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Isabelle Chaduc, Agnès Crepet, Olivier Boyron, Bernadette Charleux ...+2 more authors

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Effect of the pH on the RAFT polymerization of acrylic acid in water. Application to the synthesis of poly(acrylic acid)-stabilized polystyrene particles by RAFT emulsion polymerization.

Isabelle Chaduc,[1] *Agnès Crepet,*[2] *Olivier Boyron,*[1] *Bernadette Charleux,*[1] *Franck D'Agosto,*[1,*] *Muriel Lansalot*[1,*]

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

[2] IMP, UMR 5223, Université Claude Bernard Lyon 1, 15 Bd André Latarjet, F-69622 Villeurbanne, France

lansalot@lcpp.cpe.fr; dagosto@lcpp.cpe.fr

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ABSTRACT

The reversible addition-fragmentation chain transfer (RAFT) polymerization of acrylic acid (AA) in water was studied in detail at different pHs using 4-cyano-4-thiothiopropylsulfanyl pentanoic acid (CTPPA) as a controlling agent and 4,4'-azobis(4-cyanopentanoic acid) (ACPA) as an initiator. Well-defined hydrophilic macromolecular RAFT agents (PAA-CTPPA) were obtained and further used directly in water for the polymerization of styrene. The corresponding polymerization-induced self-assembly (PISA) process was evaluated at different pHs and it was shown that working in acidic conditions (pH = 2.5) led to well-defined amphiphilic block copolymer particles ($Đ < 1.4$) of small size (below 50 nm). When the pH increased, the control over the growth of the polystyrene block was gradually lost. Chain extension experiments of PAA-CTPPA with N-acryloylmorpholine (NAM), a hydrosoluble and non-pH sensitive monomer, performed at different pHs showed that the very first addition-fragmentation steps that occurred in water were impeded when PAA was ionized leading to partial consumption of PAA-CTPPA and thus to PS molar masses higher than expected. Varying PAA-CTPPA concentration at pH = 2.5 led in all cases to stable particles composed of well-defined block copolymers with PS segments of different molar masses.

KEYWORDS: reversible addition-fragmentation chain transfer (RAFT), acrylic acid, emulsion, amphiphilic block copolymers, particles

INTRODUCTION

Poly(acrylic acid) (PAA) is a well-known water-soluble polymer widely used in industry in the production of hydrogels, super-absorbents, membranes or coatings. Homopolymers and amphiphilic block copolymers based on PAA present original properties that can be tuned with the pH and the ionic strength. The synthesis of well-defined amphiphilic block copolymers is, however, not easy because of the opposite nature of the two segments. It was originally based on the hydrolysis of the poly(*tert*-butyl acrylate) segment of block copolymers obtained by polymerization in organic solvent. The advances of controlled radical polymerization techniques in aqueous dispersed media make now possible the direct formation of this kind of block copolymers in water.[1] The strategy is based on the in situ chain extension of a preformed water-soluble living polymer with a hydrophobic monomer that generates an insoluble segment, eventually leading to self-assembly of the block copolymers. The resulting nanoobjects are self-stabilized by their hydrophilic block and ideally constituted of identical polymer chains with a predefined and narrowly distributed molar mass. In addition, this is an easy and eco-friendly approach (recently coined as *polymerization-induced self-assembly*[2] or PISA) to generate polymer particles without the need of using low molar mass surfactants. The latter are indeed known to have detrimental effects on the latex stability upon freezing conditions or under high shear, or to induce poor film properties when exposed to water or conditions of high humidity.[3]

Focusing on the reversible addition-fragmentation chain transfer (RAFT) technique, we recently showed that the PISA strategy could be extrapolated to a two-step and one-pot process, in which both the hydrophilic and hydrophobic segments were formed in water,[4] provided that the polymerization of the monomer(s) forming the hydrophilic segment could be carried out in water up to high conversion with a good control. These criteria were effectively fulfilled for both methacrylic acid (MAA)[5] and a mixture of MAA and poly(ethylene oxide) methyl ether methacrylate.[6-8] The proof of concept of the one-pot PISA approach was also established in the case of acrylic acid[4] at acidic pH but no in-depth study was undertaken at this stage.

The literature reports a few studies dealing with the RAFT polymerization of AA. The experiments have mainly been performed in organic solvent such as DMF,[9, 10] ethanol and other protic solvents,[11, 12] and 1,4-dioxane[12]. Reactions in water or mixture of water and organic solvents have actually been scarcely described.[11, 13-17] Well-defined PAA chains with different molar masses exhibiting low dispersity were obtained in presence of trithiocarbonates and xanthates. The RAFT polymerization of AA in water was also successfully carried out under gamma and UV radiation.[15-17] However, despite the pH-dependent aqueous properties of AA and PAA, the impact of the pH on the polymerization control has never been studied.

Regarding the use of PAA macroRAFT agents (or macroRAFT) in emulsion polymerization, the reported studies rely essentially on macroRAFT ($M_n > 800$ g mol^{-1}) preformed in organic solvent. Ferguson *et al.*[18, 19] who were actually the pioneers of the PISA concept used oligomeric PAA RAFT agents (around 5 AA units) for the starved-feed emulsion polymerization of *n*-butyl acrylate (BA). Good control over both the colloidal stability and the molar masses could be achieved. Under the same starved-feed conditions, various preformed PAA macroRAFT were next used for the aqueous emulsion polymerization of hydrophobic monomers such as styrene or BA. [20, 21] More recently, Chenal et al.[22] studied the batch emulsion polymerization of BA using PAA macroRAFTs of different chain lengths and were able to form stable PBA particles with long PBA blocks (up to 176 000 g mol^{-1}).

In the context of the design of nanoparticles obtained by the PISA process and based on the consecutive RAFT polymerization of acrylic acid and styrene, the aim of the present paper is twofold. We first carried out an in-depth study on the pH effect during the RAFT polymerization of AA in water and on the transfer ability of the resulting PAA macroRAFTs in water. The resulting data were then exploited to perform the one-pot RAFT synthesis of PS nanoparticles, paying a particular attention to the pH, parameter of paramount importance for such kind of particles self-stabilized by the PAA segments.

EXPERIMENTAL SECTION

Materials. Acrylic acid (AA, Aldrich 99%), 4,4'-azobis(4-cyanopentanoic acid) (ACPA, Fluka, >98%), N-acryloylmorpholine (NAM, Aldrich, 97%), sodium hydrogen carbonate ($NaHCO_3$, Aldrich, >99.7%), were used as received. Styrene (S, Aldrich, 99%) was purified by removing the inhibitor by filtration with aluminium oxide. 4-Cyano-4-thiothiopropylsulfanyl pentanoic acid (CTPPA) was obtained by reaction of ACPA with bis(thiobenzoyl) and bis(propylsulfanylthiocarbonyl) disulfides according to the literature.[23]

One-pot procedure for the synthesis of polymer particles by emulsion polymerization in the presence of PAA macroRAFT agent.

Step 1: Synthesis of PAA macroRAFT agent in water. PAA segments were obtained in water using CTPPA as a chain transfer agent and ACPA as a radical initiator. In a typical experiment (targeted number-average molar mass, M_n ca. 4000 g mol^{-1}), the procedure was the following: in a two-necked round-bottom flask equipped with a condenser 149 mg of CTPPA (6.72×10^{-2} mol L^{-1}) and 15 mg of ACPA (6.72×10^{-3} mol L^{-1}) were dissolved in 4 mL of water and 2.02 g of AA (3.47 mol L^{-1}). 349 mg of 1,3,5-trioxane (5.79×10^{-1} mol L^{-1}) was added as an internal reference for NMR analysis. 4 mL of water were finally added. After deoxygenation by nitrogen bubbling for 30 min, the resulting mixture was immersed in an oil bath thermostated at 70 °C, which corresponded to time zero of the polymerization. The regular withdrawal of samples allowed us to follow the monomer conversion as a function of time and the evolution of molar masses and molar mass distributions as a function of monomer conversion. The monomer conversion was determined by ^{1}H NMR spectroscopy of the crude reaction medium diluted with D_2O by the relative integration of the protons of 1,3,5-trioxane and the vinylic protons of the monomer. The average molar masses (number-average molar mass M_n and weight-average molar mass M_w) and the molar-mass dispersity ($Đ = M_w/M_n$) were determined, after methylation, by size exclusion chromatography (SEC). Different PAA macroRAFT agents (PAA-CTPPA) were synthesized for the purpose of the present study (*Latexes 1-3, 5, 6* M_n = 4750 g mol^{-1}, $Đ$ = 1.06*; Latexes 4:* M_n = 4400 g mol^{-1}, $Đ$ =1.07*; Latex 7-9:* M_n = 4265 g mol^{-1}, $Đ$ = 1.12*)*.

Step 2: Emulsion polymerization procedure. The polymerization of styrene was performed at 80 °C in a two-necked round-bottom flask equipped with a condenser. In a typical experiment (*Latex* 1), 2.50 g of styrene was added to a solution of previously synthesized PAA-CTPPA (M_n = 4750 g mol^{-1}, Đ = 1.06) and the water content was adjusted so that the final concentration of styrene and macroRAFT agents were 2.4 mol L^{-1} and 5.05 × 10^{-3} mol L^{-1}, respectively. 1 mL (1.20 mol L^{-1}) of an aqueous solution of ACPA (concentration = 3.4 mg mL$^{-1,}$ neutralized by 3.5 molar equivalents of $NaHCO_3$) was added to the reaction mixture. In some cases, the pH of the medium was adjusted with NaOH 1M. The medium was purged with nitrogen during 30 min. The immersion of the round bottom flask in an oil bath thermostated at 80 °C corresponded to time zero of the polymerization. For each experiment, samples were periodically withdrawn to follow the conversion by gravimetric analysis. M_n, M_w and Đ were determined, after methylation, by SEC in THF.

Chain extension with NAM.

The polymerization of NAM was performed at 80 °C in a two-necked round-bottom flask equipped with a condenser. 3.49 g of NAM was added to a solution of previously synthesized PAA-CTPPA (M_n = 4480 g mol^{-1} and Đ = 1.11) and the water content was adjusted so that the final concentration of NAM and macroRAFT agents were 2.4 mol L^{-1} and 5.73 × 10^{-3} mol L^{-1}, respectively. 1 mL (1.20 mol L^{-1}) of an aqueous solution of ACPA (concentration = 3.4 mg mL$^{-1,}$ neutralized by 3.5 molar equivalents of $NaHCO_3$) was added to the reaction mixture. In some cases, the pH of the medium was adjusted with NaOH 1M. The medium was purged with nitrogen during 30 min. The immersion of the round bottom flask in an oil bath thermostated at 80 °C corresponded to time zero of the polymerization. The monomer conversion was determined by ^{1}H NMR spectroscopy of the crude reaction medium diluted with D_2O, from the relative integration of the protons of 1,3,5-trioxane and of the vinylic protons of the monomer. M_n, M_w and Đ were determined, after methylation, by SEC in THF.

Analytical techniques. The conversions of AA and NAM were determined by ^{1}H NMR spectroscopy in D_2O at room temperature (Bruker DRX 300). For the polymerizations of styrene in water in the presence of PAA macroRAFT agent, the monomer consumption was followed by gravimetric analysis of samples withdrawn from the polymerization medium at different times.

SEC measurements were performed in THF (THF-SEC) at 40 °C at a flow rate of 1 mL min^{-1} using toluene as a flow rate marker. Before analysis, the polymers were modified by methylation of the carboxylic acid groups using trimethylsilyl diazomethane.[24] They were analyzed at a concentration of 3 mg mL^{-1} after filtration through a 0.45 μm pore-size membrane. The separation was carried out on three columns from Malvern Instruments [T6000M General Mixed Org (300 × 8 mm)]. The setup (Viscotek TDA305) was equipped with a refractive index (RI) detector (λ = 670 nm). M_n and $Đ$ were derived from the RI signal by a calibration curve based on polystyrene standards (PS from Polymer Laboratories).

The molar masses and molar mass distributions of PAA were also determined by an aqueous SEC (ASEC) system composed of an Isochrom LC pump with a Waters 717 autosampler. A multi-angle laser light scattering (MALLS) detector (Wyatt EOS) was coupled online with a differential refractometer Wyatt Optilab T-rEX (λ = 658 nm). The separation was carried out on three columns (PSS SUPREMA linear M, 300 × 8 mm, bead diameter: 10 μm). Elution was performed at 22 °C (1 mL min^{-1}) using an aqueous buffer ($NaHCO_3$ 0.05 M, $NaNO_3$ 0.1 M, NEt_3 0.02 M, NaN_3 0.03%) after filtration on a 0.1 μm pore-size membrane. The samples were prepared at a concentration of 4 mg mL^{-1} and filtered through a 0.45 μm pore-size membrane prior to injection.

The SEC measurements for the PAA-*b*-PNAM copolymers were performed on an EcoSEC semi-micro GPC system from Tosoh equipped with a dual flow refractive index detector and a UV detector. The samples were analyzed in DMF (with LiBr at 0.01 mol L^{-1} and trifluoroacetic acid (TFA) at 0.008 mol L^{-1}) at 50 °C using a flow rate of 1 mL min^{-1}. All polymers were injected at a concentration of 3 mg mL^{-1} in DMF, after filtration through a 0.45 μm pore-size membrane. Separation was performed with 3 PSS GRAM columns (7 μm, 300 x 7.5 mm). M_n and $Đ$ were derived from the RI signal by a calibration curve based on polystyrene standards. WinGPC Unity software was used for data collection and calculation.

The particle size (hydrodynamic average diameter D_h) and the dispersity of highly diluted samples (*Poly* - the higher this value, the broader the size distribution) were measured by dynamic light scattering (DLS)

(NanoZS from Malvern Instruments). The latexes (diluted solution deposited on a carbon/formvar-coated copper grid and allowed to evaporate) were observed by transmission electron microscopy (TEM) with a Philips CM120 microscope operating at an accelerating voltage of 80 kV (Centre Technologique des Microstructures (CTμ), plateforme de l'Université Claude Bernard Lyon 1, Villeurbanne, France). The number- and mass-average particle diameter (D_n and D_w, respectively) as well as the particle-diameter dispersity (D_w/D_n) were determined using AnalySIS software (Soft Imaging System).

The number of particles N_p per unit volume of aqueous phase (mL^{-1}_{water}) was calculated using the diameter obtained from TEM (D_n, nm) according to equation (1), with τ ($g\ mL^{-1}_{water}$) the solids content of the dispersed phase ($\tau = (m_{macroRAFT} + \text{conversion} \times m_{styrene})/V_{water}$, with $m_{macroRAFT}$ and $m_{styrene}$ the initial weight of PAA-CTPPA and styrene, respectively, V_{water} the initial volume of water) and ρ the density of PS (1.05 g cm^{-3}).

$$N_p = \frac{6\tau}{\rho \pi D_n^{3}} \qquad (1)$$

The hydrolytic stability of the trithiocarbonate extremity of PAA macroRAFT agent at pH = 8 and 3.4 was studied by UV analysis. An aqueous solution of PAA-CTPPA (M_n = 4750 g mol^{-1}, c = 5.05×10^{-3} mol L^{-1}) was prepared in the same conditions as those of an emulsion polymerization experiment performed at pH = 8 or 3.4. Then the mixture was immersed in an oil bath thermostated at 80 °C. Samples were periodically withdrawn to follow the UV signal of the trithiocarbonate. UV analysis was performed using a UV/VIS spectrophotometer (JASCO V-530) and quartz cells. The measurements were carried out at the wavelength of 310 nm (absorbance of the thiocarbonyl thio) at a concentration of 4.2×10^{-5} mol L^{-1}.

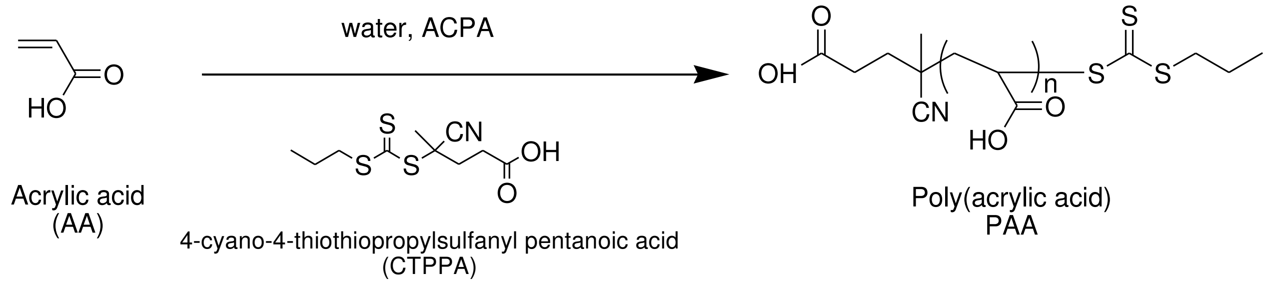
The pH value of the aqueous phase was probed by a pH-meter (Seven easy, Mettler Toledo) using a combined glass electrode (Mettler Toledo).

RESULTS AND DISCUSSION

The synthesis of PAA-stabilized polystyrene nanoparticles was performed according to the PISA concept and working in a one-pot procedure.[4-8] For this strategy to be successful, the RAFT polymerization of the hydrophilic monomer, here AA, should be performed up to high conversion with a very good control. In order to find the optimal conditions for this first step, a study was first carried out on the RAFT polymerization of AA in water.

RAFT synthesis of PAA in water.

The RAFT polymerization of AA was performed in water in presence of CTPPA as a RAFT agent (Scheme 1). CTPPA was selected here as it was successfully employed to polymerize MAA by RAFT in water under similar conditions.[25] As also observed for MAA, CTPPA is not highly soluble in water and it was thus first dissolved in AA. The polymerization medium quickly cleared up upon heating and during the first percents of conversion. The [AA]/[CTPPA] initial ratio was fixed at 52 (targeted M_n of 4000 g mol^{-1}) for all the experiments. Different parameters were studied such as the temperature and the monomer concentration and a special focus was put on the pH.



Scheme 1: Synthesis of poly(acrylic acid) by RAFT polymerization in water.

Table 1: Experimental conditions and results for the RAFT polymerizations of AA in water with [AA]/[CTPPA] = 52 [a]

Expt	$[AA]_0$ (mol L^{-1})	T (°C)	pH	Time (h)	Conv. (%)	$M_{n, theo}$ (g mol^{-1})	$M_{n, exp}$ (g mol^{-1})	$Đ = M_w/M_n$
AA-1	1	80	1.8	6	97	3895	4075^c	1.08^c
AA-2	1	70	1.8	7	95	3820	4370^c	1.09^c
AA-3	3.5	70	1.8	5.5	100	4000	4270^c	1.07^c
AA-4	3.5	70	1.8	6	98	3925	4350^c/4960^d	1.08^c/1.04^d
AA-5^b	3.5	70	4.0	22	96	3850	4765^d	1.02^d
AA-6^b	3.5	70	5.0	22	91	3650	4860^d	1.05^d
AA-7^b	3.5	70	7.0	22	99	3970	5105^d	1.08^d

[a]The RAFT polymerizations of AA were performed using ACPA as an initiator and CTPPA as a chain transfer agent [CTPPA]/[ACPA] = 10. [b] The pH was adjusted by the addition of NaOH. [c] Obtained by THF-SEC. [d] Obtained by ASEC.

Influence of the polymerization temperature and AA concentration. As mentioned above, the RAFT polymerization of AA in water has been scarcely described in the literature.[11, 13-16] Whilst the nature of the RAFT agent and the ratio [AA]/[RAFT] were investigated, no detailed study was carried out on the effect of the temperature or the monomer concentration on the polymerization control. The RAFT polymerization of AA was first performed under conditions described for MAA RAFT polymerization,[5] i.e. [AA] = 1 mol L^{-1} and T = 80 °C (AA-1, Table 1). High conversion was reached (97%) in less than 6 hours with an inhibition period of less than 30 minutes (Figure 1a). A linear increase of molar masses versus conversion was observed and the experimental molar mass values were close to the theoretical ones and narrowly distributed ($Đ < 1.10$, Figure 1b), indicating a good control of AA polymerization. However, the chromatogram obtained for the final conversion showed the presence of a small quantity of high molar mass chains (Figure 1c). The molar mass of these chains approximated twice the molar mass of the main population showing the occurrence of irreversible termination by bimolecular coupling at the end of the polymerization. As the quality of the formed PAA in this first polymerization step would impact the quality of the envisioned PISA process, the polymerization temperature was decreased to 70 °C (*AA-2*, Table 1 and Figure 1) in order to decrease the concentration of propagating radicals and hence minimize the formation of coupled chains. As shown in Figure 1d, well-defined PAA chains formed and no shoulder was observed on the chromatograms. However, to increase the polymerization rate whilst maintaining the best level of control for the same targeted molar mass (M_n = 4000 g mol^{-1}), the concentration of AA was increased from 1 mol L^{-1} (*AA-2*, Table 1) to 3.5 mol L^{-1} (*AA-3*, Table 1). The ratio [CTPPA]/[ACPA] being kept to 10, this implies that the ACPA concentration was also increased with the associated risk of increasing the occurrence of irreversible termination reactions. However, in this case, good control was kept all over the course of the polymerization (Figure 1e) and up to 100% conversion were reached in less than 6 hours (Figure 1a).

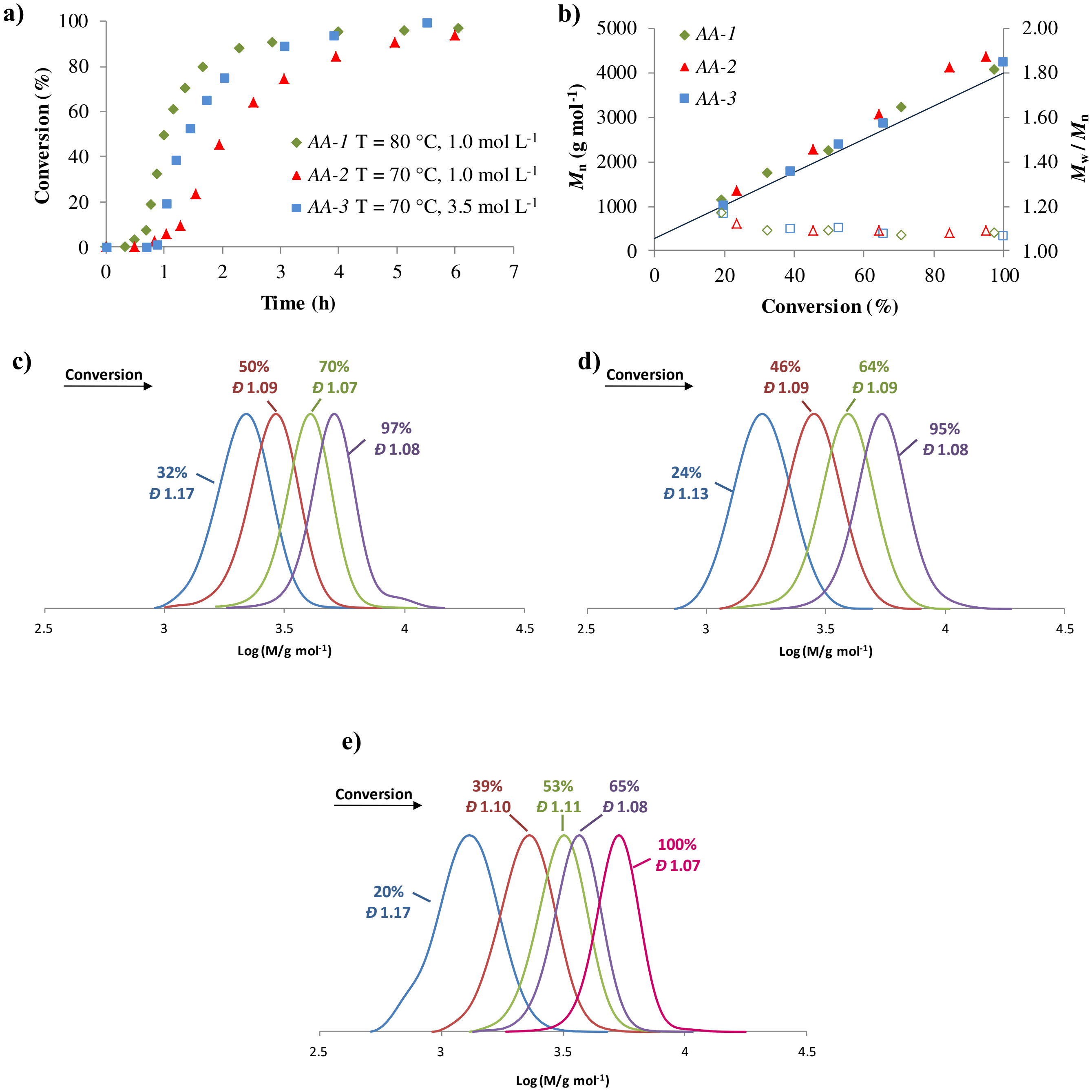


Figure 1: RAFT polymerization of AA performed in water (pH = 1.8) at different concentrations and different temperatures. [AA]/[CTPPA] = 52, [CTPPA]/[ACPA] = 10. Evolution of (a) monomer conversion versus time, (b) number-average molar mass M_n (full symbols) and $Đ = M_w/M_n$ versus (open symbols) versus conversion. The straight line corresponds to the theoretical evolution of M_n with conversion. Corresponding THF-SEC chromatogram evolution for (c) [AA] = 1 mol L^{-1} and T = 80 °C (*AA-1*), (d) [AA] = 1 mol L^{-1} and T = 70 °C (*AA-2*) and (e) [AA] = 3.5 mol L^{-1} and T = 70 °C (*AA-3*).

Influence of the pH. To the best of our knowledge, the impact of pH on the control of the RAFT polymerization of AA in water has never been described in the literature. The polymerizations were usually performed at natural pH (ca. pH ≈ 2). Increasing the pH may be insignificant on the ability of CTPPA to control RAFT polymerization of AA as long as the hydrolytic stability of the trithiocarbonate moiety is kept. However, the ionization of both the monomer and the polymer chains has been shown to impact the kinetic behaviour of the free radical polymerization of AA.[26, 27] The propagation rate constant k_p decreased by one order of magnitude when going from a non-ionized system to fully ionized monomer and polymer species likely because of the repulsion between both monomer and macroradicals (although recent results on MAA polymerization indicate that the full picture is probably more complex[28]). Besides, when an excess of salt like NaOH was added to fully ionized AA, the polymerization rate increased again. Kabanov et al.[29] explained this result by an enhancement of k_p by the presence of ions-pairs. The repulsion between the ionized species is mitigated by the increase of the ionic strength. This variation of k_p with the pH also depends on monomer concentration.[30, 31]

In this work, four experiments were carried out at pH = 1.8, 4.0, 5.0 and 7.0 (*AA-4* to *AA-7*, Table 2). As shown in Figure 2, the pH had a dramatic effect on the polymerization kinetics. After the same inhibition period (around 1h), the polymerization rate strongly decreased when the pH was increased from 1.8 to 5.0, but increased again for pH = 7.0 remaining, however, lower than in the case of pH = 1.8 but faster than when pH = 4.0. These results are consistent with observations already made for the free radical polymerization of AA in water[26, 27] and the same conclusions on the impact of pH on k_p may apply when RAFT is employed. The examination of the ASEC peaks evolution versus conversion gives additional information on the control of the RAFT process (Figure 3). Whatever the pH, the ASEC peaks are nicely shifted towards lower elution times when conversion increases and remain monomodal and narrowly distributed ($Đ < 1.1$). These findings suggest that the quality of the addition-fragmentation transfer reaction is not affected by the ionization of the species involved either during the RAFT prequilibrium (short oligomers) or the RAFT main equilibrium (macroradicals).

When comparing the experiments performed at different pHs, complete conversion was reached only at pH = 1.8 and in less than 6 hours. The following emulsion polymerization experiments were then performed with a PAA macroRAFT (PAA-CTPPA) synthesized at pH = 1.8 and 70°C.

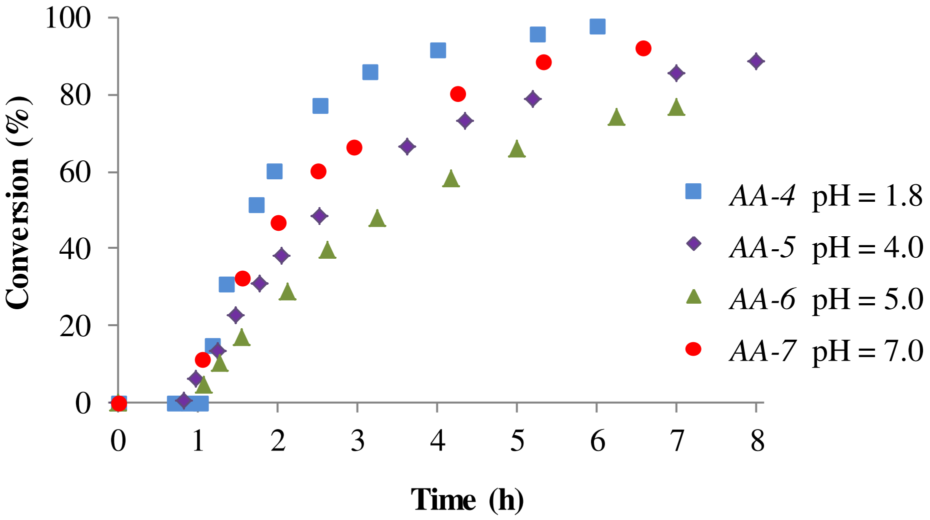


Figure 2: Evolution of monomer conversion versus time for the RAFT polymerization of AA performed in water at [AA] = 3.5 mol L^{-1} at 70 °C at 4 different pHs: pH = 1.8 (*AA-4*), pH = 4.0 (*AA-5*), pH = 5.0 (*AA-6*), pH = 7.0 (*AA-7*)). [MAA]/[CTPPA] = 52 and [CTPPA]/[ACPA] = 10.

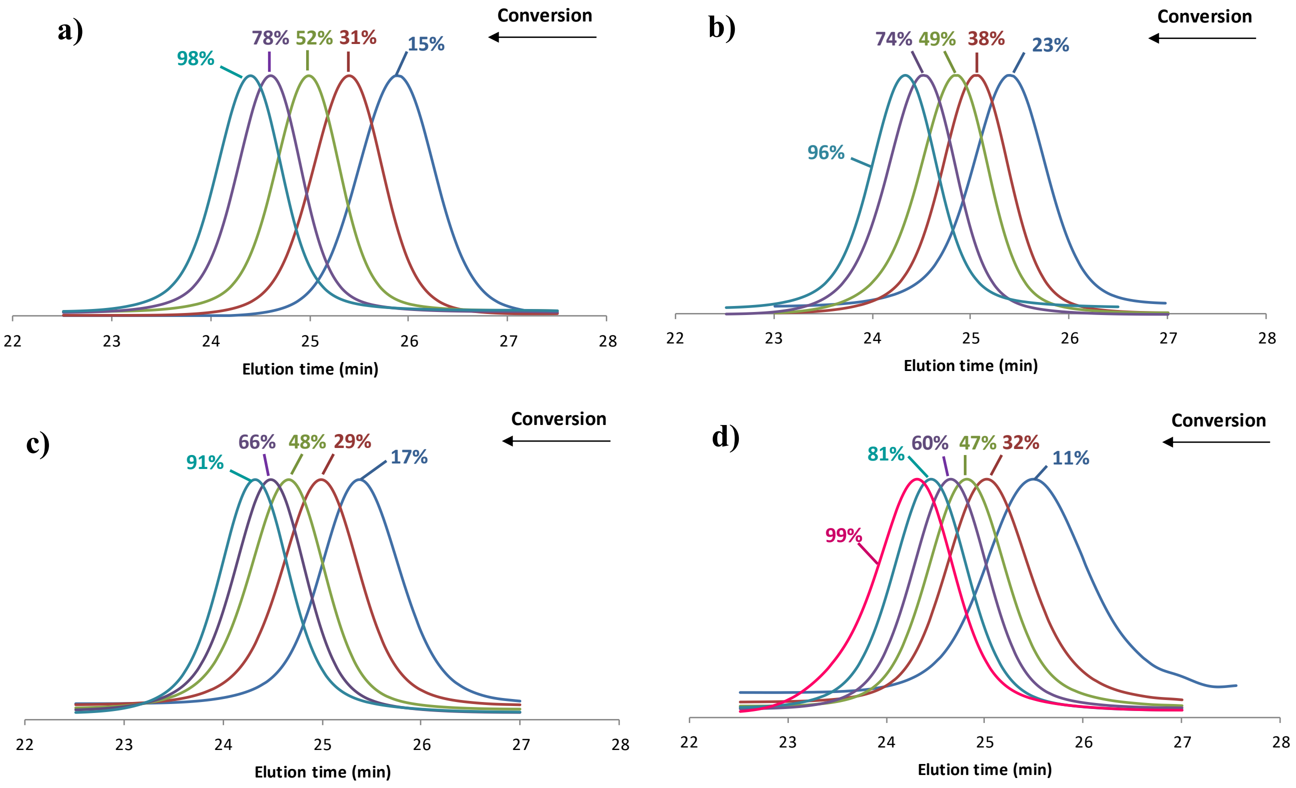


Figure 3: Evolution of the ASEC traces during the RAFT polymerization of AA performed in water at 70 °C at different pHs. [AA] = 3.5 mol L^{-1}, [AA]/[CTPPA] = 52, [CTPPA]/[ACPA] = 10. (a) pH = 1.8 (*AA-4*), (b) pH = 4.0 (*AA-5*), (c) pH = 5.0 (*AA-6*), (d) pH = 7.0 (*AA-7*).

Emulsion polymerization of styrene using PAA macroRAFT agents

The RAFT emulsion polymerization of styrene was performed at 80 °C in the presence of PAA-CTPPA. An aliquot of the medium coming out of the reactor where AA was polymerized in water at pH = 1.8 and 70°C was directly diluted with the required amount of water and styrene to target a styrene concentration close to 20 wt% (see Table 2).

Table 2: Emulsion Polymerizations of Styrene using PAA-CTPPA MacroRAFT Agents

Expt[a]	**PAA-CTPPA**		$DP_{n,theo}$	**pH**[b]	**Time (h)**	**τ (g L^{-1} water)**[c]	**Conv. (%)**
	M_n **(g mol^{-1})**	**Conc (mmol L^{-1} water)**					
Latex 1	4750	5.05	475	2.5	6	273	100
Latex 2	4750	5.05	475	3.5	7	275	100
Latex 3	4750	5.05	475	4.5	22	192	66
Latex 4	4400	5.45	440	6.0	22	215	76
Latex 5	4750	5.05	475	7.0	5	242	90
Latex 6	4750	5.05	475	8.1	5	240	89
Latex 7	4265	11.3	209	2.5	6	279	92
Latex 8	4265	5.63	427	2.5	6	264	96
Latex 9	4265	2.81	853	2.5	6	254	97

[a] All the experiments were performed at T = 80 °C with [$NaHCO_3$] / [ACPA] = 3.5; [PAA-CTPPA] / [ACPA] = 5. [b] The pH was adjusted by addition of NaOH 1M to the medium, except for pH = 2.5 which was the natural pH of the starting emulsion. [c] Global solids content taking into account the amount of PS for the given conversion and the macroRAFT agent.

In our previous study on the RAFT emulsion polymerization of styrene in the presence of poly(methacrylic acid) (PMAA-CTPPA) macroRAFT agent,[5] the occurrence of two types of nucleation mechanism was observed with the pH increase and related to PMAA conformation in water according to pH. In this particular case, it was shown that the hypercoiled conformation of the macroRAFT at pH = 3.4 would provide an important local concentration of monomer in the vicinity of the active chain end allowing a rapid addition of styrene units on the PMAA macroradical and the formation of well-defined amphiphilic copolymer nanoparticles via PISA. In contrast, the more opened water-swollen structure present at pH ≥ 6.5 and the trithiocarbonate end-group hydrolysis (effectively shown at pH = 8.0[5]) offered a less favorable environment for the growth of the PS segment and homogeneous nucleation was favored.

With the help of fluorescence studies similar to that performed with PMAA-CTPPA aqueous solutions at different pHs using Nile Red as a solvatochromic dye,[5] we preliminary showed that PAA-CTPPA does not exhibit this original hypercoiled-water swollen transition behavior (see Figure S1 in the Supporting Information).

Previous studies employing polyelectrolyte hydrophilic macroRAFT agents,[4-8] for similar PISA systems showed that the pH played a key role on the control of the formation of amphiphilic block copolymers and thus on the onset of their self-assembly (nucleation step), but also on the stability and the morphology of the final nano-objects. In order to assess the impact of the initial pH on both the kinetics and the control of styrene emulsion polymerization in the presence of PAA-CTPPA, experiments were carried out from pH = 2.5 to 8.1 (*Latexes* 1 to 6, Tables 2 and 3). As shown in Figure 4, the pH has a great impact on both the kinetics and the molar masses. An inhibition period was observed for all the experiments (Figure 4a). In a true PISA process, this period has been described as the time required for the hydrophobic polystyrene block to reach a sufficient molar mass for the amphiphilic block copolymers to start to self-assemble.[1] At pH = 2.5 (*Latex* 1), which was the natural pH of the polymerization medium, after an inhibition period of ca. 3 hours, complete conversion was reached within 4 hours. When the pH was increased, PAA being more hydrophilic, the inhibition period increased to 3.5 hours for pH = 3.5 (*Latex* 2), and to more than 8 hours for pH = 4.5 (*Latex* 3) or 6.0 (*Latex* 4). In these last two cases, however, the conversions were limited to 66% and 76% after 22 hours of polymerization. Surprisingly, for pH $\geq$ 7.0 (*Latexes* 5 and 6) the inhibition period became very short (ca. 1 hour) with lower polymerization rates (initial slope of the linear part of the conversion versus time curves, data not shown) and conversion reaching 90% in 5 hours.

Table 3: Molecular Characteristics of the Polymers and Colloidal Features of the Particles formed during the Emulsion Polymerizations of Styrene using PAA-CTPPA MacroRAFT Agents.

Expt	**pH**	$M_{\mathrm{n},\,exp}$[a] (g mol^{-1})	$M_{\mathrm{w}}/M_{\mathrm{n}}$[a]	D_{h} (nm)[b]	*Poly*[b]	D_{n} (nm)[c]	$D_{\mathrm{w}}/D_{\mathrm{n}}$[c]	N_{p} (L^{-1} $_{\mathrm{water}}$)[d]	**Coag (wt%)**[e]
Latex 1	2.5	57 160	1.36	55	0.13	33	1.08	1.38×10^{19}	4.5
Latex 2	3.5	63 100	1.81	49	0.25	26	1.23	2.85×10^{19}	4.0
Latex 3	4.5	42 140	2.42	59	0.18	24	1.28	2.52×10^{19}	3.7
Latex 4	6.0	76 830	1.40	68	0.17	27	1.15	1.99×10^{19}	6.4
Latex 5	7.0	237 680	1.79	158	0.03	106	1.05	3.70×10^{17}	3.4
Latex 6	8.1	278 450	1.96	190	0.02	145	1.04	1.43×10^{17}	3.3
Latex 7	2.5	26 540	1.26	57	0.39	25	1.05	3.25×10^{19}	3.6
Latex 8	2.5	49 460	1.37	53	0.15	26	1.10	2.73×10^{19}	5.2
Latex 9	2.5	98 560	1.52	64	0.76	43	1.07	5.81×10^{18}	6.3

[a] Obtained by THF-SEC using PS calibration. [b] Obtained by dynamic light scattering. [c] Obtained by transmission electron microscopy. [d] Calculated from the number-average diameter D_{n} obtained by TEM. [e] Based on the total weight of polymer and macroRAFT.

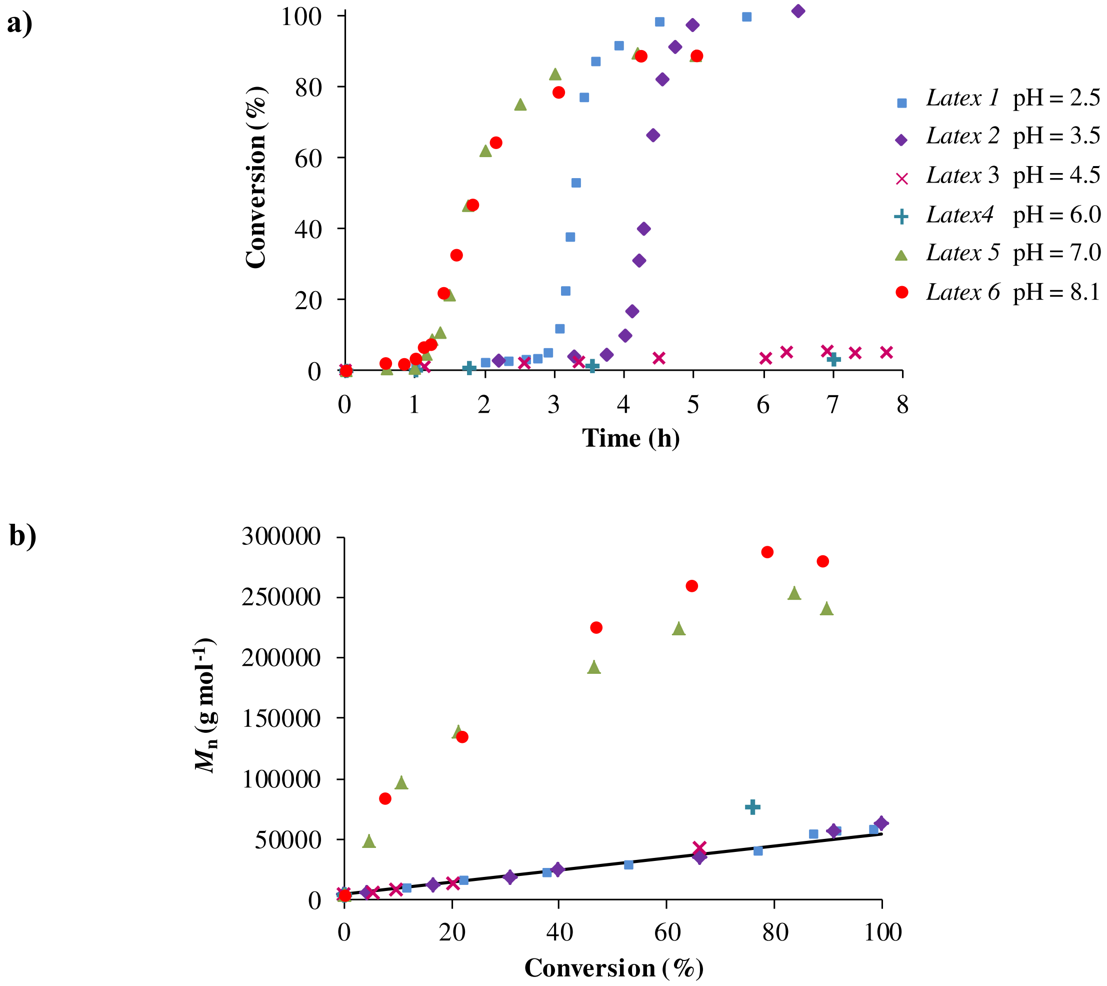


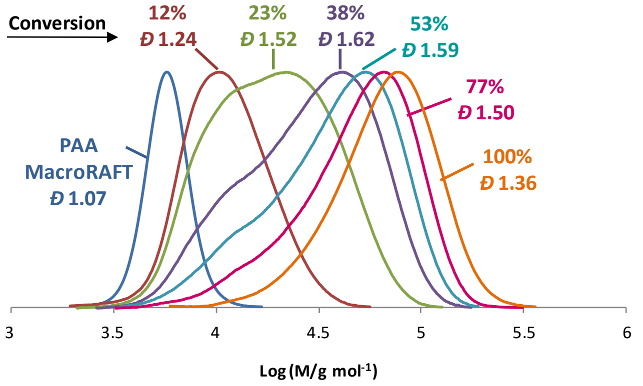
Figure 4: RAFT emulsion polymerizations of styrene performed at different pHs. *Latex* 1, pH = 2.5; *Latex* 2, pH = 3.5; *Latex* 3, pH = 4.5; *Latex* 4, pH = 6.0; *Latex* 5, pH = 7.0; *Latex 6,* pH = 8.1. Evolution of (a) monomer conversion versus time, (b) number-average molar mass M_n (full symbols) versus conversion. The straight line corresponds to the theoretical evolution of molar masses with conversion. See Table 2 for detailed experimental conditions.

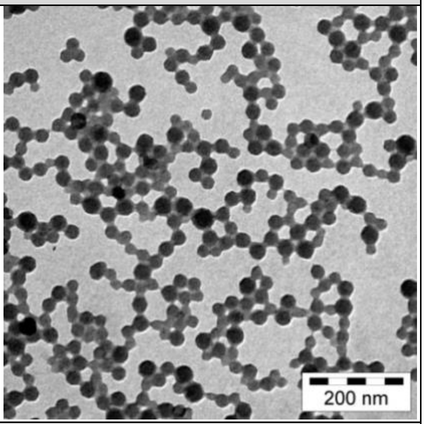
The evolution of molar masses and of molar mass distributions with conversion for Latex 1 to 6 are shown in Figure 4b and Figure 5, respectively. It is clear that the polymerization performed at pH ≥ 7 behave differently and do not display the expected features of a controlled radical polymerization in which the number of chains is controlled by the number of controlling agents.

A good control over the growth of the polystyrene block was observed at pH = 2.5 (*Latex* 1) as attested by the gradual shift towards higher molar masses of the distributions and the low final value of $Đ$ (1.36). Although PAA-CTPPA was completely consumed at the end of styrene polymerization, it was however slowly elongated (see chromatograms after 12%, 23% or 38% conversion). Indeed, in the early stage of the polymerization of styrene in water, the fragmentation towards the poly(acrylic acid) block is not favored. A similar situation was observed for pH = 3.5 (*Latex* 2), 4.5 (*Latex* 3) and 6 (*Latex* 4) with, however, a gradual loss of the polymerization control. For pH = 7.0 and 8.1 (*Latex* 5 and *Latex* 6), residual PAA-CTPPA was always observed even at high conversions (estimated for instance at ca. 80 mol% for *Latex* 6 at 89% conversion[32]) leading to a deviation from the expected molar mass values (Figure 4b) and to high final M_n (> 200 kg mol^{-1}, $Đ > 1.8$). DLS analyses and TEM observations (Table 3 and Figure 5) corroborated well these observations. Indeed, although all the latexes were stable (around 4% coagulum after 7 hours of polymerization), two ranges of particle size were obtained: small and rather polydisperse particles for *Latexes* 1-4 (D_n around 30 nm); bigger and rather isometric particles for *Latexes* 5 (D_n = 106 nm) and 6 (D_n = 145 nm). At pH = 2.5, a high number of small particles is observed ($N_p = 1.40 \times 10^{19}$ $L^{-1}{}_{water}$, D_n = 33 nm) whereas hundred times less particles with larger volume were formed at pH = 8.1 ($N_p = 1.47 \times 10^{17}$ $L^{-1}{}_{water}$, D_n = 145 nm).

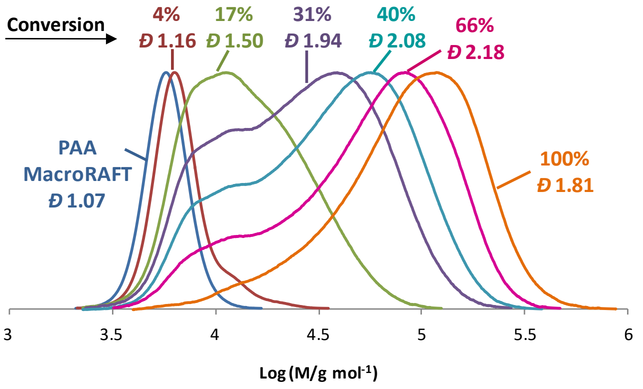
Considering the aforementioned kinetics and colloidal features of the formed latexes, two different regimes seemed to operate depending on the pH range ($2.5 \leq pH \leq 6.0$ and $pH \geq 7.0$). When pH = 2.5, all PAA macroRAFT agents are chain extended by styrene and involved in the expected PISA process. The amphiphilic block copolymers that are formed generate small particles. When the pH gradually increases up to 8.1, PAA macroRAFT is much more slowly consumed ($pH \leq 6.0$) or even not quantitatively ($pH \geq 7.0$). In these last cases, a fairly good control of the styrene polymerization is however maintained. It is of particular importance to note that, at pH = 7 for example, after 5% conversion, although unreacted PAA remained, a very nice chain extension of the PAA by styrene is observed ($Đ$ = 1.17). In addition, the high molar mass observed for the resulting block copolymer is consistent with a partial consumption of the starting PAA macroRAFT agent. The final particles (c.a. 150 nm) are thus probably mainly formed by block copolymers with a long hydrophobic block (c.a. 278 450 g mol^{-1} $Đ$ = 1.96 *Latex* 6 in Table 3). The presence of remaining PAA chains cannot be attributed to the degradation of the trithiocarbonate chain end at high pH as already observed in the case of PMAA for example.[5] Indeed, a UV study was performed at pH = 8.0 at 80 °C (see supporting information Figure S2) and showed that the absorbance of the PAA macroRAFT agent at λ = 310 nm (corresponding to the maximum absorbance of the thiocarbonylthio function) decreased after 6 hours only by 6 %. This means that under these conditions 94% of the chains still carried an active chain end.

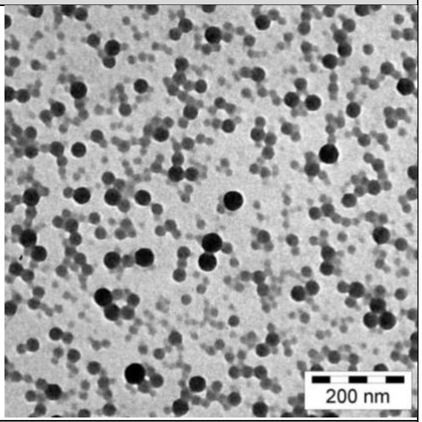
pH = 2.5 (*Latex* 1)



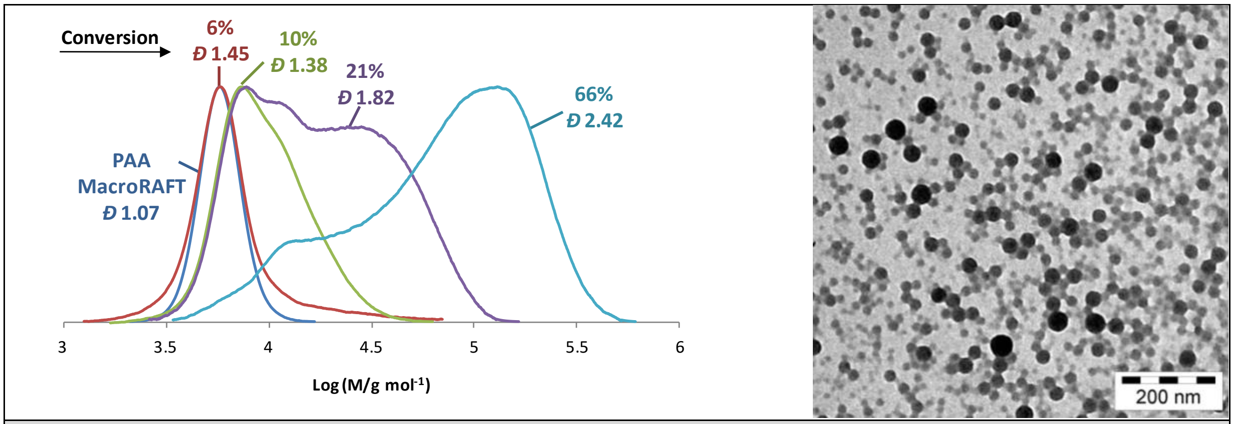


pH = 3.5 (*Latex* 2)

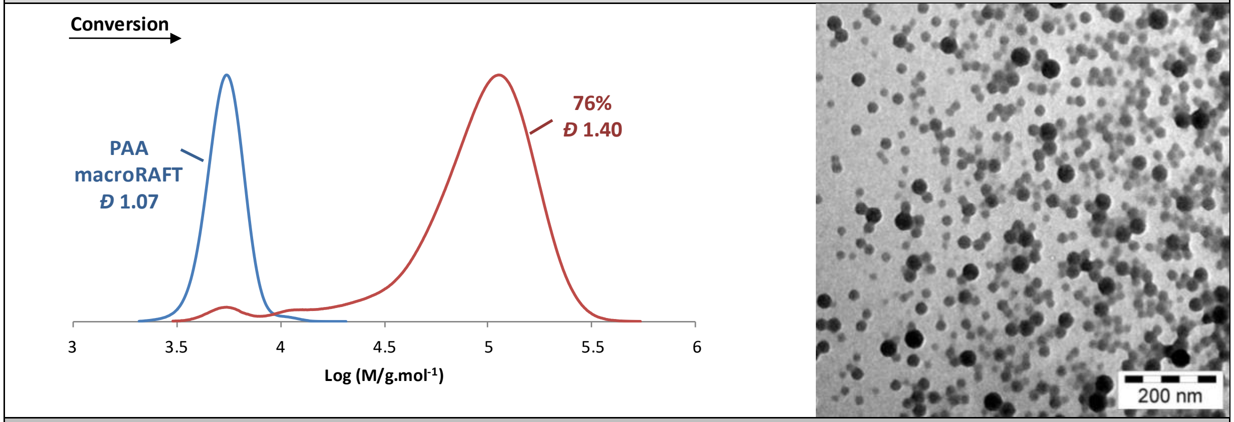




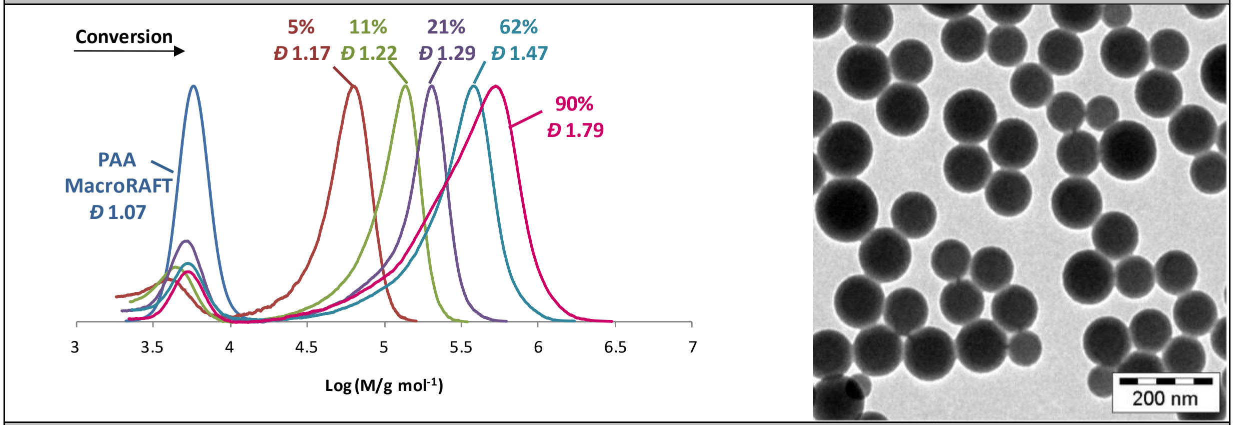
pH = 4.5 (*Latex* 3)



pH = 6.0 (*Latex* 4)



pH = 7.0 (*Latex* 5)



pH = 8.1 (*Latex* 6)

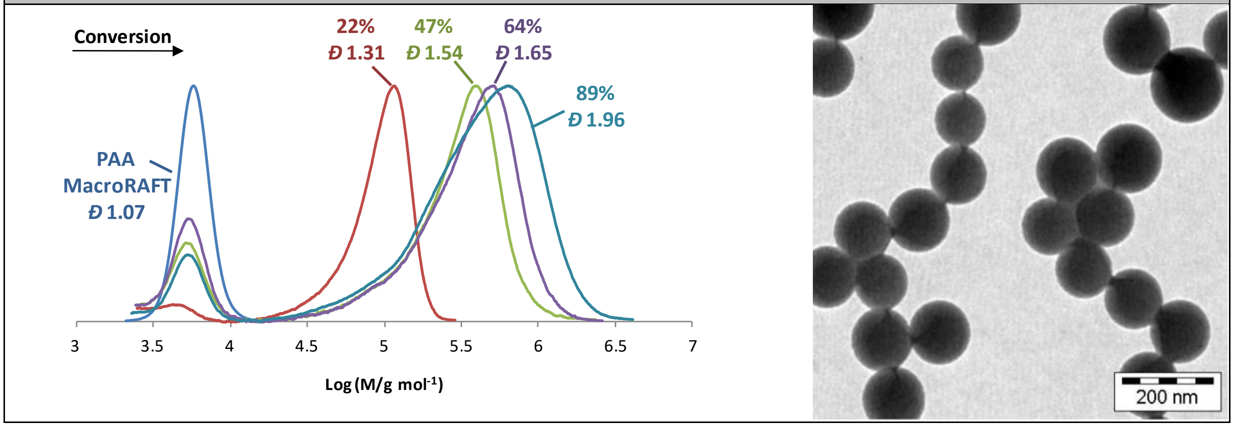


Figure 5: Evolution of the size exclusion chromatograms versus conversion and TEM images of the final latexes

for the RAFT emulsion polymerizations of styrene performed at different pHs. *Latex* 1, pH = 2.5; *Latex* 2, pH = 3.5; *Latex* 3, pH = 4.5; *Latex* 4, pH = 6.0; *Latex* 5, pH = 7.0; *Latex* 6, pH = 8.1. See Table 2 for detailed experimental conditions.

As the difference between the aforementioned regimes is only the pH, the presence of remaining PAA at pH ≥ 7 may be linked to the ionization of these chains. Indeed, at the very beginning of the polymerization and after the first fragmentation steps, styrene adds onto ionized PAA macroradicals. PS segments reach however very quickly molar masses high enough to lead to the self-assembly of these charged block copolymers. The nucleation is even faster at pH = 8.1 than at pH = 2.5 (see Figure 4a). The fast growth of the PS block at alkaline pH could be attributed to a decrease of the chain transfer constant ($C_{tr} = k_{tr}/k_p$). The propagation rate constant k_p being not impacted by the pH in the case of styrene, the decrease of C_{tr} is thus a direct consequence of a decrease of k_{tr}. This results in a slow addition reaction of charged PAA-*b*-PS$^\bullet$ radicals onto the remaining PAA-CTPPA (and also charged). Once particles are nucleated, the growth of the PS block inside the particles remains controlled as attested by the shift of the chromatograms with conversion.

It remains difficult to de-correlate the variation of C_{tr} (k_{tr}) with the pH from the impact of the dispersed state of the polymerization on the particle formation. To avoid any nucleation step and thus mimic and simplify the very beginning of the polymerization, the PAA-CTPPA mediated RAFT polymerization of a hydrosoluble non-pH sensitive monomer, namely N-acryloylmorpholine (NAM), was performed at pH = 2.5, 3.5, 6.0 and 8.0 under conditions similar to those used for the emulsion polymerization. As far as we know, the systematic study of the influence of pH on the efficiency of reinitiation of a RAFT synthesized polyelectrolyte has not been studied. In all cases the polymerization was very fast and no significant difference in the kinetics was observed with the pH (Figure 6a). Complete conversions were reached in less than 1 hour. A very good control was obtained at pH = 2.5 and 3.5 with a fast and quantitative consumption of the initial macroRAFT and narrow molar mass distributions ($Đ \leq 1.10$) (Figure 6b-c). The complete consumption of PAA-CTPPA got slower and slower when the pH increased (15 min at pH = 6.0, and ca. 30 min at pH = 8.0), while the molar mass distribution broadened (*Đ* = 1.18 and *Đ* = 1.55, Figure 6d-e). Considering the aforementioned stability of the trithiocarbonate chain end of PAA whatever the pH, this confirms that the chain transfer constant of PAA-CTPPA decreases with the increase of pH. This series of experiments is consistent with the data depicted above for the polymerization of styrene in water. Indeed, a possible hindrance of the self-assembly has already been put forward in the literature when polyelectrolytes were used as stabilizers in aqueous dispersion polymerization.[33, 34] Nevertheless, our results show that before the self-assembly takes place, the impediment of the first addition-fragmentation steps in water strongly impacts the onset of the self-assembly, i.e. the nucleation.

The polymerization performed with PAA-CTPPA at acidic pH remains the most efficient PISA system to produce latex particles composed of well-defined amphiphilic block copolymers. These conditions were further successfully employed to target different particle sizes and/or length of hydrophobic PS block for example by varying the concentration of PAA-CTPPA (M_n = 4265 g mol^{-1}, *Đ* = 1.12) in water (see Table 2 *Latexes* 7 to 9 and Figures S3 and S4 in Supporting Information). Polymerization degrees of 209, 427 and 853 were targeted for the PS segment. In all the cases, stable latexes with a PS core diameter lower than 45 nm were obtained with a good control over the PS molar mass (Table 3).

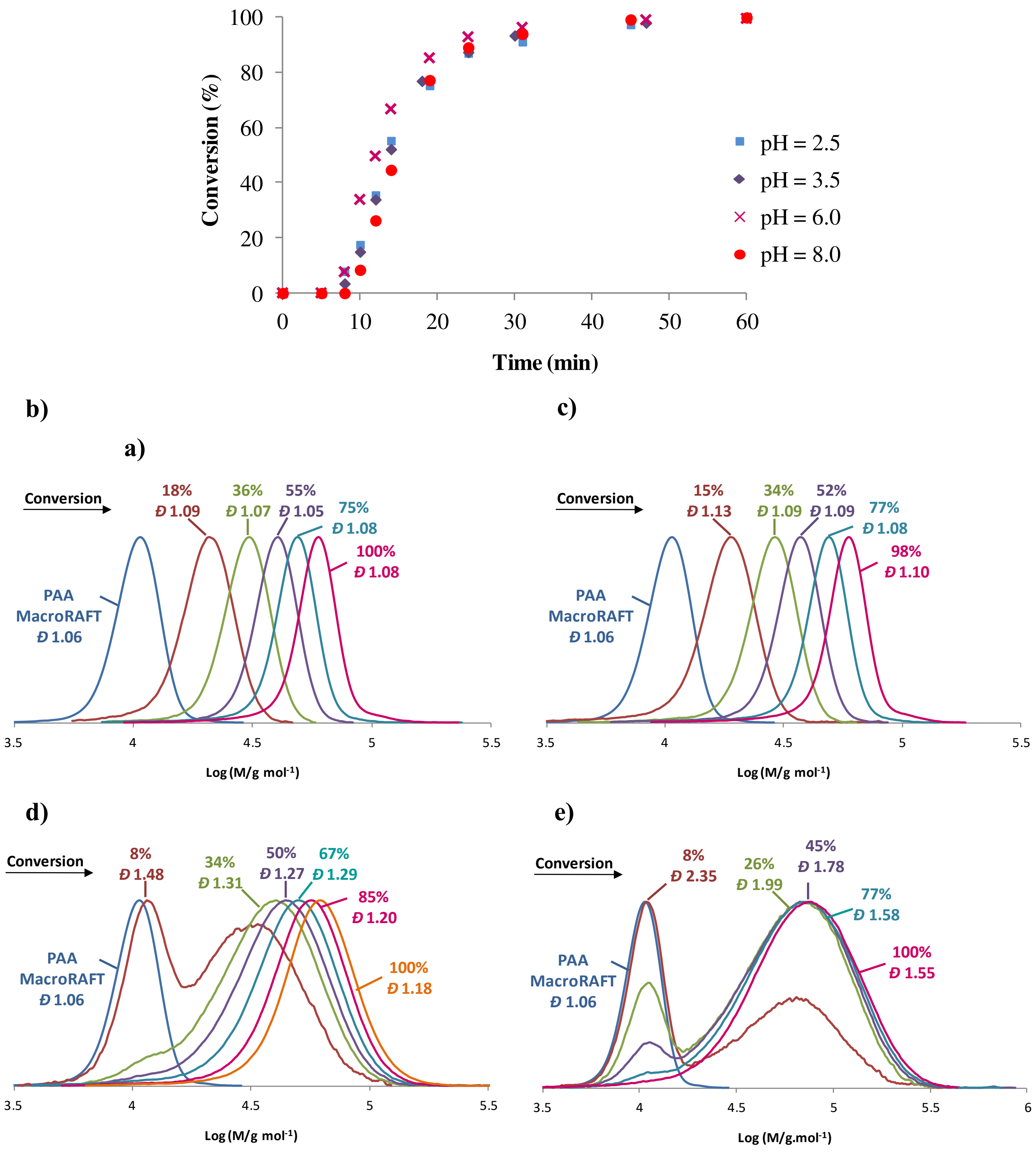


Figure 6: Chain extension experiments of PAA-CTPPA (M_n = 4480 g mol^{-1}, $Đ$ = 1.11) with NAM at different pHs at 80 °C. [NAM]/[PAA] = 400, [CTPPA]/[ACPA] = 10. Evolution of (a) monomer conversion versus time. Corresponding SEC chromatogram evolutions for (b) pH = 2.5, (c) pH = 3.5, (d) pH = 6.0 and (e) pH = 8.0.

CONCLUSION

The one-pot synthesis of self-stabilized polymer particles composed of amphiphilic block copolymers of controlled molar masses was evaluated with PAA as hydrophilic block via polymerization induced self-assembly (PISA). The RAFT polymerization of AA was first studied in detail in water at different pHs using CTPPA as a controlling agent and ACPA as an initiator. Well-defined hydrophilic macroRAFTs (PAA-CTPPA) were obtained and further used directly in water for the polymerization of styrene. The PISA process was evaluated at different pHs and it was shown that working in acidic conditions ($pH = 2.5$) led to well-defined amphiphilic block copolymer particles ($Đ = 1.36$) of small size (< 50 nm). When the pH increased, PAA was ionized and although the trithiocarbonate PAA chain end remained stable, the control over the growth of the polystyrene block was gradually lost. Indeed, chain extension experiments of PAA-CTPPA by a non-pH sensitive monomer (NAM) performed at different pHs showed that the very first addition-fragmentation steps that occurred in water – the efficiency of which determines the nucleation mechanism – were impeded when PAA was ionized. This enabled us to overcome the nucleation step and to confirm that the re-initiation of PAA-CTPPA was impacted when the pH increased due to a lower chain transfer constant. For the higher pHs ($pH \geq 7$), styrene emulsion polymerization led to partial consumption of PAA-CTPPA and thus to PS molar masses higher (> 230 000 g mol^{-1}) than expected (ca. 50 000 g mol^{-1}). Larger particle sizes (> 150 nm) were obtained. Whatever the pH the final latexes were stable. Varying PAA-CTPPA concentration at $pH = 2.5$ led in all cases to stable particles composed of well-defined block copolymers with PS segments of different molar masses. Compared with our previous studies with PMAA-CTPPA,[5] the present work additionally highlights that very similar PISA systems (employing PAA or PMAA hydrophilic macroRAFT) may involve similar nucleation mechanisms originating in however different chemical or physico-chemical events.

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