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Amphiphilic Poly(vinyl acetate)-*b*-poly(*N*-vinylpyrrolidone) and Novel Double Hydrophilic Poly(vinyl alcohol)-*b*-poly(*N*-vinylpyrrolidone) Block Copolymers Prepared by Cobalt-Mediated Radical Polymerization

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ABSTRACT: Well-defined amphiphilic block copolymers of poly(vinyl acetate) (PVAc) and poly(*N*-vinylpyrrolidone) (P*N*VP) were synthesized by cobalt-mediated radical polymerization (CMRP). The *N*VP polymerization initiated by poly(vinyl acetate) end-capped by the cobalt(II)acetylacetonate complex met the criteria of controlled polymerization, i.e., first-order kinetic in *N*VP, increase of the molar mass with the *N*VP conversion, and narrow molar mass distribution. Therefore, the length of the two blocks can be tuned by the [VAc]/[Co(acac)$_2$] and the [*N*VP]/[PVAc] ratios for the synthesis of the macroinitiator and the polymerization of the second monomer, respectively. These amphiphilic PVAc-*b*-P*N*VP block copolymers were easily converted into the double hydrophilic PVOH-*b*-P*N*VP counterparts by selective methanolysis of the PVAc block. These two types of copolymers were prone to self-association into micelles in appropriate solvents.

Introduction

Controlled radical polymerization (CRP) was developed in the recent past as an answer to the steadily increasing demand for new materials with controlled properties. This concept is indeed a valuable strategy to provide a large range of polymers with well-defined molecular characteristics (length, composition and architecture), under non very demanding conditions.[1−3] Although, the CRP of most vinyl monomers is very effective, that one of non conjugated monomers, such as vinyl acetate (VAc) and *N*-vinylpyrrolidone (*N*VP), is more challenging but worthy. Indeed, poly(vinyl acetate) (PVAc) is involved in major applications, such as adhesives and paints, and its hydrolyzed version, poly(vinyl alcohol), is the hydrosoluble synthetic polymer produced on the largest scale.[4] Poly(vinylpyrrolidone) (P*N*VP) is also an extremely attractive polymer because of its high solubility in water and organic solvents, complexation capability and excellent biocompatibility.[5] Recently, effective controlled radical polymerization of VAc were developed such as degenerative-iodine transfer,[6] macromolocular design via interchange of xanthate (MADIX),[7] organotellurium-mediated living radical polymerizations[8] and cobalt-mediated radical polymerization (CMRP) via cobalt porphyrins[9] and cobalt(II) acetylacetonate complexes.[10] CMRP of VAc was successfully carried out both in bulk and in aqueous dispersed media,[11] and used to prepare high molar mass PVAc, PVAc containing block copolymers,[12] and solid substrates, such as fullerene, grafted by PVAc.[13] Today, few systems can impart control to the radical polymerization of *N*-vinylpyrrolidone. Good control was reported for a chain transfer process based on xanthates,[14] dithiocarbamates[15] and trithiocarbonates.[14b,16] Synthesis of P*N*VP-*b*-PVAc copolymers by MADIX was also briefly reported.[14e] A group-transfer technique that involves organostilbine[17] and more recently organobismuthine compounds[18] is another valuable approach for the control of the *N*VP polymerization.

Recently, Matyjaszewski et al. tried to extend the cobalt-mediated radical polymerization technique to *N*VP.[19] However, the control of this polymerization was not as good as that one of VAc more likely because of the lower deactivation rate of the P*N*VP growing chains by the cobalt complex (cobalt(II) acetylacetonate; Co(acac)$_2$). Nevertheless, statistical PVAc-*co*-P*N*VP copolymers were prepared in a controlled manner.[19] This paper aims at reporting for the first time the synthesis of well-defined amphiphilic PVAc-*b*-P*N*VP block copolymers by CMRP. Initiated by a PVAc−Co(acac)$_2$ macroinitiator, the polymerization of *N*VP is controlled. Moreover, methanolysis of the PVAc block is an easy way to prepare a novel class of biocompatible double hydrophilic PVOH-*b*-P*N*VP block copolymers. These two families of diblock copolymers are prone to self-assemble into micelles, in water for the amphiphilic PVAc containing copolymers and in organic media for the double hydrophilic block copolymers.

Experimental Section

Materials. Vinyl acetate (VAc) (>99%, Acros) was dried over calcium hydride, degassed by several freeze-thawing cycles before being distilled under reduced pressure and stored under argon. *N*-Vinylpyrrolidone (Aldrich) was degassed by several freeze-thawing cycles before being distilled under reduced pressure and stored under argon. Toluene was distilled from sodium benzophenone complex, whereas anisole (Aldrich) and dimethylformamide (DMF) were dried over molecular sieves. All the solvents were degassed by bubbling argon for 30 min. 2,2′-azobis(4-methoxy-2,4-dimethyl valeronitrile) (V-70) (Wakko), cobalt(II) acetylacetonate (Co(acac)$_2$) (>98%, Acros), potassium hydroxide (KOH), 2,2,6,6-tetramethylpiperidine 1-oxy (TEMPO) (98%, Aldrich), hexamethyldisiloxane (HMDS) (Aldrich, NMR purity) were used as received. Membrane Spectra/Pore (cutoff : 6000−8000 Da) was used for dialysis.

Characterization. ^{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*-P*N*VP and PVOH-*b*-P*N*VP were recorded with the same spectrometer at 353 K in DMSO-d_6 and D$_2$O, respectively. ($D_1 =$ 5 s, 32 scans, 5 wt % of polymer).

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Size exclusion chromatography (SEC) of poly(vinyl acetate) was carried out in THF (flow rate: 1 mL min^{-1}) at 40 °C with a Waters 600 liquid chromatrograph 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). Polystyrene standards were used for calibration. Size exclusion chromatography (SEC) of poly(vinyl acetate)-*b*-poly(*N*-vinylpyrrolidone) was carried out in dimethylformamide containing 25 mM LiBr (flow rate : 1 mL min^{-1}) at 55 °C with a Waters 600 liquid chromatrograph equipped with a 410 refractive index detector and four Waters Styragel columns [HR 1 (100−5000), HR 3 (500−30000), HR 4 (5000−500000), and HR 5 (2000−4000000) (7.8 × 300 mm)]. Poly(methyl methacrylate) standards were used for calibration.

Infrared spectra were recorded with a Perkin-Elmer FT-IR instrument from 4000 to 600 cm^{-1}. PVAc-*b*-P*N*VP copolymers were dissolved in CH$_2$Cl$_2$ and solvent-cast on a NaCl disk, whereas PVOH-*b*-P*N*VP copolymers were mixed with potassium bromide and compressed before IR analysis.

Inductively coupled plasma mass spectrometry (ICPMS) was carried out with a spectrometer Elan DRC-e Perkin-Elmer SCIEX. Samples were prepared by dissolving a small amount (30 mg) of polymer in 5 mL of HNO$_3$ (65%). This solution was heated until complete dissolution and then diluted with 50 mL of bidistilled water at room temperature.

Dynamic light scattering (DLS) was performed on a Malvern CGS-3 equipped with a He−Ne laser (633 nm) at an angle of 90°. A bath of filtered toluene surrounded the scattering cell, and the temperature was controlled at 25 °C. The polydispersity index (PDI) was defined as the μ_2/Γ_1^2 ratio, where μ_2 is the second cumulant and Γ_1 is the first cumulant. The DLS data were also analyzed by the CONTIN routine, a method based on a constraint inverse Laplace transformation of the data, which gives access to a size distribution histogram for the aggregates.

General Recipe for the Synthesis of Poly(vinyl acetate) Macroinitiators End-Capped by Cobalt(II) Acetylacetonate. Co(acac)$_2$ (0.363 g, 1.42 mmol) and V-70 (1.42 g, 4.60 mmol) were added into a round-bottom flask capped by a three-way stopcock and purged by three vacuum−argon cycles. After addition of degassed vinyl acetate (30 mL, 28 g, 370 mmol), the reaction mixture was heated at 30 °C under stirring. After 56 h, the viscosity of the medium increased substantially, and the monomer conversion was estimated gravimetrically (conversion = 45%). The residual monomer was evaporated under reduced pressure, and the pink poly(vinyl acetate) macroinitiator was stored under inert atmosphere. $M_{\mathrm{n,SEC}} = 11\,500$ g/mol; $M_{\mathrm{w}}/M_{\mathrm{n}} = 1.13$. $M_{\mathrm{n,NMR}} = 86.09 \times [3 \times (-\mathrm{C}H-\mathrm{OCOCH_3}, \mathrm{PVAc})/(-\mathrm{OC}H_3, \mathrm{V\text{-}70})] = 11\,300$ g/mol. Cobalt content was determined by ICP = 5672 ppm.

PVAc macroinitiators with different molar masses were prepared by the same recipe, merely by changing the [VAc]/[Co] ratio.

General Recipe for the Synthesis of PVAc-*b*-P*N*VP Block Copolymers. The PVAc−Co(acac)$_2$ macroinitiator (5 g, $M_{\mathrm{n,NMR}} = 11\,300$ g/mol, $M_{\mathrm{n,SEC}} = 11\,500$ g/mol, $M_{\mathrm{w}}/M_{\mathrm{n}} = 1.13$) was added into a 100 mL round-bottom flask, that was purged by three vacuum-argon cycles before addition of 15 mL a dry and degassed anisole/toluene (9/1 : v/v) mixture. After complete dissolution of PVAc, distilled and degassed *N*-vinylpyrrolidone (15 mL, 15.6 g) was added. A first sample was picked out and used as a reference for the monitoring of the monomer conversion. The reaction medium was stirred in a thermostated bath at 20 °C. After 6 h, the medium was highly viscous, and the polymerization was terminated by addition of a solution of TEMPO (0.5 g of TEMPO in 5 mL of degassed toluene). Stirring was maintained at room temperature overnight. The monomer conversion was determined by ^{1}H NMR in DMSO-d_6 based on the *N*VP resonance at 4.3 ppm (two olefinic protons) with respect to the resonance at 4.8 ppm characteristic of PVAc ($-\mathrm{CH_2}-\mathrm{C}H(\mathrm{OAc})-$) used as an internal reference (*N*VP conversion = 65%).

After elimination of the residual monomer and solvents under reduced pressure at 30 °C, the PVAc-*b*-P*N*VP block copolymer was dissolved in THF, precipitated into cold diethyl ether, filtered, and dried in vacuo. This purification step was repeated two times, and 11.7 g of a slightly yellow PVAc-*b*-P*N*VP block copolymer was collected. $M_{\mathrm{n,SEC}} = 51\,000$ g/mol, $M_{\mathrm{w}}/M_{\mathrm{n}} = 1.35$. Before ^{1}H NMR analysis, samples were dried in vacuo for 2 h at 170 °C. ^{1}H NMR (250 MHz, 353 K, DMSO-d_6) δ (ppm) : 4.79 (m, 1H, $\mathrm{C}H-$OCOCH$_3$ PVAc), 3.72 and 3.56 (1H, C*H*-NCO P*N*VP), 3.16 (2H, $\mathrm{C}H_2-\mathrm{NCO}-$ P*N*VP), 2.20 and 2.09 (2H, $-\mathrm{NCOC}H_2-$ P*N*VP), 1.92 (3H, $-\mathrm{OCOC}H_3$ PVAc), 1.9−1.3 ($-\mathrm{N}-\mathrm{CH_2}-\mathrm{C}H_2-\mathrm{CH_2}-\mathrm{CO}-$ and $-\mathrm{C}H_2-\mathrm{CH}-\mathrm{NCO}-$ of P*N*VP, $\mathrm{C}H_2-\mathrm{CH}-\mathrm{OCOCH_3}$ of PVAc). The molar mass of the P*N*VP block was calculated from the ^{1}H NMR data of the diblock and M_{n} of the PVAc macroinitiator determined by NMR: PVAc(11300)-*b*-P*N*VP(33900). Cobalt content determined by ICP = 293 ppm. Further purification of the copolymer by filtration of a solution in methanol through silica decreased the cobalt content to 22 ppm.

The same general procedure was repeated by changing temperature, *N*VP conversion and molar mass of the PVAc macroinitiator.

General Recipe for the Synthesis of PVOH-*b*-P*N*VP Block Copolymers. In a 200 mL round-bottom flask, a solution of PVAc(11300)-*b*-P*N*VP(33900) (4 g) in methanol (p.a. 150 mL), was added with a solution of potassium hydroxide (2 g) in methanol (50 mL, p.a.), degassed by of bubbling argon for 10 min and stirred at room temperature. After 20 h, part of the methanol was eliminated under reduced pressure, and the residual PVOH-*b*-P*N*VP solution (30 mL) was diluted by bidistilled water and dialyzed against water through a Spectra/Pore membrane (cutoff : 6000−8000 Da) in order to eliminate methanol, potassium hydroxide and methyl acetate residues. The aqueous solution of PVOH-*b*-P*N*VP was finally lyophilized, and a fluffy and colorless PVOH-*b*-P*N*VP (2.6 g) was recovered.

^{1}H NMR (250 MHz, 353K, D$_2$O), δ (ppm): 3.85 (1H, $\mathrm{C}H-\mathrm{OH}$ PVOH), 3.58 and 3.42 (1H, $\mathrm{C}H-\mathrm{NCO}$ P*N*VP), 3.10 (2H, $\mathrm{C}H_2-\mathrm{NCO}-$ P*N*VP), 2.20 and 2.10 (2H, $-\mathrm{NCOC}H_2-$ P*N*VP), 1.81 (2H, $-\mathrm{N}-\mathrm{CH_2}-\mathrm{C}H_2-\mathrm{CH_2}-\mathrm{CO}-$P*N*VP), 1.6−1.3 ($\mathrm{C}H_2-\mathrm{CH}-\mathrm{OH}$ of PVAc and $-\mathrm{C}H_2-\mathrm{CH}-\mathrm{NCO}-$ of P*N*VP). The molar mass of the PVOH block was calculated from the ^{1}H NMR spectrum of the diblock and M_{n} of the P*N*VP:PVOH(5600)-*b*-P*N*VP(33900). Cobalt content determined by ICP = 348 ppm.

PVOH-*b*-P*N*VP block copolymers with different compositions and molar masses were prepared by the same procedure.

Micellization of the P*N*VP Containing Diblock Copolymers. Polymeric micelles consisting of a hydrophobic PVAc core and hydrophilic P*N*VP shell were prepared in water. Typically, 0.01 g of a PVAc-*b*-P*N*VP copolymer was dissolved in 1 mL of methanol, followed by the dropwise addition of 10 mL of bidistilled water. The mixture was stirred at room temperature for 24 h and passed through a 1.0 μm filter before analysis by dynamic light scattering (DLS). Solutions of PVAc-*b*-P*N*VP with a PVAc block shorter than 12.0 K were passed through a 0.2 μm filter.

Polymeric micelles with a PVOH core and a P*N*VP shell were prepared in methanol. Typically, 0.01 g of copolymer was dissolved in 1 mL of bidistilled water, followed by the dropwise addition of 10 mL of methanol. The mixture was stirred at room temperature for 24 h and then passed through a 1.2 μm filter before analyzis by dynamic light scattering (DLS). Solutions of PVOH-*b*-P*N*VP with a PVOH block smaller than to 6.0 K were passed through a 0.2 μm filter.

Results and Discussion

A series of well-defined poly(vinyl acetate) macroinitiators with a molar mass in the 5K−25K range, were prepared by bulk cobalt-mediated radical polymerization (CMRP), as reported elsewhere (Table 1).[10a] Typically, the vinyl acetate polymerization was initiated by V-70 at 30 °C in the presence of cobalt(II) acetylacetonate (Co(acac)$_2$). The control of the polymerization, assessed by reasonable agreement between the experimental and theoretical molar masses and quite narrow molar mass distribution, results from the mediating role of the cobalt complex. From a mechanistic point of view, it was recently reported that VAc bulk polymerization conducted in

Table 1. Synthesis of the Poly(vinyl acetate) Macroinitiators End-Capped by $Co(acac)_2$ with Polymerization at 30 °C

PVAc macroinitiator	$[VAc]_0/[Co]_0/[V\text{-}70]_0$[a]	time (h)	convn[b] (%)	$M_{n,th}$[c] (g/mol)	$M_{n,NMR}$[d] (g/mol)	$M_{n,SEC}$[e] (g/mol)	M_w/M_n	f[f]
1	115/1/3.3	74	49	4850	5600	6000	1.10	0.86
2	115/1/3.3	79	52	5150	5900	6600	1.28	0.87
3	230/1/3.3	56	45	8900	11 300	11 500	1.13	0.79
4	406/1/3.3	27	56	19 600	24 300	23 600	1.17	0.81

[a] Initial concentrations. [b] Determined gravimetrically after elimination of the residual monomer in vacuo at 40 °C. [c] Calculated from the initial [VAc]/[Co] ratio and the monomer conversion. [d] $M_{n,NMR} = 86.09 \times [3\times (-CH-OCOCH_3, \text{PVAc})/(-OCH_3, \text{V-70})]$. [e] SEC with PS standards. [f] $f = M_{n,th}/M_{n,NMR}$.

Scheme 1. Preparation of Amphiphilic PVAc-*b*-P*N*VP and Double Hydrophilic PVOH-*b*-P*N*VP Block Copolymers by Cobalt-Mediated Radical Polymerization (CMRP)

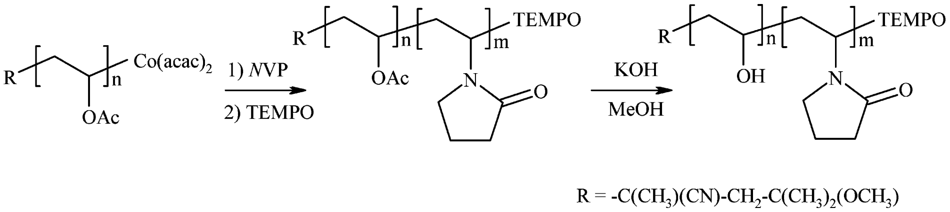

Table 2. *N*VP Polymerization Initiated by a PVAc−$Co(acac)_2$ Macroinitiator at Different Temperatures[a]

				PVAc-*b*-P*N*VP before purif.		PVAc-*b*-P*N*VP after purif[b]			
entry	T (°C)	t (h)	convn[c] (%)	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,NMR,PNVP}$[e] (g/mol)	$M_{n,th,PNVP}$ (g/mol)
1	30	8	80	37 200	1.41	40 100	1.37	34 700	14 000
2	20	8	78	36 200	1.35	38 200	1.27	34 400	13 500
3	6	88	87	38 400	1.40	41 200	1.34	36 000	15 300

[a] [PVAc−Co **1**] (0.18 mmol, 1 g, 5600 g/mol), *N*VP (28.1 mmol, 3 mL), 3 mL anisole/toluene (9/1) mixture. [b] The copolymer was precipitated three times in cold diethyl ether. [c] Determined by ^1H NMR (see Experimental Section). [d] SEC calibrated by PMMA standards. [e] Determined by ^1H NMR (see Experimental Section).

the presence of cobalt complexes and an excess of V-70 is a degenerative chain transfer process, whereas this mechanism turns into a reversible-termination process by cleavage of the Co−C bond when amino compounds that coordinate the cobalt complex, are added.[20]

The poly(vinyl acetate) macroradicals were directly recovered by elimination of the residual monomer in vacuo and stored at −20 °C under inert atmosphere. The pink color testified to the persistence of the active cobalt complex at the chain end, which is no longer the case when the chains are exposed to air. These PVAc chains are thus potential macroinitiators of the CMRP of the same monomer or not. In this work, attention was paid to *N*-vinylpyrrolidone (*N*VP) with the purpose to prepare not yet reported well-defined PVAc-*b*-P*N*VP amphiphilic copolymers and the PVOH-*b*-P*N*VP double hydrophilic counterparts by methanolysis of the PVAc block. (Scheme 1)

Synthesis of Poly(vinyl acetate)-*b*-poly(*N*-vinylpyrrolidone) Copolymers. CMRP of *N*-vinylpyrrolidone initiated by PVAc macroinitiators was investigated under different experimental conditions. Whenever the Co−C bond is cleaved in the presence of *N*VP, the released poly(vinyl acetate) radicals can initiate the *N*VP polymerization, whose the propagation might be mediated by the cobalt complex.

The first experiment was carried out at 30 °C, which is the ideal temperature for the CMRP of VAc. However, as mentioned in the introduction, deactivation of the P*N*VP growing chains by $Co(acac)_2$ is less efficient than that one of the PVAc chains.[19] One reason might be the competitive complexation of the cobalt(II) acetylacetonate by the carbonyl group of the *N*VP units, which shifts the equilibrium between dormant and active species toward the active species, as pyridine does.[20] Temperature was then decreased in order to restore a more favorable position of this equilibrium. Experiments were conducted at 20 °C and 6 °C, respectively, which would not have been possible in the case of *N*VP homopolymerization initiated by V-70 in the presence $Co(acac)_2$, because of the low decomposition rate of the initiator at these temperatures.

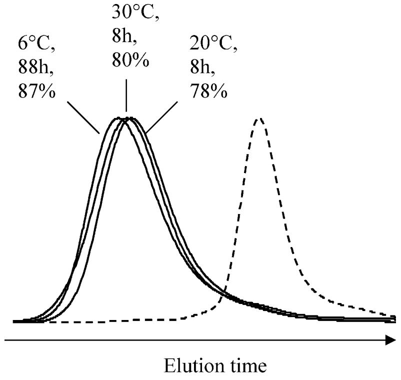

Figure 1. SEC chromatograms of the three PVAc-*b*-P*N*VP block copolymers prepared by resumption of the *N*VP polymerization by the same PVAc−Co macroinitiator **1** (5600 g/mol, dotted line) at different temperatures (Table 2). The chromatograms were recorded before purification.

The [*N*VP]/[PVAc] ratio was kept constant in the experiment carried out at different temperatures with the same macroinitiator. Copolymerization data are listed in Table 2, and the SEC chromatograms are shown in Figure 1.

At 30 °C, the polymerization rate was quite high and the medium was rapidly viscous, consistent with previous observations for the homopolymerization of *N*VP by CMRP.[19] The monomer conversion, determined by ^1H NMR analysis of *N*VP with PVAc as an internal reference, was 80% after 8 h. The polymerization rate was quite comparable at 20 °C, and much lower at 6 °C at which a monomer conversion in the 80% range needed a much longer period of time. Nevertheless, the block copolymerization was effective whatever the temperature, as

Table 3. *N*VP Polymerization Initiated by a PVAc−Co(acac)$_2$ Macroinitiator at 20 °C[a]

			PVAc-*b*-P*N*VP before purif		PVAc-*b*-P*N*VP after purif[b]			
entry	time (h)	convn[c] (%)	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,NMR,PNVP}$[e] (g/mol)	$M_{n,th,PNVP}$ (g/mol)
1	2	32	21 000	1.35	23 600	1.25	14 700	5600
2	4	50	27 100	1.36	29 300	1.29	21 400	8700
3	6	67	33 800	1.37	37 800	1.31	31 700	11 600
4	8	78	36 200	1.35	38 200	1.27	34 400	13 500

[a] [PVAc−Co **1**] (0.18 mmol, 1 g, 5600 g/mol), *N*VP (28.1 mmol, 3 mL), 3 mL anisole/toluene (9/1), at 20 °C. [b] The copolymer was precipitated three times in cold diethyl ether. [c] Determined by ^{1}H NMR (see Experimental Section). [d] SEC calibrated by PMMA standards. [e] Determined by ^{1}H NMR (see Experimental Section).

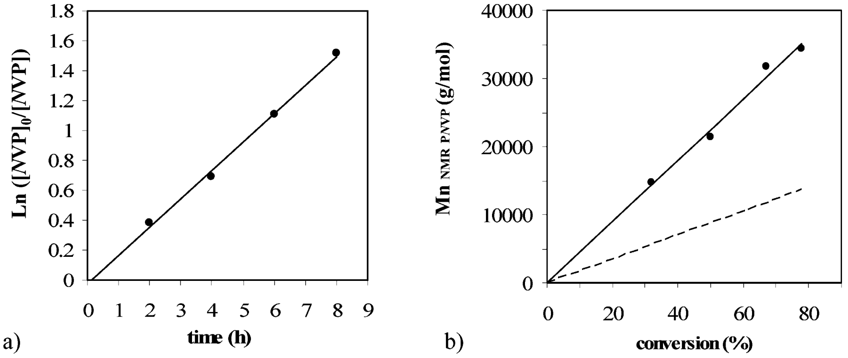

Figure 2. (a) Plot of ln([*N*VP]$_0$/[*N*VP]) vs time and (b) dependence of molar mass of the P*N*VP block ($M_{n,NMR}$) on *N*VP conversion, for the *N*VP polymerization initiated by the PVAc−Co macroinitiator **1** ($M_{n,NMR}$ = 5600 g/mol) at 20 °C. The dotted line shows the dependence of the theoretical molar mass of the P*N*VP block on the monomer conversion.

illustrated by the SEC chromatograms for the PVAc macroinitiator and the three copolymers collected at quite a comparable *N*VP conversion (Figure 1). The elution peak for the macroinitiator is completely shifted toward higher molar masses for the copolymers before purification, leaving very few unreacted PVAc chains behind. The reproducibility of the three syntheses is quite remarkable, and the polydispersity of the PVAc-*b*-P*N*VP copolymers is reasonably low (M_w/M_n ∼ 1.35−1.40), and slightly lower than that of homo P*N*VP and P*N*VP-*co*-PVAc random copolymers by CMRP with Co(acac)$_2$.[19] Consistent with the SEC data, the molar mass of the P*N*VP block, determined by ^{1}H NMR and reported in Table 2, is essentially independent of the temperature at similar *N*VP conversion. Moreover, a substantial discrepancy is observed between the theoretical and the experimental molar masses of the P*N*VP blocks determined after repeated precipitations. The partial fractionation of the copolymer, in line with a lower polydispersity after precipitation, might be an explanation without precluding that not all the macroinitiator chains initiated the *N*VP polymerization.

In order to know whether the P*N*VP blocks are growing according to a controlled process or not, a series of independent copolymerization experiments were conducted at 20 °C and stopped at different polymerization times. The *N*VP conversion and the molecular parameters of the copolymers, before and after purification, are listed in Table 3.

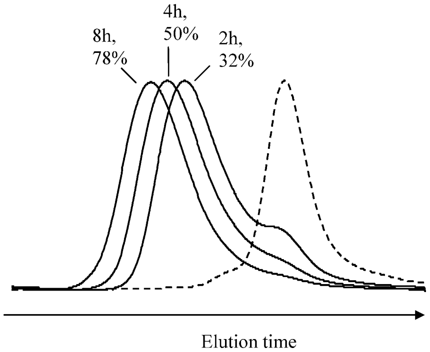

Figure 3. SEC chromatograms of the PVAc−Co macroinitiator **1** (dotted line) and PVAc-*b*-P*N*VP copolymers prepared at 20 °C. (Table 3) The chromatograms were recorded before purification of the copolymers.

Kinetics of the *N*VP polymerization initiated at 20 °C by the PVAc−Co(acac)$_2$ was first order in monomer as assessed by the linear dependence of ln([M]$_0$/[M]) on time (Figure 2a), which indicates that the radical concentration is constant during the polymerization. Consistent with a controlled polymerization, the molar mass of the P*N*VP block increased with the monomer conversion (Figure 2b). Figure 3 shows a substantial shift of the original chromatogram of the PVAc−Co(acac)$_2$ macroinitiator toward higher molar mass in agreement with the formation of a PVAc-*b*-P*N*VP block copolymer. At 32% *N*VP conversion, all the macroinitiator chains were not consumed and the copolymer polydispersity was higher than that of the PVAc-macroinitiator (1.35 vs 1.10). Although it cannot definitely be precluded that the residual peak of the PVAc is due to irreversible termination, only a very faint tail persists on the low molar mass side at higher monomer conversion, which seems to indicate a slow initiation of the *N*VP polymerization by the PVAc macroinitiator compare to the propagation. An explanation might be the formation of PVAc chains end-capped by a primary alkyl cobalt adduct (CHOAc−CH$_2$−Co), as result of head-to-head monomer addition followed by radical deactivation. Activation of this Co−C bond might be too slow at 20 °C for block copolymer with low polydispersity to be prepared. This hypothesis is consistent with the stability of the cobalt−carbon bond, that drastically decreases from a primary carbon to an increasingly substituted carbon.[21] A similar behavior was reported for the organotellurium-mediated radical polymerization of vinyl acetate.[8] Moreover, in contrast to the preparation of the PVAc macroinitiator, the N*V*P polymerization occurs in the absence of an external radical source, whereas coordination of the cobalt by the pyrrolidone units could favor a reversible-termination mechanism rather than a degenerative chain transfer process. A change in the polymerization mechanism of the two

Table 4. Synthesis of PVAc-*b*-P*N*VP Block Copolymers with Different P*N*VP Chain Length[a]

				PVAc-*b*-P*N*VP before purif		PVAc-*b*-P*N*VP after purif[b]			
entry	[*N*VP]/[PVAc]	*t* (h)	convn[c] (%)	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,NMR,PNVP}$[e] (g/mol)	$M_{n,th,PNVP}$ (g/mol)
1	84	4	61	17 800	1.32	21 700	1.20	14 600	5700
2	168	6	67	33 800	1.37	37 800	1.31	31 700	12 500
3	280	4	65	42 200	1.34	43 800	1.34	37 800	20 200

[a] PVAc−Co(acac)$_2$ **1** (5600 g/mol, 1 g), *N*VP/anisole/toluene (5/4.5/0.5 v/v), at 20 °C. [b] The copolymer was precipitated three times in cold diethyl ether. [c] Determined by ^{1}H NMR (see Experimental Section). [d] SEC calibrated by PMMA standards. [e] Determined by ^{1}H NMR (see Experimental Section).

Table 5. Synthesis of PVAc-*b*-P*N*VP Block Copolymers with Different PVAc Macroinitiators[a]

				PVAc-*b*-P*N*VP before purif		PVAc-*b*-P*N*VP after purif[b]				
entry	$M_{n,NMR,PVAc}$	*t* (h)	convn[c] (%)	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,SEC}$[d] (g/mol)	M_w/M_n	$M_{n,NMR,PNVP}$[e] (g/mol)	$M_{n,th,PNVP}$ (g/mol)	wt % P*N*VP
1	5900	6	72	41 500	1.40	45 800	1.34	25 000	13 200	80
2	11 300	6	65	50 300	1.37	51 000	1.35	33 900	22 900	75
3	24 300	6	67	87 900	1.49	86 400	1.49	60 100	50 600	71
4	24 300	1	25	46 100	1.32	47 700	1.29	15 700	18 900	40

[a] PVAc−Co(acac)$_2$ **2**, **3** and **4** (5 g), *N*VP (140 mmol, 15.6 g, 15 mL), 15 mL anisole/toluene (9/1), at 20 °C. [b] The copolymer was precipitated three times in cold diethyl ether, [c] Determined by ^{1}H NMR (see Experimental Section). [d] SEC calibrated by PMMA standards. [e] Determined by ^{1}H NMR (see Experimental Section).

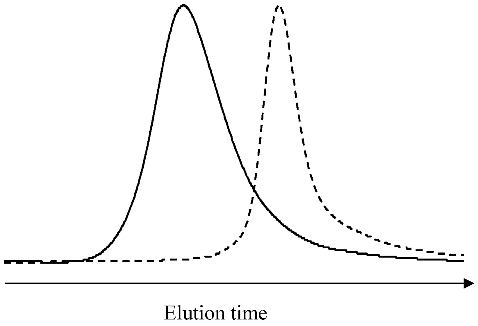

Figure 4. SEC chromatograms for the PVAc(24300)-*b*-P*N*VP(60100) copolymer (full line) and the PVAc−Co macroinitiator (dotted line). (Table 5, entry 3)

comonomers might also contribute to the broadening of the molar mass distribution.

That the growth of the P*N*VP block is reasonably well controlled was confirmed by another set of experiments in which the [*N*VP]/[PVAc] ratio was changed and the same monomer conversion was targeted. The same macroinitiator being used, the length of the P*N*VP block was expected to change, which was actually the case (Table 4). Indeed, M_n of the P*N*VP block was increased by 2.2, when the [*N*VP]/[PVAc] ratio was two times higher (from 84 to 168). A further increase of this ratio by 3.3 (from 84 to 280) resulted in a smaller increase in M_n (by 2.6) than expected. Partial fractionation during precipitation in diethyl ether might however perturb the calculation of $M_{n,PNVP}$ and account for some apparent discrepancy.

Finally, PVAc macroinitiators with different chain lengths were used to initiate the *N*VP polymerization and to prepare well-defined PVAc-*b*-P*N*VP block copolymers with different molar masses and compositions, which is crucial when specific properties are desired (Table 5).

A diblock copolymer with a P*N*VP block of M_n as high as 60100 g/mol was successfully prepared, with however a higher polydispersity (1.5), which more likely results from the unavoidable tail on the low molar mass side due to irreversible termination reactions and/or inactive PVAc macroinitiator chains (Figure 4).

Synthesis of Poly(vinyl alcohol)-*b*-poly(*N*-vinylpyrrolidone) Copolymers. Basic hydrolysis of poly(vinyl acetate) in methanol is the traditional technique for preparing hydrosoluble poly(vinyl alcohol). Therefore, amphiphilic PVAc-*b*-P*N*VP block copolymers prepared in this work are typical precursors of novel double hydrophilic PVOH-*b*-P*N*VP copolymers (step 2, Scheme 1), provided that the pyrrolidone subunits remain untouched. In this respect, P*N*VP is known to resist hydrolysis except under severe conditions (strong bases in molten P*N*VP above 200 °C).[22] Moreover, it was confirmed in this work that homo P*N*VP was unaffected by the conditions used for the methanolysis of the PVAc block, i.e., potassium hydroxide in methanol at room temperature. IR and ^{1}H NMR analyses of P*N*VP before and after treatment are provided as Supporting Information.[23]

Figure 5 confirms that the methanolysis of the PVAc(24300)-*b*-P*N*VP(60100) copolymer (Table 5, entry 3) under the aforementioned conditions results in the complete disappearance of the IR absorptions typical of PVAc (C═O stretching at 1738 cm^{-1}), whereas the absorptions characteristic of P*N*VP persists (C═O stretching at 1667 cm^{-1}), in agreement with the formation of a fully hydrolyzed PVOH-*b*-P*N*VP block copolymer. Additional evidence was found in the NMR spectra of the original PVAc-*b*-P*N*VP copolymer and the final hydrosoluble PVOH-*b*-P*N*VP counterpart recorded at 353 K in DMSO-d_6 and D_2O, respectively (Figure 6). The simultaneous disappearance of the PVAc signals (a−c), particularly the signal b at 4.79 ppm (C*H*−OCOCH$_3$), the appearance of the signals typical of PVOH (C*H*−OH at 3.85 ppm) and the persistence of the P*N*VP (d−h) confirmed the selective hydrolysis of the PVAc block.

A range of PVOH-*b*-P*N*VP copolymers were accordingly prepared by methanolysis of the PVAc-*b*-P*N*VP copolymers listed in Table 5. The molar mass of the PVOH block was calculated from the ^{1}H NMR spectrum of the diblock and M_n of the unaffected P*N*VP block (Table 6). The agreement between the PVOH molar mass determined by ^{1}H NMR and the theoretical value in the case of complete methanolysis of the acetate groups indicates that the methanolysis is at least as extensive as 95%.

Finally, all cobalt-mediated radical polymerizations of *N*VP were quenched by an excess of TEMPO in order to displace the cobalt complex from the chain end and purify the PVAc-*b*-P*N*VP copolymers, as reported previously for PVAc.[10b] Although not complete, the displacement reaction was confirmed by the drastic loss of cobalt measured by inductively coupled plasma (ICP) analysis. For example, the cobalt content of the

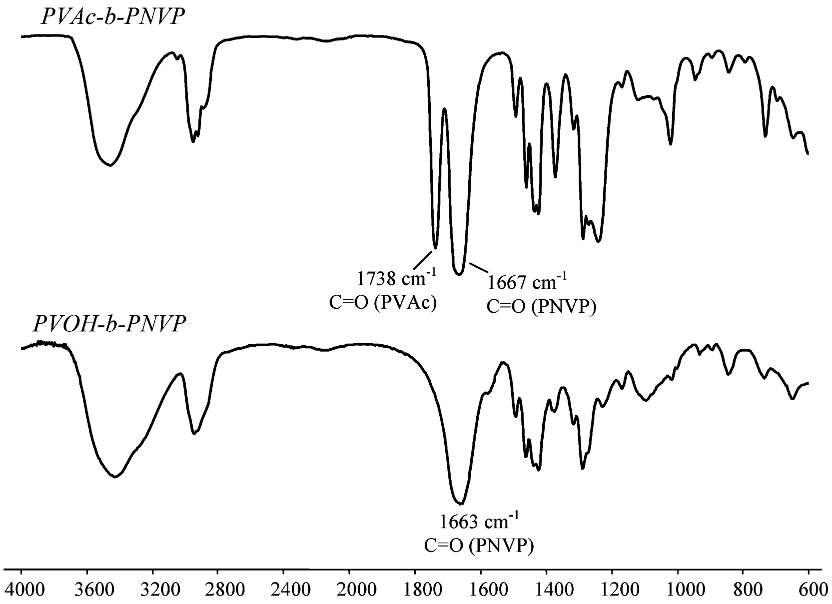

Figure 5. Infrared spectra for the original PVAc(24300)-*b*-P*N*VP(60100) before and after methanolysis of the PVAc block.

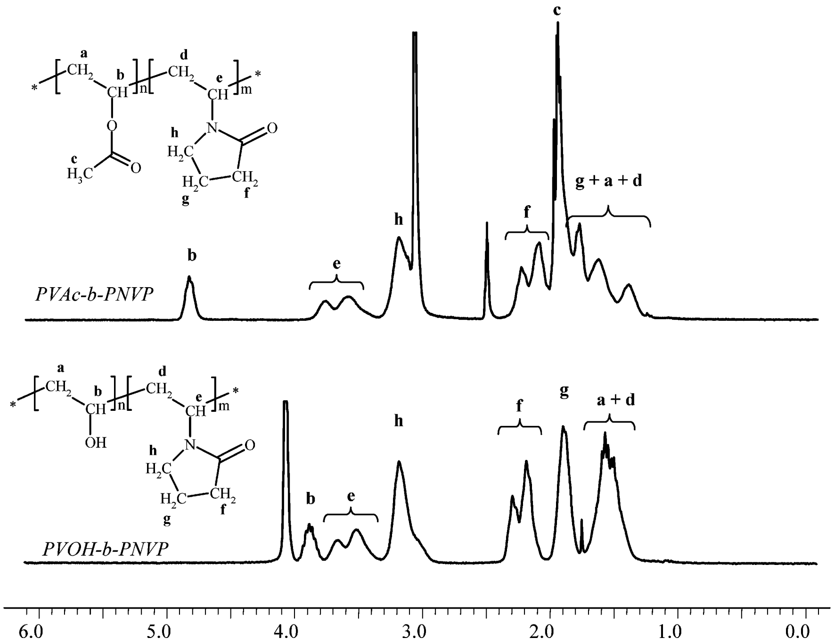

Figure 6. ^{1}H NMR spectra at 353 K for the original PVAc(24300)-*b*-P*N*VP(60100) (Table 5, entry 3) in DMSO-d_6 and the final PVOH-*b*-P*N*VP (Table 6, entry 3) in D_2O after selective methanolysis of the PVAc block.

Table 6. Synthesis of PVOH-*b*-P*N*VP Block Copolymers by Selective Methanolysis of PVAc-*b*-P*N*VP

entry	PVAc-*b*-P*N*VP (g/mol)	PVOH-*b*-P*N*VP (g/mol)
1	PVAc (5900)-*b*-P*N*VP (25000)	PVOH (2900)-*b*-P*N*VP (25000)
2	PVAc (11300)-*b*-P*N*VP (33900)	PVOH (5600)-*b*-P*N*VP (33900)
3	PVAc (24300)-*b*-P*N*VP (60100)	PVOH (11900)-*b*-P*N*VP (60100)
4	PVAc (24300)-*b*-P*N*VP (15700)	PVOH (13400)-*b*-P*N*VP (15700)

PVAc macroinitiator (Table 1, entry 3) was estimated to be 5672 ppm whereas only 293 ppm of metal was detected in the PVAc(11300)-*b*-P*N*VP(33900) copolymer after treatment with TEMPO. As expected, a slightly higher concentration of cobalt residues was measured in the corresponding PVOH(5600)-*b*-P*N*VP(33900) copolymer (348 ppm) as a result of the loss of the ester groups. The complexation capabilities of P*N*VP might explain that the elimination of cobalt is not quantitative for the P*N*VP containing copolymers. Moreover, the copolymer PVAc-*b*-P*N*VP was further purified by filtration of a copolymer solution in methanol through silica. The residual cobalt content decreased from 293 to 22 ppm. This purification effort will be continued in the future.

Solution Behavior of Poly(vinyl acetate)-*b*-poly(*N*-vinylpyrrolidone) and Poly(vinyl alcohol)-*b*-poly(*N*-vinylpyrrolidone) Copolymers in Solution. Micellization of amphiphilic block copolymers in a solvent selective of one constitutive block is a well-known phenomenon with great potential in the design of a drug delivery system. For instance, amphiphilic derivatives of poly(vinylpyrrolidone) were investigated as drug carriers[24] and stabilizers of liposomes in vivo.[25] Micellization of the two types of block copolymers synthesized in this work (Table 6) was investigated by dynamic light scattering (DLS).

Whenever a dilute solution of the PVAc-*b*-P*N*VP diblocks in methanol was added dropwise with water at room temperature, micellar aggregates were formed with a quite narrow size distribution (Figure 7). The polydispersity was in the 0.07–

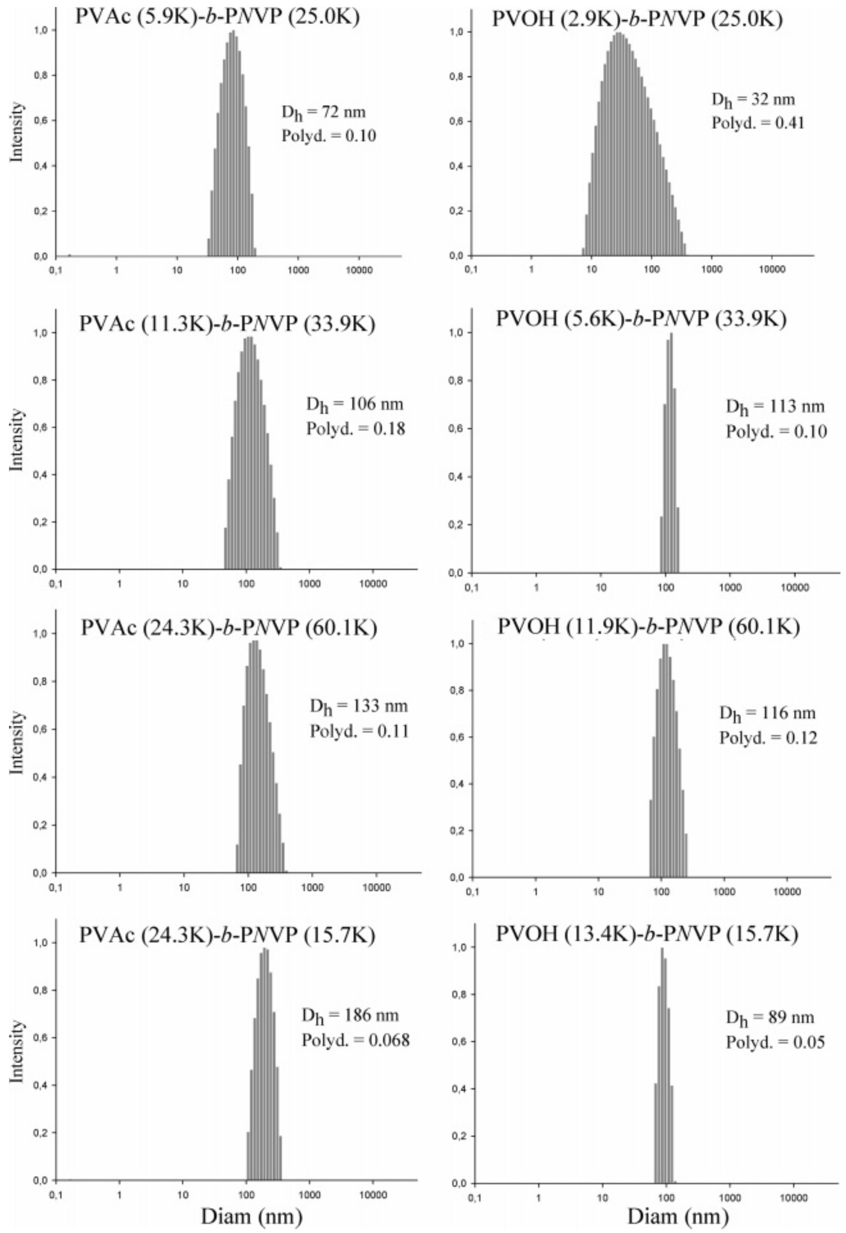

Figure 7. Size distribution of PVAc-*b*-P*N*VP and PVOH-*b*-P*N*VP micelles formed in water and methanol, respectively.

0.12 range. For the three copolymers, in which P*N*VP is the major block (70−80 wt %), the size of the micelles increases with the molar mass from 72 to 133 nm. The mutual repulsion of these solvated P*N*VP chains in the shell is responsible for a strong curvature of the core/shell interface and thus for the spherical geometry. Surprisingly, the copolymer with a comparatively shorter hydrophilic block (PVAc(24300)-*b*-P*N*VP-(15700)) leads to micellar aggregates with a diameter as high as 186 nm. This figure must be compared to 133 nm for the diblock with the same PVAc block (24300 g/mol) and a much longer P*N*VP one (60100 g/mol). An explanation might be found in the steric repulsion of the P*N*VP blocks in the micellar shell, which is lower for the shorter blocks. As a result, the curvature of the core−corona interface lower and the micelles can grow further.[26] Moreover, the quite low polydispersity (0.07) strongly suggests the formation of monodisperse objects, which is usually the case for spheres and also possible for vesicles, whereas the polydispersity of cylinders is commonly much higher than 0.2.

Although the PVOH-*b*-P*N*VP block copolymers are double hydrophilic, they can form micelles in an organic solvent selective for one block, e.g., in methanol selective for P*N*VP. Thus, a large amount of methanol was added to an aqueous solution of the diblock copolymers. As soon as PVOH started to precipitate at the appropriate content of methanol in water, micelles were formed with a narrow size distribution, except for the block copolymer with a shorter PVOH block (2900 g/mol). In this case, the distribution is broad (polyd. = 0.41), more likely because the solubility of PVOH decreases slowly with the addition of methanol and the smooth phase separation that occurs leads to ill-defined core−shell structures. Another striking observation is the drastic reduction of micellar size shown by the PVAc(24300)-*b*-P*N*VP(15700) (diameter = 186 nm) upon methanolysis of the PVAc block [PVOH(13400)-*b*-P*N*VP(15700); diameter = 89 nm]. This might merely reflect the substantial decrease in the molar mass of the copolymer as result of the PVAc conversion into PVOH.

Conclusions

This paper reports for the first time the synthesis of well-defined poly(vinyl acetate)-*b*-poly(vinylpyrrolidone) block copolymers by the cobalt-mediated radical polymerization. It was shown indeed that the polymerization of *N*-vinylpyrrolidone was effectively initiated by PVAc macroinitiators and controlled as assessed by the first-order kinetics in *N*VP and the increase of the molar mass of the P*N*VP with the monomer conversion. Therefore, the length of the two blocks can be merely tuned by the [VAc]/[Co(acac)$_2$] and the [*N*VP]/[PVAc] ratios for the synthesis of the macroinitiator and the polymerization of the second monomer, respectively. The reverse experiment that consists in initiating the polymerization of VAc by a P*N*VP macroinitiator was disregarded because CMRP of *N*VP is not under a control good enough for yielding very effective macroinitiators. The amphiphilicity of the PVAc-*b*-P*N*VP copolymers was confirmed by micellization in water. Upon hydrolysis of the PVAc block of these copolymers, double hydrophilic PVOH-*b*-P*N*VP copolymers of well-defined structure and composition were collected. Finally, driven by the insolubility of PVOH into methanol, these diblocks self-assembled into micelles in this solvent.

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Supporting Information Available: Text discussing the evidence for the integrity of P*N*VP upon treatment by potassium hydroxide at room temperature in methanol and figures showing IR and ^{1}H NMR spectra for P*N*VP. This material is available free of charge via the Internet at http://pubs.acs.org.

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