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Synthesis of Novel Well-Defined Poly(vinyl acetate)-*b*-poly(acrylonitrile) and Derivatized Water-Soluble Poly(vinyl alcohol)-*b*-poly(acrylic acid) Block Copolymers by Cobalt-Mediated Radical Polymerization

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ABSTRACT: Poly(vinyl acetate)−Co(acac)$_2$ macroinitiators, prepared by cobalt-mediated radical polymerization of vinyl acetate (VAc), were used to synthesize well-defined poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc-*b*-PAN) block copolymers. Different solvents and temperatures were tested for the polymerization of the acrylonitrile segment by cobalt-mediated radical polymerization (CMRP), and copolymers with low polydispersity were obtained provided that dimethylformamide was used as solvent at 0 °C. The mechanism of control was assumed to change from a degenerative chain transfer mechanism for the VAc polymerization to a reversible-termination process for the AN polymerization. The hydrolysis of the ester groups of the PVAc block and the nitrile groups of the PAN sequence of the copolymer by potassium hydroxide in an ethanol/water mixture provided the double hydrophilic and pH-responsive poly(vinyl alcohol)-*b*-poly(acrylic acid) block copolymer. Finally, the pH responsiveness of these copolymers was demonstrated by DLS pH titration with formation of aggregates at pH < 3.

Introduction

The increasing availability of novel synthetic polymers sustains the development of emerging technologies in the fields of medicine, microelectronics, and many others. In order to provide materials able to fulfill more and more strict requirements, requested for such specialty applications, new macromolecular synthetic tools have been made available during these past decades. Among them, controlled radical polymerization (CRP),[1] based on the limitation of irreversible termination reactions between the growing radical chains, is one of the most rapidly developing techniques due to the undemanding conditions and applicability to a large range of monomers. This type of controlled polymerization process notably allows the synthesis of well-defined block copolymers which combine properties of both segments and present particular behaviors.

Indisputably, nitroxide-mediated radical polymerization (NMP),[2,3] atom transfer radical polymerization (ATRP),[4–6] and degenerative transfer processes (radical addition fragmentation chain transfer[7–11] and macromolecular design via interchange of xanthate[12–15]) are three of the most widely used CRP methods. Another technique called "cobalt-mediated radical polymerization" (CMRP) and based on the reversible deactivation of the radicals by the metallic species has known a constant development since the advent of CRP, particularly in the past few years.[16–21] One major advantage of this system is its high efficiency for the control of the bulk polymerization of vinyl acetate (VAc), a nonconjugated and industrially important monomer.[20,22–25] Compatibility of the process with aqueous dispersed media such as suspension and miniemulsion was also demonstrated.[21,26] Moreover, hydrolysis of the ester functions of well-defined poly(vinyl acetate) (PVAc) containing materials prepared by CMRP provides the corresponding water-soluble poly(vinyl alcohol) (PVOH)-based polymer.[27] Finally, CMRP gave access to novel well-defined PVAc and PVOH containing block copolymers.[28–31] The general strategy consists of the sequential polymerization of VAc and other monomers such as styrene,[28,29] ethylene,[30] or *N*-vinylpyrrolidone[31] in the presence of the cobalt complex, possibly followed by hydrolysis of the PVAc blocks.

Among vinyl monomers, acrylonitrile (AN) appears as a very interesting comonomer due to the numerous possible transformations of polyacrylonitrile (PAN) and the large range of applications it covers. As a consequence, the control of the polymerization of this monomer has been extensively investigated by NMP,[32–34] ATRP,[35–37] and RAFT.[38–41] However, few studies have reported on the synthesis of pure polyacrylonitrile (PAN) containing block copolymers.[33,38,42] Poly(acrylonitrile) (PAN) is an extremely attractive polymer because it is the precursor for carbon fibers[43] by pyrolysis. Self-assembly of PAN containing block copolymers followed by pyrolysis of the PAN block lead to ordered carbon nanostructures[44–47] and nanoobjects such as carbon nanoparticles[48] and nanocapsules.[49] Moreover, PAN can be easily hydrolyzed into poly(acrylic acid) (PAA), an important hydrosoluble and biocompatible polymer, whose pH-responsive properties are largely used for drug delivery.[50–54]

In this paper, we reported for the first time the synthesis of a range of well-defined PVAc-*b*-PAN block copolymers by cobalt-mediated radical polymerization. Different temperatures and solvents were tested in order to obtain low polydispersed PVAc-*b*-PAN by CMRP. Only one tentative synthesis of this type of copolymer was reported in the literature using a photochemical process,[55] but the copolymer was ill-defined and largely contaminated by both homopolymers. Finally, hydrolysis of both blocks of the PVAc-*b*-PAN was a straightforward way to synthesize a novel class of biocompatible, double hydrophilic, and pH-responsive PVOH-*b*-PAA block copolymers, material of potential interest in the biomedical field (Scheme 1).

Experimental Part

Materials. Vinyl acetate (>99%, Aldrich) and acrylonitrile (>99%, Aldrich) were dried over calcium hydride, degassed by several freeze–thawing cycles before being distilled under reduced pressure and stored under argon. 2,2′-Azobis(4-methoxy-2,4-

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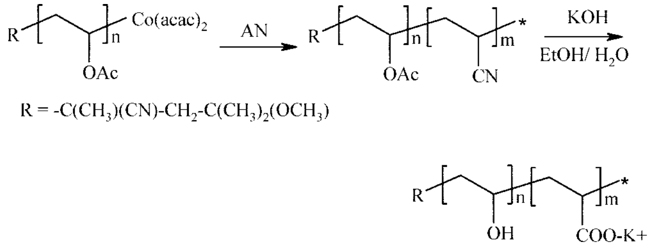
Scheme 1. General Strategy for the Preparation of Well-Defined Poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc-*b*-PAN) and Double Hydrophilic Poly(vinyl alcohol)-*b*-poly(acrylic acid) (PVOH-*b*-PAA) Block Copolymers by Cobalt-Mediated Radical Polymerization (CMRP) Using Cobalt(II) Acetylacetonate ($Co(acac)_2$)



dimethylvaleronitrile) (V-70) (Wako), cobalt(II) acetylacetonate ($Co(acac)_2$) (>98%, Merck), and 2,2,6,6-tetramethylpiperidine-1-oxy (TEMPO) (98%, Aldrich) were used as received. Membrane Spectra/Pore (cutoff: 6000–8000 Da) was used for dialysis.

Characterization. Size exclusion chromatography (SEC) of poly(vinyl acetate) was carried out in tetrahydrofuran (THF) (flow rate: 1 mL min^{-1}) at 40 °C with a Waters 600 liquid chromatograph equipped with a 410 refractive index detector and styragel HR columns (four columns HP PL gel 5 μm: 10^5, 10^4, 10^3, and 10^2 Å). The molar mass of PVAc determined by SEC with PS calibration was in good agreement with that determined by ^{1}H NMR whenever the α-end group of the initiator ($-OCH_3$ at $\delta = 3.13$ ppm) could be observed and compared to the $-CHOCOCH_3$ proton at $\delta = 4.8$ ppm of the monomer unit, as reported elsewhere.[20,21] SEC of both PVAc and PVAc-*b*-PAN were carried out in dimethylformamide (DMF) containing some LiBr (0.025 M) at 55 °C (flow rate: 1 mL min^{-1}), with a Waters 600 liquid chromatograph equipped with a 410 refractive index detector and styragel HR columns (HR1, 100−5000; HR3, 500–30 000; HR4, 5000–500 000; HR5, 2000–40 000 000). In all the cases, polystyrene standards ranging from 580 to 225 × 10^4 g/mol were used for calibration.

^{1}H NMR spectra of the PVAc macroinitiators were recorded at 298 K with a Bruker spectrometer (250 MHz) in $CDCl_3$ ($D_1 = 2$ s, 16 scans, 5 wt % of polymer). ^{1}H NMR spectra of PVAc-*b*-PAN and PVOH-*b*-PAA were recorded with the same spectrometer at 298 K in deuterated dimethyl sulfoxide (DMSO-d_6) or DMF-d_7 and deuterated water (D_2O), respectively ($D_1 = 5$ s, 32 scans, 5 wt % of polymer).

Infrared spectra were recorded with a Perkin-Elmer FT-IR instrument from 4000 to 450 cm^{-1}. PVAc-*b*-PAN and PVOH-*b*-PAA copolymers were mixed with potassium bromide and compressed before IR analysis.

Light scattering titrations (LS-T) were performed on an ALV light scattering instrument equipped with an ALV-5000 digital correlator, a Spectra-Physics 2000 1 W argon ion laser operated at a wavelength of 514.5 nm and a scattering angle (θ) of 90°, and a Schott-Geräte computer-controlled titration setup to control sequential addition of titrant and cell stirring. A refractive index matching bath of filtered *cis*-decalin surrounded the cylindrical scattering cell, and the temperature was controlled at 21.7 ± 0.3 °C using a Haake F3-K thermostat. The pH was measured with a combined Ag/AgCl glass electrode. The recorded mV values were converted into pH values after calibration of the electrode with five buffers of known pH ($3 \leq pH \leq 7$). After every dosage of 0.1 M HCl or NaOH, pH, 90° light scattering intensity, $I_{90°}$, and the second-order correlation function, $G_2(t)$, were recorded, the latter two 5 times during a period of 50 s. Averaged values of the intensity, $I_{90°}$, and hydrodynamic radius, $R_{h,90°}$ (CONTIN), are reported as a function of pH.

Typical Procedure for the Synthesis of PVAc-*b*-PAN in Anisole/Toluene. $Co(acac)_2$ (0.103 g, 0.402 mmol) and V-70 (0.401 g, 1.30 mmol) were added into a 50 mL flask and degassed by three vacuum−nitrogen cycles. Vinyl acetate (15.0 mL, 162 mmol) was then added with a syringe under nitrogen. The purple mixture was stirred at 30 °C. After 48 h, a sample was withdrawn in order to evaluate the monomer conversion gravimetrically (conversion = 55%) and measure the molecular parameters of the PVAc macroinitiator by SEC analysis in THF ($M_{n,SEC,THF} = 1.90 \times 10^4$ g/mol; $M_w/M_n = 1.19$) and DMF ($M_{n,SEC,DMF} = 7.51 \times 10^4$ g/mol; $M_w/M_n = 1.13$). The residual monomer was evaporated under reduced pressure at room temperature, and the pink poly(vinyl acetate) macroinitiator was stored under an inert atmosphere. A mixture of degassed anisole and toluene (9/1; v/v; 15 mL) was added to dissolve the polymer at 0 °C, followed by the addition of cold acrylonitrile (10.0 mL, 0.152 mol). The pink reaction medium was stirred at 0 °C. Upon AN polymerization, the medium became viscous but remained homogeneous and the color turned dark pink-brown. Samples were regularly picked out the reaction flask for monitoring the conversion and SEC profiles in DMF. The results are presented in Figure 3.

Finally, the unreacted PVAc macroinitiator that contaminates the desired PVAc-*b*-PAN copolymer was removed by Soxhlet extraction with methanol for 48 h. The purified copolymer (8.5 g) was then analyzed by SEC in DMF ($M_{n,SEC,DMF} = 16.3 \times 10^4$ g/mol; $M_w/M_n = 1.38$) and ^{1}H NMR. ^{1}H NMR (250 MHz, 298 K, DMF-d_7) δ (ppm): 4.78 (1H, $CH{-}OCOCH_3$ of PVAc), 3.14 (1H, $CH_2{-}CH{-}CN$ of PAN), 2.06 (2H, $CH_2{-}CH{-}CN$ of PAN), 1.97 (3H, $-OCOCH_3$ of PVAc), 1.75 (2H, $-CH_2{-}CH{-}OCOCH_3$ of PVAc). The molar mass of the PVAc block was given by the SEC analysis of the PVAc macroinitiator carried out in THF, whereas the molar mass of the PAN block was calculated from the ^{1}H NMR data by comparison of the intensities of the signals corresponding to $CH_2{-}CH{-}CN$ of PAN (at 3.14 ppm) and $CH_2{-}CH{-}OCOCH_3$ of PVAc (at 4.78 ppm): PVAc(19000)-*b*-PAN(20300), $PVAc_{220}$-*b*-PAN_{382}.

Typical Procedure for the Synthesis of PVAc-*b*-PAN in DMF. $Co(acac)_2$ (1.03 g, 4.02 mmol) and V-70 (4.01 g, 13.0 mmol) were added in a 500 mL flask and degassed by three vacuum−nitrogen cycles. Vinyl acetate (150 mL, 1.62 mol) was then added with a syringe under nitrogen, and the purple mixture was stirred at 30 °C. After 26 h, a sample was withdrawn in order to evaluate the monomer conversion gravimetrically (conversion = 46%) and measure the molecular parameters of the PVAc macroinitiator by SEC analysis in THF ($M_{n,SEC,THF} = 1.93 \times 10^4$ g/mol; $M_w/M_n = 1.19$) and DMF (0.025 M LiBr) ($M_{n,SEC,DMF} = 6.56 \times 10^4$ g/mol; $M_w/M_n = 1.19$). The residual monomer was then evaporated under reduced pressure at room temperature, and the pink poly(vinyl acetate) macroinitiator was stored under inert atmosphere. The flask was then cooled to 0 °C, and 150 mL of degassed and distilled DMF was added, followed by addition of 100 mL of acrylonitrile. The reaction medium was stirred at 0 °C for about 22 h (monomer conversion = 60%). The medium became viscous upon AN polymerization but remained homogeneous, and the color changed from pink to gray-black. The reaction medium was then diluted with DMF followed by precipitation of the copolymer in a methanol/water (20/80) mixture. This purification step was repeated two times, and the collected copolymer (~90 g) was analyzed by SEC DMF (0.025 M LiBr) ($M_{n,SEC,DMF} = 18.7 \times 10^4$ g/mol; $M_w/M_n = 1.16$) and ^{1}H NMR. The molar mass of the PAN block was calculated from the ^{1}H NMR data of the diblock in DMSO-d_6 and M_n of the PVAc macroinitiator determined by SEC in THF. The molar mass of the PVAc block was given by the SEC analysis of the PVAc macroinitiator carried out in THF, whereas the molar mass of the PAN block was calculated from the ^{1}H NMR data by comparison of the intensities of the signals corresponding to $CH_2{-}CH{-}CN$ of PAN (at 3.14 ppm) and $CH_2{-}CH{-}OCOCH_3$ of PVAc (at 4.78 ppm): PVAc (19.3K)-*b*-PAN(22.7K), $PVAc_{224}$-*b*-PAN_{430}.

PVAc-*b*-PAN block copolymers with different compositions and molar masses were prepared by the same procedure (Table 1).

Typical Procedure for the Synthesis of PVOH-*b*-PAA. In a 5 L flask, a solution of $PVAc_{224}$-*b*-PAN_{430} (30 g) in ethanol (p.a., 600 mL) was added with an aqueous solution of potassium hydroxide (120 g of KOH in 2700 mL of water). The mixture was stirred at 75 °C for 48 h under reflux. During the first hours, the

Table 1. Synthesis of Poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc-*b*-PAN) Block Copolymers from PVAc−Co^{III} Macroinitiator at 0 °C in Dimethylformamide (DMF), Precursors of Poly(vinyl alcohol)-*b*-poly(acrylic acid) (PVOH-*b*-PAA) Block Copolymers

	PVAc−Co		PVAc-*b*-PAN				PVOH-*b*-PAA
entry	M_n[a] ($\times 10^3$ g/mol)	M_w/M_n[a]	M_n[b] ($\times 10^3$ g/mol)	M_w/M_n[b]	$M_{n,NMR,PAN}$[c] ($\times 10^3$ g/mol)	DP_n[d]	DP_n[d]
1	20.8	1.19	109.3	1.17	9.8	PVAc$_{241}$-*b*-PAN$_{185}$	PVOH$_{241}$-*b*-PAA$_{150}$
2	19.3	1.19	186.8	1.16	22.7	PVAc$_{224}$-*b*-PAN$_{430}$	PVOH$_{224}$-*b*-PAA$_{454}$
3	26.5	1.16	255.3	1.29	48.8	PVAc$_{308}$-*b*-PAN$_{918}$	PVOH$_{308}$-*b*-PAA$_{843}$

[a] Number-average molar mass (M_n) and weight-average molar mass (M_w) were determined by size exclusion chromatography (SEC) calibrated by PS standards in tetrahydrofuran. [b] M_n and M_w were determined by SEC calibrated by PS standards in DMF. [c] M_n of the PAN block was determined by ^{1}H NMR (see Experimental Part). [d] The degree of polymerization (DP_n) was determined by ^{1}H NMR (see Experimental Part).

copolymer slowly dissolved in the reaction medium with the formation of an homogeneous solution. After hydrolysis, ethanol was removed under vacuum, and the aqueous solution of the copolymer was dialyzed for 48 h against water through a Spectra/Pore membrane (cutoff: 6000–8000 Da) and then lyophilized, after which the copolymer was recovered as a white powder.

^{1}H NMR (250 MHz, 298 K, D_2O) δ (ppm): 3.9 (1H, C*H*−OH of PVOH), 2.05 (1H, C*H*−COO$^-$K$^+$ of PAA), 1.80–1.0 (2H, C*H*$_2$−CHOH of PVOH and 2H, C*H*$_2$−CH−COO$^-$K$^+$ of PAA). The molar mass of the PVOH block was calculated from the ^{1}H NMR spectrum of the diblock. The molar ratio PVOH/PAA calculated from the ^{1}H NMR spectrum was very similar to the PVAc/PAN ratio of the starting copolymer (PVOH$_{224}$-*b*-PAA$_{454}$ vs PVAc$_{224}$-*b*-PAN$_{430}$).

PVOH-*b*-PAA block copolymers with different compositions and molar masses were prepared by the same procedure (Table 1).

Results and Discussion

As a rule, for a block copolymerization to be effective, it is necessary to start the process with the most reactive monomer; otherwise, initiation of the second monomer from the first block might be slow or partial, leading to polydispersed block copolymer or contamination by the unreacted homopolymer. On the basis of the reactivity ratios mentioned in the literature,[56] it is clear that acrylonitrile should ideally be polymerized first followed by vinyl acetate in order to obtained well-defined PVAc-*b*-PAN block copolymers by CMRP. However, such an approach requires that the homopolymerization of acrylonitrile can be controlled by the Co(acac)$_2$, but nothing is known about it yet. Therefore, the CMRP of AN was tested for the first time using V-70 as initiator and Co(acac)$_2$ as the controlling agent at 30 °C in anisole using a stoichiometric amount of V70 and Co(acac)$_2$. The choice of this solvent was driven by recent success in the *N*-vinylpyrrolidone (*N*VP) copolymerization by CMRP[31,57] carried out in anisole. However, under these conditions, only a very poor control of the AN polymerization was observed as well as a lack of solubility of the PAN formed.

Despite this failure, it appeared interesting to us to initiate the AN polymerization from a PVAc−Co(acac)$_2$ macroinitiator preformed by CMRP. Indeed, the formation of the dormant species in the early stage of the CMRP process could be bypassed and possibly lead to PVAc-*b*-PAN block copolymers with a controlled PAN sequence.

Synthesis of PVAc-*b*-PAN in Anisole/Toluene Mixture. Poly(vinyl acetate) macroinitiators end-capped by Co(acac)$_2$ were synthesized in a well-controlled manner by bulk polymerization of vinyl acetate initiated by V-70 in the presence of Co(acac)$_2$ at 30 °C, as previously reported ([VAc]/[V70]/[Co(acac)$_2$] = 286/3.25/1).[20] After 40 h, the residual vinyl acetate was evaporated under reduced pressure at room temperature (monomer conversion = 52%), and the recovered PVAc−Co(acac)$_2$ macroinitiator ($M_{n,SEC,THF}$ = 15 800 g/mol; M_w/M_n = 1.22) was sequentially added with a degassed anisole/toluene mixture (9/1; v/v) and acrylonitrile ([AN]/[PVAc-Co(acac)$_2$] = 330). Heating the reaction medium at 30 °C led to the very fast polymerization of AN, and the monomer conversion reached 88% in less than 30 min. In this case, the SEC analyses, performed in DMF/LiBr, clearly evidenced the formation of the PVAc-*b*-PAN diblock copolymer (Figure 1). Indeed, the SEC peak of the macroinitiator was shifted toward higher molar masses. However, this chain extension experiment was accompanied by the broadening of the molar mass distribution from 1.14 to 1.44 due to some unreacted macroinitiator. However, this contamination problem can merely be solved by extraction of the unreacted homopolymer by methanol, a selective solvent for PVAc, using a Soxhlet apparatus for 24 h (Figure 1). Increasing the extraction time to 48 h did not allow further removing of residual macroinitiator. After the purification process, the peak corresponding to the PVAc-*b*-PAN was almost symmetrical, and the polydispersity decreased to 1.37. The recovered block copolymer was then analyzed by ^{1}H NMR in DMF-d_7 for the determination of its composition and the degree of polymerization (DP) of the PAN sequence. The molar mass of the PAN block was calculated from the ^{1}H NMR data of the diblock and M_n of the PVAc macroinitiator determined by SEC in THF (DP = 184, M_n = 15 800 g/mol; the SEC analysis of PVAc carried out in THF using a PS calibration was demonstrated to provide a molar mass very close to the real molar mass).[58] The integration of the signal characteristic of −CH$_2$−C*H*(OAc)− of PVAc at 4.78 ppm and the signal characteristic of −CH$_2$−C*H*(CN)− of PAN at 3.14 ppm allowed to determine the DP of the second block (DP = 305, M_n = 16 200 g/mol) (Figure 2).

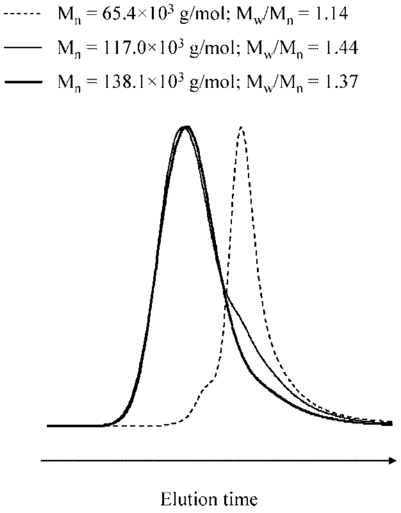


Figure 1. Size exclusion chromatograms carried out in dimethylformamide for the poly(vinyl acetate) macroinitiator (PVAc−Co^{III}) (dotted line) and the PVAc-*b*-poly(acrylonitrile) block copolymer prepared in anisole/toluene at 30 °C before (full line) and after methanol extraction (bold line) (number-average molar mass (M_n), weight-average molar mass (M_w)). Conditions: [AN]/[PVAc−Co^{III} ($M_{n,SEC,THF}$ = 15.8 × 10^3 g/mol; M_w/M_n = 1.22)] = 330, DMF/AN = 1.5 (v/v), 30 °C, 25 min.

Although block copolymers could be prepared by this strategy, copolymers with a polydispersity around 1.40–1.50

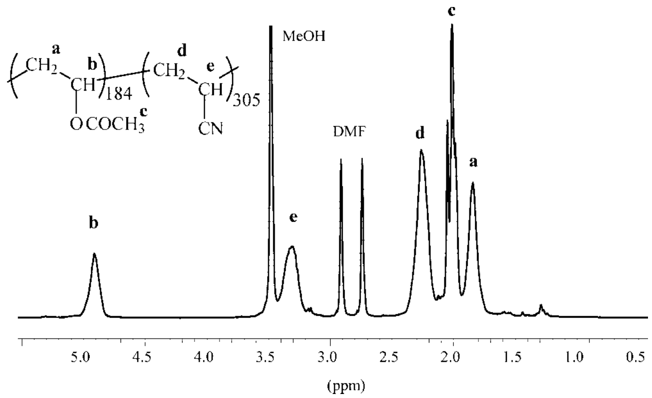


Figure 2. ^{1}H NMR spectrum in deuterated dimethylformamide (DMF-d_7) for the poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc$_{184}$-*b*-PAN$_{305}$) block copolymer after methanol extraction. Conditions: [AN]/[PVAc−Co^{III} ($M_{n,SEC,THF}$ = 15.8 × 10^3 g/mol; M_w/M_n = 1.22)] = 330, DMF/AN = 1.5 (v/v), 30 °C, 25 min.

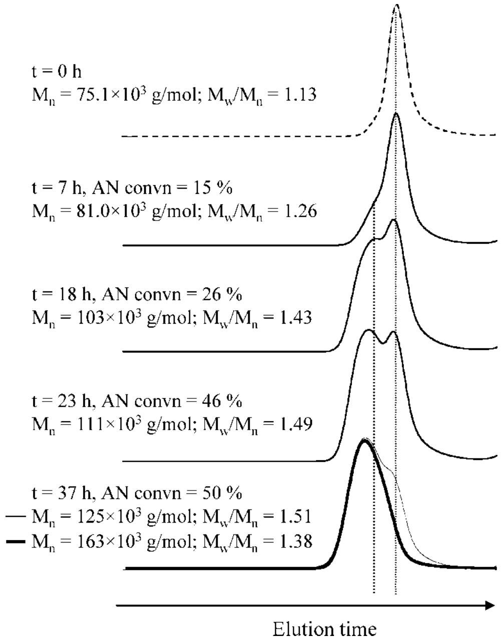


Figure 3. Size exclusion chromatograms (SEC) carried out in dimethylformamide (DMF) for the synthesis of poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc-*b*-PAN) block copolymers in anisole/toluene at 0 °C, starting from a PVAc−Co^{III} macroinitiator (dotted line). In the last chromatogram, the bold line corresponds to the PVAc-*b*-PAN copolymer after extraction with methanol. Conditions: [AN]/[PVAc−Co^{III} ($M_{n,SEC,THF}$ = 20.8 × 10^{3}g/mol; M_w/M_n = 1.18)] = 458, anisole/toluene (9/1, v/v)/AN = 1.5 (v/v), 0 °C (number-average molar mass (M_n), weight-average molar mass (M_w)).

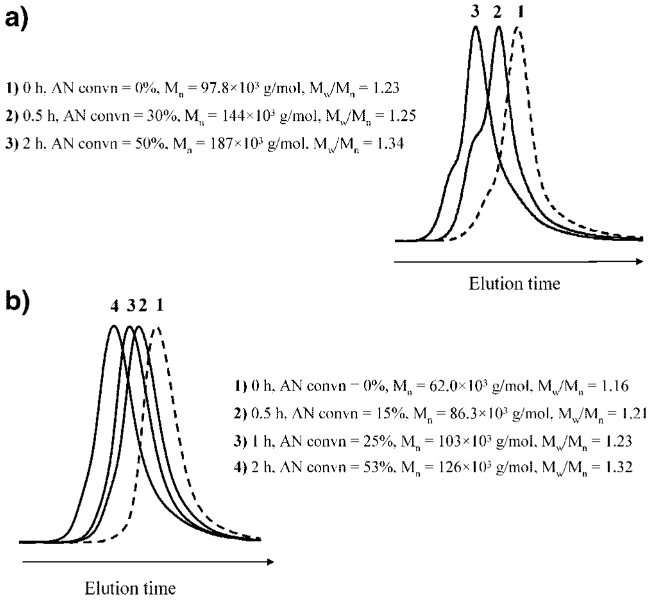


Figure 4. Size exclusion chromatograms (SEC) for the acrylonitrile polymerization initiated at 30 °C in dimethylformamide (DMF) by a preformed poly(vinyl acetate)−Co^{III} macroinitiator (dotted line) with (b) and without (a) addition of 2,2,6,6-tetramethylpiperidine-1-oxy in the sample prior SEC analysis carried out in DMF (number-average molar masses (M_n) and weight-average molar masses (M_w)). Conditions: [AN]/[PVAc−Co^{III}] = 445, DMF/AN = 1.5 (v/v), 30 °C.

before methanol extraction and 1.30–1.40 after extraction were commonly observed. In a tentative approach for improving the control of the AN polymerization, which was quite fast at 30 °C, the polymerization of the second sequence was carried out at 0 °C. The kinetics of the acrylonitrile polymerization initiated by the PVAc−Co(III) at 0 °C was followed by SEC in DMF (Figure 3). At the early stages of the polymerization, besides the peak corresponding to the PVAc macroinitiator, a second peak, assigned to the growing PVAc-*b*-PAN copolymer, was shifted toward higher molar masses with the time (Figure 3). The intensity of this block copolymer signal increased compared to the one of the macroinitiator peak along the reaction. Although some irreversible termination of the PVAc macroinitiator cannot be excluded, the broad polydispersity of the sample and the bimodal profile can also be explained as follows. The release of the PVAc radicals from the macroinitiator might be slow compared to the initiation and propagation of the AN leading to the contamination of the PVAc-*b*-PAN diblock copolymer by unreacted PVAc macroinitiator, as evidenced by the SEC analysis. Again, this residual PVAc was extracted with methanol in a Soxhlet for 48 h to provide pure PVAc-*b*-PAN block copolymer (bold curve in Figure 3). The degree of polymerization of both PVAc and PAN blocks was then evaluated by ^{1}H NMR at 220 and 382, respectively (PVAc(19 000)-*b*-PAN(20 300)).

Synthesis of PVAc-*b*-PAN in Dimethylformamide. The polymerization of acrylonitrile initiated by a PVAc macroinitiator (M_n = 23 700 g/mol; M_w/M_n = 1.25) was then carried out at 30 °C in DMF, which is known to be a better solvent for PAN than the anisole/toluene mixture. In such conditions, the polymerization was fast (50% monomer conversion after 2 h), and the SEC peak of the PVAc macroinitiator completely shifted toward the higher molecular weight side with the monomer conversion, in agreement with a fast initiation of AN by the PVAc macroinitiator (Figure 4a). The polydispersity of the PVAc-*b*-PAN block copolymer remained low all along the polymerization process. Almost no residual PVAc macroinitiator was left at the end of the polymerization. Although the polydispersity was low, the SEC chromatograms showed a shoulder on the high molar mass which was twice that one of the main peak, suggesting the occurrence of a coupling reaction (Figure 4a). This ratio of 2 between the molar masses of the two chain populations did not change with the polymerization time, which suggested that the coupling reaction occurred during the polymer recovery rather than all along the polymerization. The occurrence of coupling reactions during the polymer recovery indicated that the chains ends were very reactive.

In order to avoid this side reaction, a spin trap, 2,2,6,6-tetramethylpiperidinoxy (TEMPO), was added to the samples picked out during the polymerization process. TEMPO reacted irreversibly with the activated chains and thus avoided coupling reaction during the polymer recovery, as reported previously.[22,25]

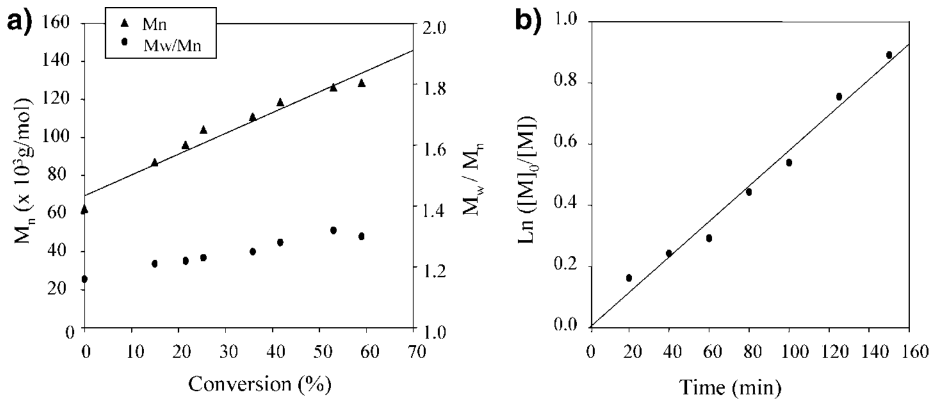


Figure 5. Acrylonitrile (AN) polymerization initiated at 30 °C by a preformed poly(vinyl acetate) macroinitiator (PVAc−Co^{III}) in dimethylformamide (DMF). (a) Evolution of the number-average molar mass (M_n) and polydispersity (M_w/M_n) with the monomer conversion. The samples were added with 2,2,6,6-tetramethylpiperidine-1-oxy prior size exclusion chromatography (SEC) analysis carried out in DMF. (b) Dependence of ln([M]$_0$/[M]) vs time. Conditions: [AN]/[PVAc−Co^{III} ($M_{n,SEC,THF}$ = 19.8 × 10^3 g/mol; M_w/M_n = 1.15)] = 445, DMF/AN = 1.5 (v/v), 30 °C.

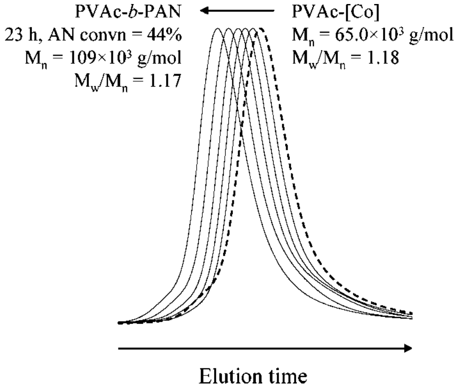


Figure 6. Size exclusion chromatograms (SEC) for the acrylonitrile polymerization initiated at 0 °C in dimethylformamide (DMF) by a preformed poly(vinyl acetate) macroinitiator (PVAc−Co^{III}) (dotted line). The samples were added with 2,2,6,6-tetramethylpiperidine-1-oxy prior size exclusion chromatography (SEC) analysis in order to avoid postcoupling reactions (number-average molar masses (M_n) and weight-average molar masses (M_w)). Conditions: [AN]/[PVAc−Co^{III} ($M_{n,SEC,THF}$= 20.8 × 10^3 g/mol; M_w/M_n = 1.19)] = 450, DMF/AN = 1.5 (v/v), 0 °C.

No shoulder on the SEC chromatograms was thus observed, and very well-defined PVAc-*b*-PAN diblock copolymers were thus obtained (Figure 4b). The linear dependence of the molar mass of the copolymer with the monomer conversion (Figure 5a) and ln([M]$_0$/[M]) with time (Figure 5b), together with the low polydispersity (1.15 ≤ M_w/M_n ≤ 1.30; Figure 5a), evidenced of a well-controlled process. Clearly, the use of DMF as solvent instead of anisole/toluene induced a fast initiation compared to propagation of AN, leading to well-defined PVAc-*b*-PAN copolymers which did not require further purification.

As expected, when the block copolymerization was carried out in DMF at 0 °C instead of 30 °C, the polymerization of AN was much slower (44% monomer conversion after 24 h of reaction). Despite the low temperature, the SEC chromatogram of the PVAc−Co(acac)$_2$ macroinitiator was shifted toward the higher molecular weight side from the very beginning of the polymerization (Figure 6), in agreement with a fast initiation and a complete consumption of the PVAc chains, in contrast to the observations done in anisole/toluene. Criteria for a controlled polymerization of AN were fulfilled, i.e., molar mass increasing with monomer conversion (Figure 7a) and first-order kinetics in monomer (Figure 7b). The polydispersity were also lower compared to the same polymerization carried out at 30 °C (1.15 ≤ M_w/M_n ≤ 1.20 at 0 °C vs 1.15 ≤ M_w/M_n ≤ 1.30 at 30 °C; Figure 7a). A series of PVAc-*b*-PAN copolymers with different molar masses and compositions were synthesized in DMF at 0 °C from PVAc macroinitiators with various chain lengths. Data are listed in Table 1.

Obviously, the choice of the solvent is critical for the block copolymerization of VAc and AN by CMRP. In contrast to the experiment carried out in the anisole/toluene mixture, the use of DMF as solvent prevents the resumption of the acrylonitrile from a PVAc−Co(acac)$_2$ to be slow, allowing the preparation of well-defined PVAc-*b*-PAN copolymers. In order to propose a reasonable hypothesis for this phenomenon, it is necessary to come back to the intimate CMRP mechanism.

Although the homopolymerization of VAc initiated by V70 in the presence of Co(acac)$_2$ in the bulk at 30 °C seems to be governed by a degenerative transfer mechanism (DT),[24] the polymerization of acrylonitrile initiated by the PVAc−Co(acac)$_2$ at 0 °C most probably mainly follows a reversible-termination (RT) mechanism by cleavage of the Co−C bond at the ω-chain end rather than a chain transfer process. Indeed, it was previously shown that amino compounds, able to coordinate the cobalt complex, turned the CMRP mechanism of VAc into a reversible-termination process by simple cleavage of the Co−C bond.[24] In the case of block copolymerization of acrylonitrile initiated by PVAc−Co(acac)$_2$ in DMF, the sixth coordination site of the cobalt complex in the polymer−Co(acac)$_2$ dormant species is most probably occupied by the solvent (DMF), which disfavors the DT process. Moreover, the residual V70 azo-initiator present in PVAc−Co$^{(III)}$ is not active at 0 °C and thus cannot produce the slight excess of chains generally necessary for systems purely governed by a degenerative transfer mechanism. In addition, the complexation of the cobalt complex at the ω-chain end of PVAc−Co(acac)$_2$ by DMF might activate the homolytic cleavage of the C−Co bond, preventing the slow initiation process observed when the copolymerization was carried out in the anisole/toluene mixture. Further effort is presently devoted to the deep understanding of the effect of DMF.

On the basis of these good results in DMF, the homopolymerization of AN was initiated by V-70 in the presence of Co(acac)$_2$ in DMF at 30 °C. The initial purple polymerization medium turned progressively black, and after 2 h, it turned gray-black while the viscosity was progressively increasing, indicating that polymerization occurred. However, as was the case when carried out in anisole, the reaction medium became inhomogeneous due to the lack of solubility of the homopolyacrylonitrile in DMF at high concentration at 30 °C. The low solubility of the PAN was most probably responsible for the poor level of control observed under these conditions. For instance, at 10 and 60% of AN conversion, the molar masses were equal to 4000

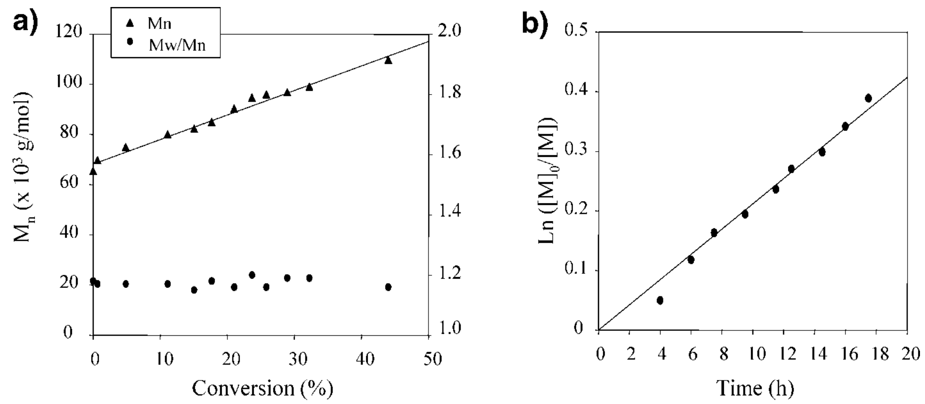


Figure 7. Acrylonitrile (AN) polymerization initiated at 0 °C by a preformed poly(vinyl acetate) macroinitiator (PVAc$-$Co^{III}) in dimethylformamide (DMF). (a) Evolution of the number-average molar mass (M_n) and polydispersity (M_w/M_n) with the monomer conversion. Samples were added with 2,2,6,6-tetramethylpiperidine-1-oxy prior analysis by size exclusion chromatography (SEC) in DMF. (b) Dependence of ln([M]$_0$/[M]) vs time. Conditions: [AN]/[PVAc$-$Co^{III} ($M_{n,SEC,THF} = 20.8 \times 10^3$ g/mol; $M_w/M_n = 1.19$)] = 450, DMF/AN = 1.5 (v/v), 0 °C.

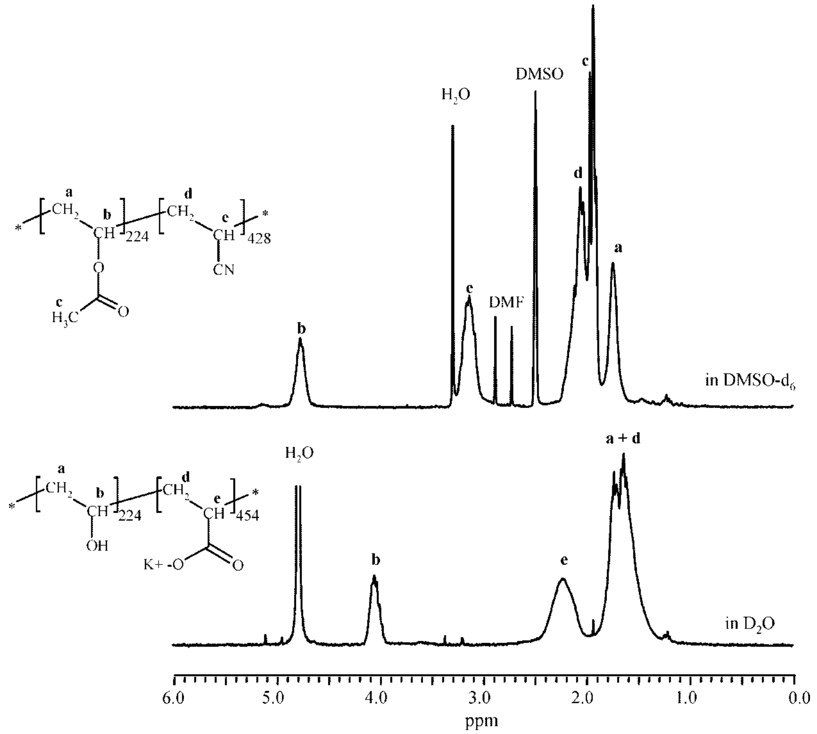


Figure 8. ^{1}H NMR spectra for the poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc(19.3K)-*b*-PAN(22.7K)) copolymer and the derivatized poly(vinyl alcohol)-*b*-poly(acrylic acid) (PVOH(9.8K)-*b*-PAA(32.7K)) copolymer obtained by hydrolysis of both ester and nitrile groups.

and 10 000 g/mol, which is well beyond the expected values (1000 and 6500 g/mol, respectively). Moreover, the molar mass distributions were broad, i.e., 1.65 and 1.90, respectively. So far, the controlled radical homopolymerization of AN by CMRP remains an important challenge that requires an in-depth study that will be discussed in a forthcoming paper.

Hydrolysis of PVAc-*b*-PAN into PVOH-*b*-PAA. Poly(vinyl acetate) is known to be a good precursor of hydrosoluble poly(vinyl alcohol) upon hydrolysis in basic medium, whereas biocompatible and pH-responsive poly(acrylic acid) can be obtained from PAN by hydrolytic treatment. Therefore, PVAc-*b*-PAN block copolymers prepared in this work are precursors of novel double hydrophilic PVOH-*b*-PAA copolymers (step 2, Scheme 1). After optimization, ideal conditions for the complete transformation of both block were found and consists in treating the PAN and PVAc containing block copolymer with a large excess of potassium hydroxide in a water/ethanol mixture (4.5/1, v/v) at 75 °C for 48 h. The solubility of the polymer in water after treatment was a first indication of the success of the transformation. The ^{1}H NMR analysis of a pure PVAc-*b*-PAN copolymer before and after treatment of the copolymer definitely evidenced the successful hydrolysis of both blocks (Figure 8). Disappearance of the PVAc (a$-$c) and PAN (d, e) signals, and particularly signal b at 4.79 ppm corresponding to the C*H*$-$OCOCH$_3$ proton and signal d at 3.15 ppm corresponding to the C*H*$-$CN proton, and appearance of the signals typical of PVOH (C*H*$-$OH at 3.80 ppm) and PAA (C*H*$-$COOH at 2.2 ppm) confirmed the formation of the desired PVOH-*b*-PAA block copolymer. Additional evidence for the successful hydrolysis of both PVAc and PAN sequences of the copolymer was provided by the comparison of infrared spectra of the copolymer before and after treatment, which shows the disappearance of the absorption band of the ester groups of PVAc at 1738 cm^{-1} and the nitrile groups of PAN at 2245 cm^{-1} (Figure 9).

A range of PVOH-*b*-PAA copolymers were accordingly prepared by hydrolysis of the PVAc-*b*-PAN copolymers listed

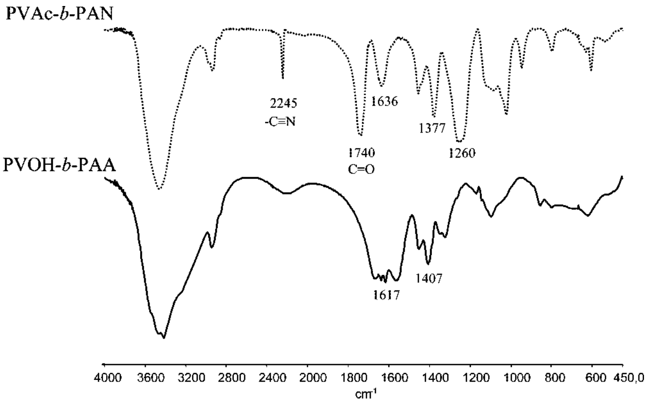


Figure 9. Infrared spectra for the poly(vinyl acetate)-*b*-poly(acrylonitrile) (PVAc(19.3K)-*b*-PAN(22.7K)) copolymer and the derivatized poly(vinyl alcohol)-*b*-poly(acrylic acid) (PVOH(9.8K)-*b*-PAA(32.7K)) copolymer obtained by hydrolysis of both ester and nitrile groups.

in Table 1. The molar mass of the PVOH and PAA block was calculated from the ^{1}H NMR spectrum in D_2O of the diblock. The PVOH/PAA molar ratio was similar (within the experimental errors) to the PVAc/PAN ratio of the starting copolymer, demonstrating the quantitative hydrolysis of both sequences.

Aqueous Solution Behavior of the pH-Responsive PVOH-*b*-PAA Copolymers. All these PVOH-*b*-PAA were perfectly soluble in water at room temperature under neutral and basic conditions, where the carboxylic acid groups are deprotonated. At low pH, the block copolymer may self-assemble into aggregates due to the protonation of the PAA carboxylic acid groups, which enables H-bonding between PAA and PVOH units and is reported to decrease PAA solubility. Note, however, that the degree of PAA solubility is dependent on polymer tacticity,[59] and the polymer may be unimerically water-soluble down to pH = 2.

In order to evaluate the pH responsiveness of these PVOH-*b*-PAA block copolymers, their solution behavior was monitored by pH light scattering titrations (pH LS-T) between pH 2 and 8. For example, the pH of a 0.1 wt % PAA_{454}-*b*-$PVOH_{224}$ solution was gradually decreased (Figure 10). While the solution was clear at high pH, it is opaque for low pH values although no precipitate was observed during or after the pH LS-T (i.e., for pH ≥ 2). Two fractions were observed in the size distribution plots for pH ≥ 3 (Figure 10a). The "fast mode" ($R_{h,90°} = 5 \pm 1$ nm) can be assigned to unimerically dissolved polymers, while the "slow mode" ($R_{h,90°} = 98 \pm 8$ nm) most likely corresponds to a small fraction of aggregates consisting of H-bonded polymers. The fast mode disappears for pH < 3, indicating that the polymer is no longer unimerically soluble, and only aggregates were observed at pH 2. The onset of the precipitation of the PAA-*b*-PVOH polymer was also confirmed by the increase in intensity (Figure 10b) for pH ≤ 2.7. These results are in excellent agreement with those by Khutoryanskiy et al.,[60] who reported a critical pH (pH_{cr}) of 2.67 ± 0.05 for a mixture of PAA and PVOH homopolymers in salt-free solution ($M_{w,PAA} = 450K$, $M_{w,PVOH} = 205K$, [PAA] = [PVOH] = 0.01 M in base-mole units), which the authors define as the pH value where the solution became opaque and turbidity increased sharply in a narrow pH range due to the formation of insoluble polycomplexes.[60] Moreover, when the pH of the aggregates solution was increased from 2 to 8, the scattering intensity decreased. Moreover, at pH 8, the scattering intensity was equal to the value obtained at the same pH before the pH titration cycle and corresponds to the starting unimerically soluble polymer, which proves the reversibility of the pH behavior of the PVOH-*b*-PAA copolymer.

As a conclusion, hydrosolubility and biocompatibility of both PVOH and PAA as well as pH-sensitive properties of the PAA segment make these PVOH-*b*-PAA copolymers promising materials in the biomedical field.

Conclusion

Well-defined PVAc-*b*-PAN block copolymers with a low polydispersity were successfully prepared by cobalt-mediated radical polymerization (CMRP), providing that PVAc−$Co(acac)_2$ was used as the first sequence. The block copolymerization was the most efficient in DMF at 0 °C, while a slow initiation compared to the propagation was observed in an anisole/toluene mixture. The controlled mechanism turned from a degenerative transfer for the bulk polymerization of VAc to a reversible termination process for the AN polymerization initiated by PVAc−$Co(acac)_2$.

Hydrolysis of both sequences of PVAc-*b*-PAN in an ethanolic solution of potassium hydroxide at 75 °C led to the novel double hydrophilic poly(vinyl alcohol)-*b*-poly(acrylic acid) (PVOH-*b*-PAA) block copolymer. Moreover, the pH-responsive properties of these copolymers were demonstrated by LS pH titrations with aggregate formation at pH < 3 due to H-bonding between the PAA and PVOH monomers. The reversibility of the process was also successfully demonstrated.

Finally, the ability of these PAA-*b*-PVOH copolymers to form complex coacervate core micelles (C3Ms)[61] by addition of an aqueous solution of poly(2-methylvinylpyridinium iodide)-*block*-poly(ethylene oxide) (P2MVP-*b*-PEO) will be reported in a forthcoming paper.

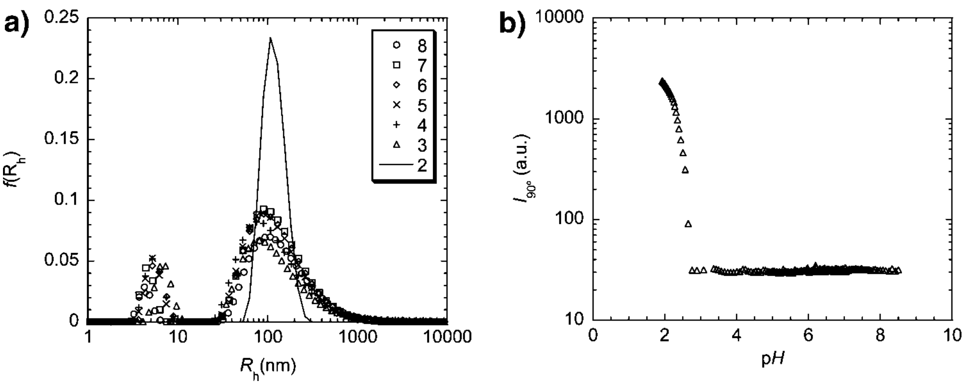


Figure 10. Dynamic light scattering (a) and static light scattering (b) results for the titration of a 0.1 wt % PAA_{368}-*b*-$PVOH_{192}$ solution by 0.1 M HCl for pH 2–8. (a) Equal area representation ($\theta = 90°$) of size distributions determined by CONTIN at pH 2−8. Note that the shown area ratio is an intensity average; i.e., a small amount of large aggregates may result in a larger peak area compared to a large amount of small, unimerically dissolved polymers. (b) Intensity (in kHz L g^{-1}, i.e., $I_{90°}$ in kHz is divided by polymer concentration in g L^{-1} to correct for dilution during the titration) vs pH.

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