, with K the equilibrium constant between active and dormant chains

$$PDMA{-}SG1 \underset{k_c}{\overset{k_d}{\rightleftharpoons}} PDMA^{\bullet} + SG1^{\bullet}; \quad K = k_d/k_c$$

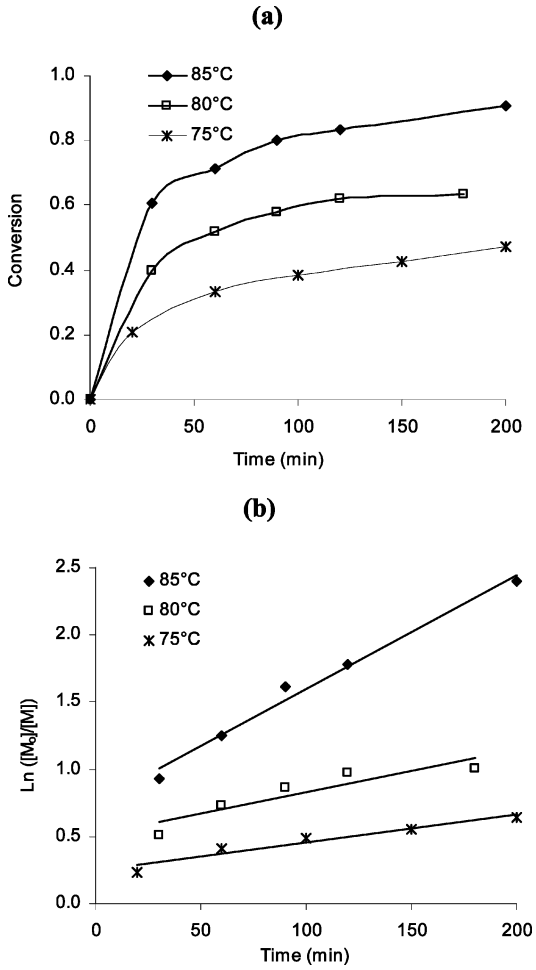


Figure 5. Monomer conversion of aqueous polymerization of sodium 4-styrenesulfonate (SSNa) at 75, 80, and 85 °C with [SSNa]/[sodium MAMA-SG1] = 126, 139, and 124, respectively. (a) Conversion vs time, (b) ln([M_0]/[M]) vs time.

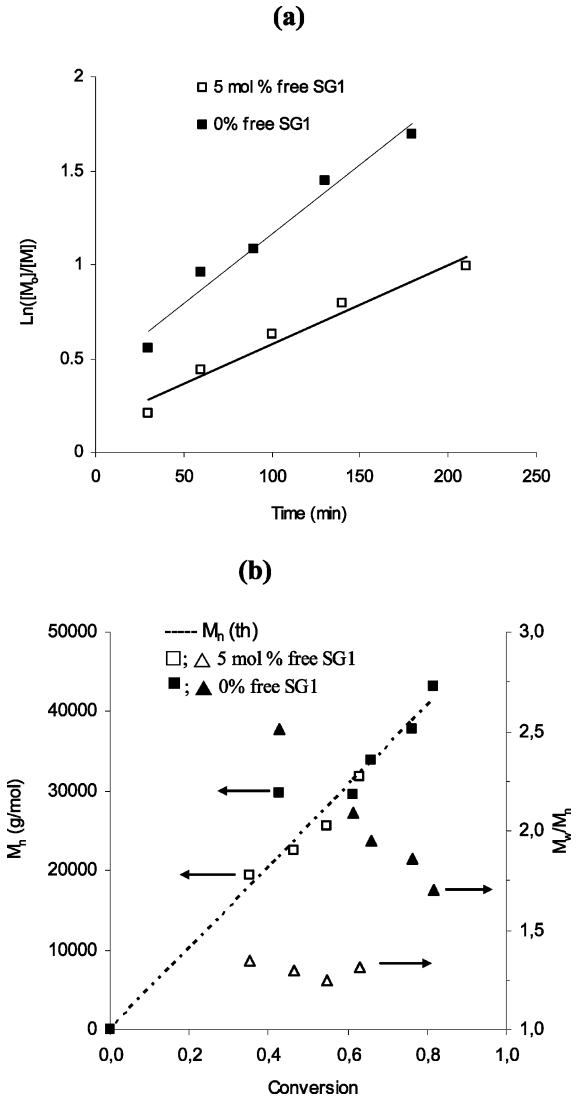


Figure 6. Influence of the presence of free SG1 on the aqueous polymerization of sodium 4-styrenesulfonate using sodium MAMA-SG1 at 85 °C. (a) Evolution of ln([M_0]/[M]) vs time data. (b) Evolution of M_n and M_w/M_n with conversion; M_n estimated by using calibration curve established with poly(sodium 4-styrenesulfonate) standards. Experimental conditions: [SSNa]/[sodium MAMA-SG1] = 241; [monomer + initiator] in water = 25 wt %; T = 85 °C.

k_t the rate constant of self-termination, and k_p the rate constant of propagation.[33,39,41]

In general, a larger excess of nitroxide than the calculated values was used.[33] As no reliable and trustable values of k_p and k_t are available for dimethylacrylamide in the literature, it is difficult for us to calculated precisely the excess of nitroxide SG1 required. The usual [SG1]/[alkoxyamine based SG1] ratio used by other authors and reported in the literature is comprised between 5% and 15%.[29,42,43] In the present work, a internal preliminary DMA polymerization was performed with a [SG1]/[MAMA-SG1] ratio of 0.08 at 110 °C, showing a fast polymerization kinetic (95% conversion within 3 h) and giving PDMA homopolymers with large polydispersities (PDI > 1.6). By taking into account of this result, we fixed a [SG1]/[MAMA-SG1] ratio equal to 0.15 for other DMA polymerizations. The presence of this excess of nitroxide which is certainly not an optimized one but with such system we had a good compromise between kinetics and polymerization control as shown in the discussion below.

DMA was polymerized in water at 100 and 110 °C under a pressure of 2 bar by employing sodium MAMA-SG1 as initiator. As expected, the polymerization rate was significantly higher at 110 °C than at 100 °C (Figure 1a). Indeed, the cleavage rate constant k_d depends on the dissociation energy of the alkoxyamine bond and Arrhenius temperature while cross-combination constant k_c shows non-Arrhenius temperature dependencies.[44] The polymerization proceeds to high conversion (75%) within 3 h at 110 °C. Figure 1b shows a linear relationship between ln([M_0]/[M]) vs time for both cases, which indicates not only the first order with respect to the monomer but also the constant concentration of radicals in these systems. Control over the growth of polymer chains was furthermore evidenced by the linear evolution of molecular weight with conversion as well as a acceptable polydispersitiy index of 1.4 and unimodal aqueous SEC chromatograms (Figures 2 and 3).

The living character of the PDMA polymer chains produced with the sodium MAMA-SG1 system at 110 °C has been further confirmed by chain extension using a second addition of the same monomer DMA. An amount of 5 g of PDMA (Table 1, M_n = 24 500 g mol^{-1}, PDI = 1.4) was employed as a macroalkoxyamine agent for chain extension experiment. The M_n of the chain-extended polymer was increased to 60 000 g mol^{-1}. The presence of 10 mol % of free SG1 in the polymerization medium allowed once again obtaining a reasonable low polydispersity index (PDI = 1.45, Table 2). These results indicate that the PDMA homopolymer is effectively functionalized with nitroxide end groups. The aqueous chro-

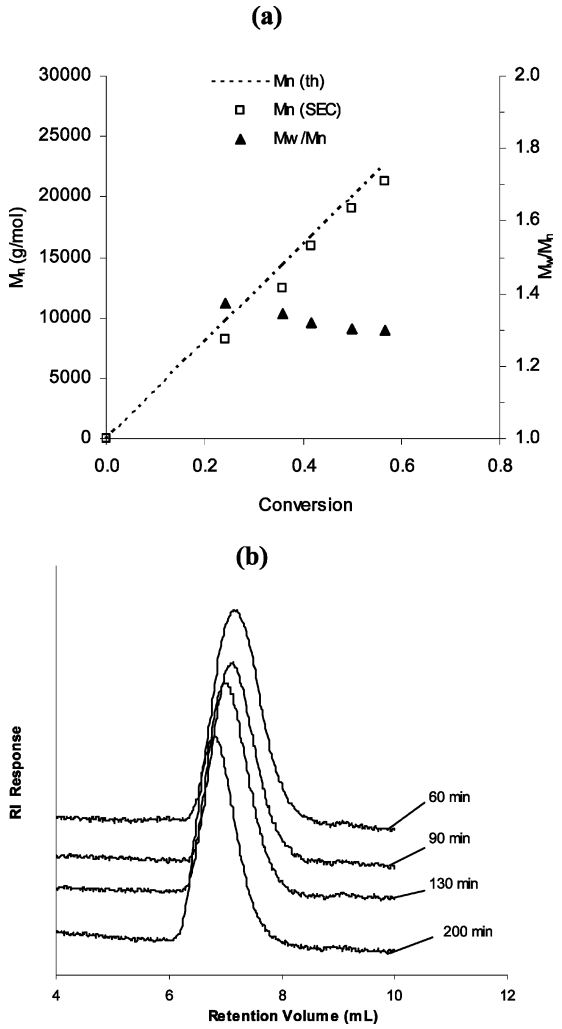


Figure 7. (a) Evolution of M_n and M_w/M_n with conversion; M_n estimated by using calibration curve established with poly(sodium 4-styrenesulfonate) standards. (b) Aqueous size exclusion chromatograms for a poly(sodium 4-styrenesulfonate) homopolymer evolution as a function of time (eluent: 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$ at a flow rate of 1 mL min^{-1}; detector: differential refractive index). Experimental conditions: [SSNa]/[sodium MAMA-SG1] = 192; [SG1]/[sodium MAMA-SG1] = 0.05; [monomer + initiator] in water = 25 wt %; T = 85 °C.

matogram of the chain extended product shifts to lower elution volumes compared to PDMA macroalkoxyamine after chain extension experiment, while still being unimodal (Figure 4). To our knowledge, the present experiment gives the first example of molecular weight control, with living characteristics of the polymerization of *N*,*N*-dimethylacrylamide in dilute aqueous solution via NMP.

3.2. Aqueous NMP of Sodium 4-Styrenesulfonate. Sodium 4-styrenesulfonate is a functional monomer which forms interesting double hydrophilic water-soluble AB diblock copolymers owning stimuli-responsive properties in water. The polymerization of this monomer by ionic polymerization often required protection and subsequent deprotection was sometimes problematic. With recent advances in CRP techniques in aqueous media, Chiefari et al.[8] were the first ones who demonstrated that sodium 4-styrenesulfonate could be polymerized directly in water by the RAFT method to yield an homopolymer with low polydispersity index (1.13) at 70% conversion. This single example initiated other works examining the potential of CRP methods with respect to homogeneous aqueous polymerization of sodium 4-styrenesulfonate.[23,35,45,46]

In the present study, sodium 4-styrenesulfonate was polymerized in dilute aqueous phase (25 wt % of monomer) using sodium MAMA-SG1 as initiator. The effect of temperature on the polymerization rate was investigated at 75, 80, and 85 °C (Table 3, entries 1−3). Polymerization proceeded without addition of free SG1. Figure 5a shows the monomer conversion vs time; as expected, the polymerization rate was increased with temperature. Figure 5b gives the first-order kinetic plot. The linearity observed in the plots of $\ln([M_0]/[M])$ vs time indicates the constant concentration of radicals in the systems. Nevertheless, the first-order kinetic plot is slightly deviated early on and its intercept is not zero, which is characteristic of the fast monomer polymerization as already observed in other studies.[23,35,45] The molar mass of PSSNa homopolymers and their polydispersities, determined by aqueous SEC, are summarized in Table 4. The results show that the experimental M_n is very close to theoretical values. However, the polydispersities remained too high (PDI = 1.7−1.9) to be acceptable.

With the aim to improving the control of sodium 4-styrenesulfonate polymerization, the effect of the addition of free SG1 was investigated. When two same experiments (Table 3, entries 4 and 5) were carried out at 85 °C without and with 5 mol % of free SG1, the polymerization kinetic without addition of free SG1 was faster than that with addition of 5 mol % of free SG1 (Figure 6a). Both present an evolution of experimental M_n, determined by aqueous SEC, agreed well with the theoretical values based on conversion (Figure 6b). The polydipersities decreased significantly, from 1.8 to 1.3, when polymerization performed with the presence of 5 mol % of free SG1 compared to that without addition of free SG1. In spite of the fast homolysis rate of MAMA-SG1 alkoxyamine ($t_{90\%}$ = 140 s at 90 °C),[47] which makes the formation of the macroalkoxyamine in a short time with respect to the polymerization time, while because of the fast polymerization of SSNa, an excess of free SG1 must add to the medium to increase the efficiently scavenging of the growing radical by the nitroxide and thus allow to obtain a better control of the SSNa polymerization.

From these results, an other SSNa aqueous polymerization was performed in the presence of 5 mol % free SG1 at 85 °C to subsequently prepare the hydrophilic block. The [monomer]/[sodium MAMA-SG1] ratio was such that a theoretical molar mass of 40 000 g mol^{-1} at 100% conversion was expected (Table 3, entry 6). The time−conversion relationship as well as the first-order kinetic plot (curves not presented) is similar to those obtained from the previous experiments. The derived M_n values (Figure 7a), determined by aqueous SEC, grow linearly with conversion and correspond very closely to the theoretical values, while polydispersities decreased with conversion, which indicates that the polymerization of sodium 4-styrenesulfonate using sodium MAMA-SG1 occurred in a controlled fashion. The poly(sodium 4-styrenesulfonate), so-called PSSNa-6, produced with M_n = 21 300 g mol^{-1} was obtained after 200 min at 85 °C (Table 4, entry 6). The homopolymer is near-monodisperse, with polydispersity index about 1.27, well below the theoretical lower limit of 1.5 for classical free-radical polymerization. Our results are comparable to those reported by Nicolay et al.[23] These authors reported the synthesis of PSSNa in aqueous media using 2,2,5-trimethyl-4-*p*-methylbenzoate-3-azahexane 3-nitroxide. The homopolymer had a M_n (as determined by aqueous SEC) of 38 300 g mol^{-1} and a polydispersity index of 1.18, with 63% conversion being achieved after 24 h at 95 °C.

The aqueous SEC traces (Figure 7b) show the continuous shift to smaller retention volumes with increasing time and are

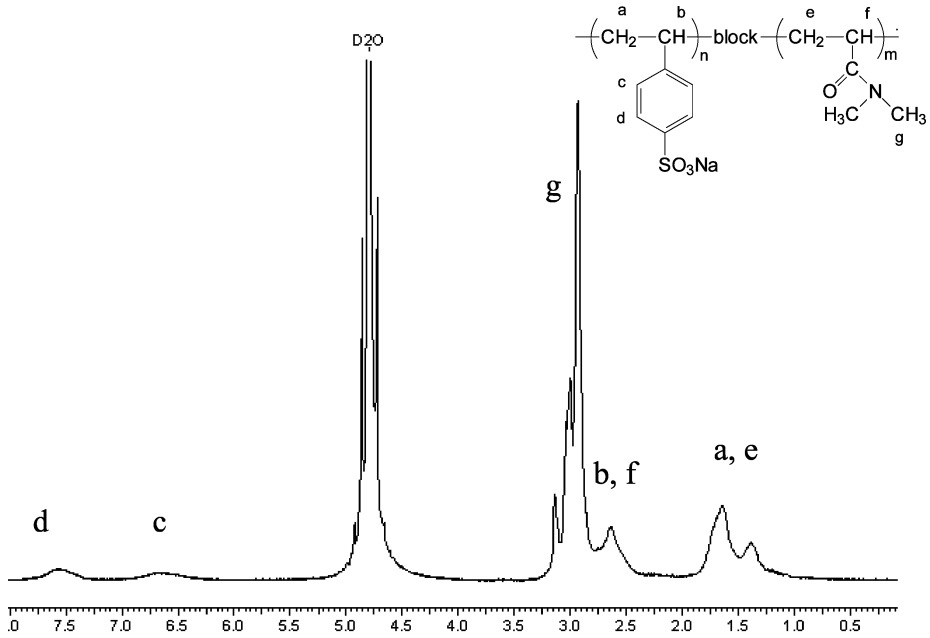


Figure 8. ^{1}H NMR spectrum of poly(sodium 4-styrenesulfonate-*block*-dimethylacrylamide) copolymer in D_2O.

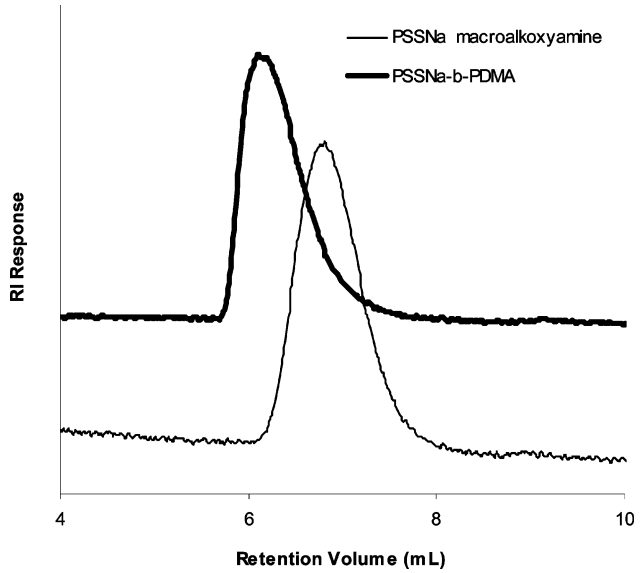


Figure 9. Aqueous SEC traces (eluent: 20 wt % acetonitrile/80 wt % 0.1 M $NaNO_3$; detector: differential refractive index) of poly(sodium 4-styrenesulfonate) macroalkoxyamine (sample from kinetic study 200 min at 85 °C, M_n = 22 300 g mol^{-1}, PDI = 1.3) and poly(sodium 4-styrenesulfonate-*block*-dimethylacrylamide) (PSSNa-*b*-PDMA) copolymer with M_n = 50 200 g mol^{-1}, PDI = 1.3. M_n and PDI were calculated according to the relative calibration curve established with poly(sodium 4-styrenesulfonate) standards. Experimental conditions: [DMA]/[PSSNa macroalkoxyamine] = 599; [SG1]/[PSSNa macroalkoxyamine] = 0.1; [monomer + macroinitiator] in water = 40 wt %; T = 110 °C; P = 2 bar; t = 120 min.

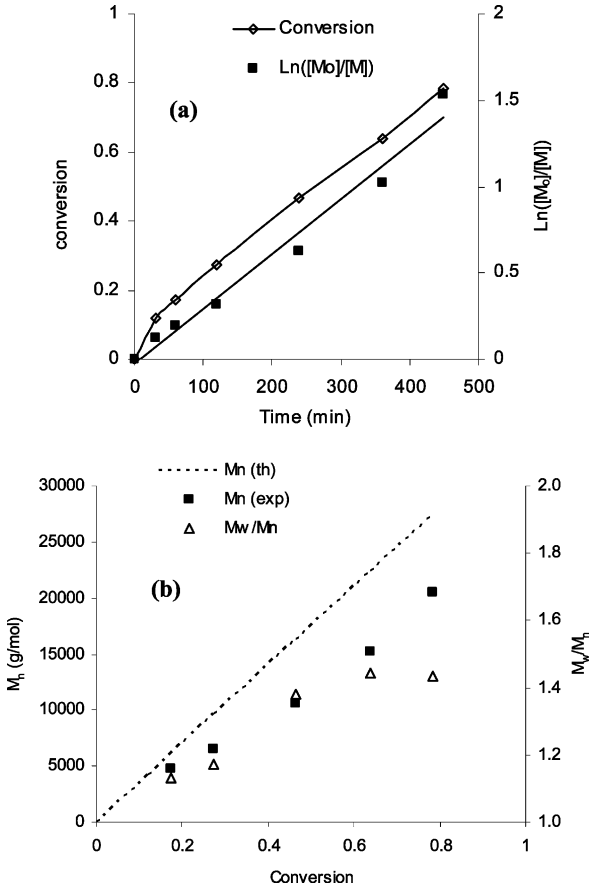


Figure 10. Polymerization of 2-(acryloyloxy)ethylbenzyldimethylammonium chloride (ABC) in water using sodium MAMA-SG1 at 95 °C. (a) Evolution of conversion and ln([M_0]/[M]) vs time data. (b) Evolution of M_n and M_w/M_n with conversion. M_n estimated from calibration with poly(ethylene oxide) standards. Experimental conditions: [ABC]/[sodium MAMA-SG1] = 130; [SG1]/[sodium MAMA-SG1] = 0.1; [monomer + initiator] in water = 40 wt %; T = 95 °C.

all unimodal with no evidence of high molecular weight species that may be indicative of uncontrolled polymerization and/or termination by coupling of poly(sodium 4-styrenesulfonate) propagating radicals.

The ability to synthesize controlled architectures, such as AB diblock copolymers, is one of the features that distinguish "pseudo-living" free radical from conventional free radical polymerization. The polymerization of sodium 4-styrenesulfonate, reported here, produce a homopolymer with nitroxide chain end functionality which can be used as macroalkoxyamine for the block copolymerization of *N*,*N*-dimethylacrylamide (Table 1). The second polymerization step was conduced for 2 h and achieved at a high conversion (83%, as determined by ^{1}H NMR) compared to the homopolymerization of DMA in the same conditions. A summary of the molar mass, polydispersity,

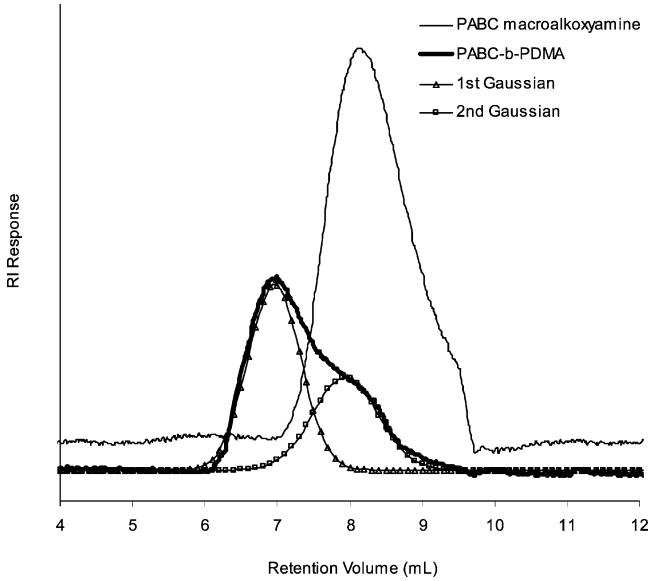


Figure 11. Aqueous SEC traces of poly(2-(acryloyloxy)ethylbenzyldimethylammonium chloride) (PABC) macroalkoxyamine (sample from kinetic study 450 min, M_n = 22 000 g mol^{-1}, PDI = 1.4) and poly(2-(acryloyloxy)ethylbenzyldimethylammonium chloride-*block*-dimethylacrylamide) (PABC-*b*-PDMA) copolymer. Eluent: 0.5 M acetic acid containing 0.3 M Na_2SO_4 at a flow rate of 1 mL min^{-1}. Detector: differential refractive index. Experimental conditions: [DMA]/[PABC macroalkoxyamine] = 501; [SG1]/[PSSNa macroalkoxyamine] = 0.1; [monomer + macroinitiator] in water = 40 wt %; T = 110 °C; P = 2 bar; t = 120 min. The curves under PABC-*b*-PDMA peak are the fit of the first Gaussian function (empty triangles) and the second Gaussian function (empty squares) as calculated by nonlinear regression analysis using Microsoft Excel Solver.

and block copolymer composition is given in Table 2. According to elemental analysis, the polymer product is composed of 25.5 wt % of PSSNa and 74.5 wt % of PDMA; the integration of the signal of the ^{1}H NMR spectrum recorded in D_2O (Figure 8) is in good agreement. The observed molar mass (based on near-monodisperse poly(sodium 4-styrenesulfonate) standards) for the poly(sodium 4-styrenesulfonate-*block*-*N*,*N*-dimethylacrylamide) (PSSNa-*b*-PDMA) hydrophilic block copolymer is significantly lower than the theoretical molar masses due to the lack of suitable standards. Figure 9 compares the aqueous SEC traces of the PSSNa macroalkoxyamine and block copolymer. The signal of the polymer after blocking experiment is shifted to lower evolution volumes compared to the signal of the macroalkoxyamine as well as the narrowness of the chromatogram proved the success of the chain extension polymerization.

Consequently, double hydrophilic block copolymer PSSNa-*b*-PDMA with a number-average molar mass M_n of 50 200 g mol^{-1} and a low PDI of 1.3 was efficiently produced by aqueous nitroxide-mediated polymerization. To our knowledge, this is the first example of AB hydrophilic diblock copolymer synthesized directly in homogeneous aqueous media via NMP.

3.3. Aqueous NMP of 2-(Acryloyloxy)ethylbenzyldimethylammonium Chloride. Polymers and copolymers containing acryloyloxyethylammonium salts find a wide range of industrial use. Applications include cholesterol-lowering ion-exchange resins,[48,49] flocculants for industrial wastewater treatment,[50,51] binders for coated paper,[52] and antistatic coatings.[53,54] The polymerization of these cationic acrylates was usually performed by conventional free radical polymerization. As far as we are aware, there have been only few reports of the polymerization of cationic acrylates by living radical polymerization.[55,56] In this study, 2-(acryloyloxy)ethylbenzyldimethylammonium chloride was polymerized at 95 °C in water by employing sodium MAMA-SG as initiator. We choose to work at this temperature because the internal preliminary experiments shown that below 95 °C the kinetic of ABC polymerization was extremely slow; for example, at 85 °C, ABC polymerization achieved a conversion of 75% for 22 h. However, at 95 °C, the polymerization proceeds to 80% conversion within a reasonable time (7 h) and follows first-order kinetics up to high conversion (Figure 10a). Because of their positive charge, cationic polymers are particularly difficult to separate on a SEC column, in worst cases being completely adsorbed on the oppositely charged packing material. In order to avoid this problem, eluent containing 0.5 M acetic acid and 0.3 M Na_2SO_4 was used. The aqueous SEC elugrams (not given here) shift steadily to lower elution volumes with increasing conversion. The evaluation of the molar mass from the calibration of the aqueous SEC with the narrow poly(ethylene oxide)

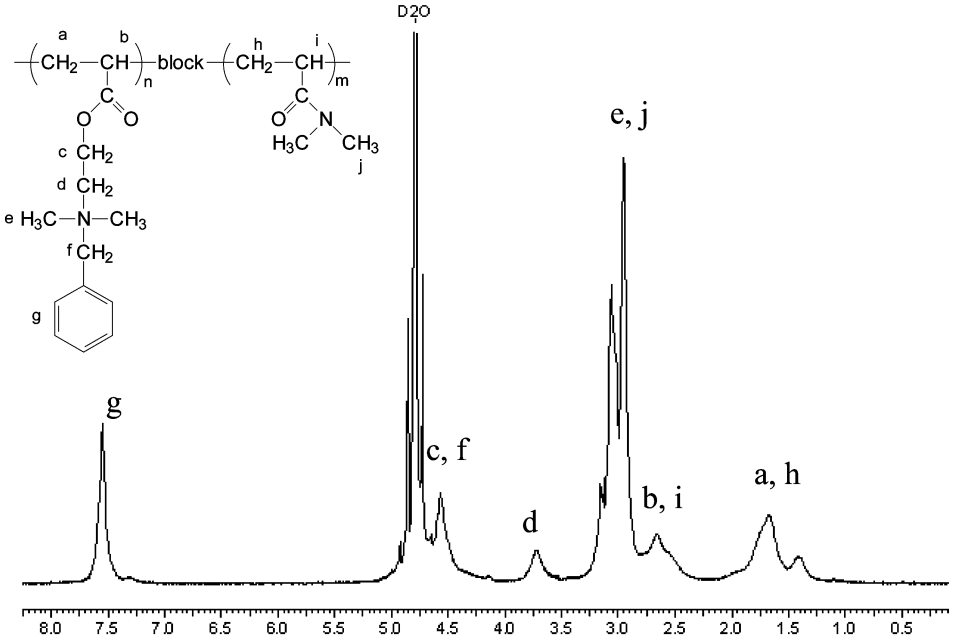


Figure 12. ^{1}H NMR spectrum recorded in D_2O of poly(2-(acryloyloxy)ethylbenzyldimethylammonium chloride-*block*-dimethylacrylamide) copolymer.

standards indicated acceptable polydispersities (about 1.4) and molar masses increasing linearly with the conversion (Figure 10b). However, the apparent M_n values are considerably lower than the theoretical values based on conversion as the polymer standard is not appropriate.

Poly(2-(acryloyloxy)ethylbenzyldimethylammonium chloride) (PABC) macroalkoxyamine was used as initiator for the blocking of *N*,*N*-dimethylacrylamide at 110 °C in water under a pressure of 2 bar. The second polymerization step was conduced for 2 h and reached a conversion of 33% (Table 1). Figure 11 compares the aqueous SEC traces of the PABC macroalkoxyamine and PABC-*b*-PDMA diblock copolymer. The signal of the copolymer after the blocking experiment is shifted to lower elution volumes ($V_e = 7.2$ mL) compared to the signal of the PABC macroalkoxyamine ($V_e = 8.3$ mL) but shows a shoulder at the same elution volume of PABC macroalkoxyamine. The shoulder in the elugram is putatively attributed to inactive PABC homopolymer resulting from the termination reactions due to the long polymerization time (7 h) of 2-(acryloyloxy)ethylbenzyldimethylammonium chloride. The nonlinear regression analysis using Microsoft Excel Solver was used to fit the multiple Gaussian functions of the chromatography peaks.[57−59] The fitting curves are presented in Figure 11. According to the modeling results, the first Gaussian curve is attributed to the PABC-*b*-PDMA diblock copolymer and represents about 70% of sample, whereas the second Gaussian curve is attributed to the PABC "dead" homopolymer and which represents 30% of sample.

Evaluation of the aqueous SEC elugrams based on the calibration curve established with poly(ethylene oxide) standards gave a nominal M_n of 38 000 g mol^{-1} for the synthesized diblock copolymer with a polydispersity of 1.35. The diblock copolymer was also characterized by ^{1}H NMR spectroscopy (Figure 12). Contrary to the precedent experiment (PSSNA-*b*-PDMA diblock copolymer), the contamination of PABC-*b*-PDMA diblock copolymer by PABC "dead" homopolymer yields the estimation of the PDMA molar mass by ^{1}H NMR analysis basing on the PABC molar mass incorrect. The PABC-*b*-PDMA hydrophilic diblock copolymer contaminated by PABC homopolymer is composed of 48 wt % of PABC according to the proton NMR analysis. The characteristics of hydrophilic block copolymer are presented in Table 2.

4. Conclusion

Nitroxide-mediated polymerization of different hydrophilic monomers (DMA, SSNa, and ABC) in homogeneous aqueous medium was achieved using tertiary SG1-based alkoxyamine bearing carboxylic acid group. These polymerizations present the typical features of controlled/living polymerization, such as first-order kinetic up to high conversions, a linear increase of the molecular weight with conversion, good agreement between experimentally determined and theoretical expected M_n values, acceptable polydispersity index (about 1.25−1.4), and efficient synthesis of block copolymers. The NMP in water yields well-defined polymers with acrylamide, acrylate, and styrene based water-soluble monomers at 110, 95, and 85 °C. The rate of polymerization of acrylamide-based monomer is low in the NMP process below 100 °C. Long polymerization time (7 h to yield 80% conversion) was necessary to reach high conversions in the polymerization of acrylate-based monomer; thus, some termination reactions interfere with the polymerization in water, causing a medium blocking efficiency.

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