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Switching the Inside and the Outside of Aggregates of Water-Soluble Block Copolymers with Double Thermoresponsivity

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Abstract: Water-soluble block copolymers were prepared from the nonionic monomer *N*-isopropylacrylamide (NIPA) and the zwitterionic monomer 3-[*N*-(3-methacrylamidopropyl)-*N*,*N*-dimethyl]ammoniopropane sulfonate (SPP) by sequential free radical polymerization via the RAFT process. Such block copolymers with two hydrophilic blocks exhibit double thermoresponsive behavior in water: the poly-NIPA block shows a lower critical solution temperature, whereas the poly-SPP block exhibits an upper critical solution temperature. Appropriate design of the block lengths leads to block copolymers which stay in solution in the full temperature range between 0 and 100 °C. Both blocks of these polymers dissolve in water at intermediate temperatures, whereas at high temperatures, the poly-NIPA block forms colloidal hydrophobic associates that are kept in solution by the poly-SPP block, and at low temperatures, the poly-SPP block forms colloidal polar aggregates that are kept in solution by the poly-NIPA block. In this way, colloidal aggregates which switch reversibly can be prepared in water, and without any additive, their “inside” to the “outside”, and vice versa. The aggregates provide microdomains and surfaces of different character, which can be controlled by a simple thermal stimulus.

Introduction

Two different types of water-soluble block copolymers are typically distinguished, namely amphiphilic block copolymers and double-hydrophilic block copolymers. Amphiphilic block copolymers are typically composed of a hydrophobic, water-insoluble block that associates in aqueous solution and of a hydrophilic block that prevents the aggregates from precipitation.[1] Due to the similarity of such aggregates to micelles made from low molar mass surfactants,[2−5] amphiphilic block copolymers are often referred to as "macrosurfactants”. Such macrosurfactants are, for example, discussed for enzyme encapsulation, or the transport and targeting of drugs.[6−10]

The particular structure of double-hydrophilic block copolymers,[11−18] i.e., of copolymers combining two different hydrophilic blocks, enables one of the blocks to undergo physical or chemical transformations in aqueous solution which render them insoluble, while the copolymer stays in solution by virtue of the hydrophilicity of the other block. Within other possible uses, such polymers find increasing interest in ion sequestering in water,[15,16] or in the transfection of cells.[17,18]

An interesting combination of the two types of block copolymers described above is double-hydrophilic block copolymers in which one of the hydrophilic blocks is thermoresponsive, i.e., undergoes a transition from soluble to insoluble in water.[14] Typically, most reports on such systems exploit the wide-spread occurrence of a lower critical solution temperature (LCST) of nonionic polymers in water. When passing above the critical temperature, one of the hydrophilic blocks collapses, thus creating hydrophobic microdomains in analogy to macro-

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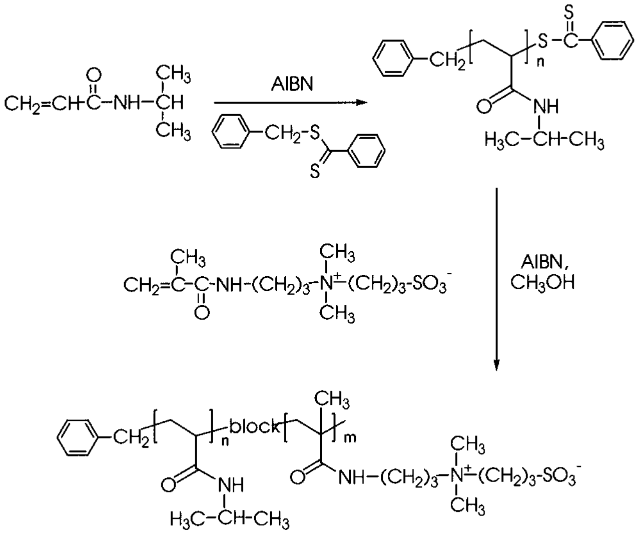
surfactants. Or, applying the thermal stimulus in the other direction, the aggregates formed by such block copolymers are dissociated by lowering the temperature below a critical value. This strategy can be used to trigger the release of encapsulated materials, e.g. for controlled drug delivery.[19] Alternatively, though rarely done, the existence of an upper critical solution temperature (UCST) can be exploited for thermoresponsive behavior, too.[20,21]

Unfortunately, the synthesis of block copolymers containing hydrophilic blocks is inherently difficult, because hydrophilic monomer units typically contain electrophilic and/or nucleophilic fragments that interfere with most living polymerization methods. Therefore, amphiphilic block copolymers[22−24] are more frequently encountered than double-hydrophilic ones. Most of the systems reported are made by anionic polymerization (including group transfer polymerization) using ethylene-oxide,[5,14,23] or monomers with a tertiary amine moiety,[24−27] due to their chemical inertness under such conditions. Other often used hydrophilic blocks are made from *tert*-butylacrylate and methacrylate, requiring a second reaction step after polymerization to hydrolyze the hydrophobic ester groups into polar acid ones.[1,4,7,14,24] Characteristically, the hydrophilicity of tertiary amines and of carboxylic acids depends on the extent of their protonation, or deprotonation, respectively, i.e., hydrophilicity varies strongly with the pH.

Recently, more complex thermoresponsive polymers were reported having two blocks presenting a LCST each. In this way, the block copolymers are dissolved in water molecularly, or in colloidal form, or they are insoluble, depending on the temperature and the ionic strength or the pH.[25,26] Most recently, a system was reported based on poly(propylene oxide)-*block*-(2-(diethylamino)ethyl methacrylate) (PPO-*b*-DEAEM) that exploits the different pH dependencies of the LCSTs of both blocks.[27] Thus, the nature of the micellar core of the aggregates is determined by the conditions, allowing the inside and outside block to change by a combined pH and temperature stimulus. This most interesting approach requires nevertheless the use of additives that will accumulate after repeated switching and thus inevitably limit the number of possible switching cycles.

We have now addressed a new type of complex, switchable block polymers with double thermoresponsivity, using two blocks of which one presents a LCST whereas the other presents an UCST. Depending on the relative positions of the UCST and the LCST, such a design can result in polymers which either are associated at low and at high temperatures, but are insoluble at intermediate temperatures, or, as studied by us, form colloidal aggregates at low and at high temperatures, while being dissolved at intermediate temperatures (cf. Scheme 1). Importantly, this design leads to a thermally triggered exchange of the molecular fragments which form the inner core of the aggregate and those which form the hydrophilic "corona" around the core.

Scheme 1. Outline of the Synthesis of the Block Copolymers by the RAFT Method



Results and Discussion

(a) Synthesis of the Block Polymers. Water-soluble block copolymers were prepared from the nonionic monomer *N*-isopropylacrylamide (NIPA) and the zwitterionic monomer 3-[*N*-(3-methacrylamidopropyl)-*N*,*N*-dimethyl]ammoniopropane sulfonate (SPP). The homopolymer of NIPA is known to exhibit a lower critical solution temperature (LCST) in aqueous solution in the range of 32−34 °C,[28,29] while the polymer of SPP exhibits an upper critical solution temperature (UCST). Whereas the position of the LCST of poly-NIPA depends only a little on the molar mass when exceeding 10^4 Da,[28] and becomes virtually independent for molar masses higher than 5×10^4 Da,[29] the UCST of poly-SPP increases markedly with the molar mass. Block copolymers were prepared by the RAFT (Reversible Addition Fragmentation chain Transfer) process, a recent method of "controlled" free radical polymerization.[30] Good control on molar masses with monomer conversion, on polydispersities, and on end-group functionalization is achieved in this process by adding a dithioester,[30,31] or related compounds,[32] as chain transfer agents. Because the RAFT agent terminates the growing polymer chain by transferring the functional moiety, the terminated polymer will serve as a macromolecular chain transfer agent itself, thus leading to degenerative chain transfer. Moreover, such end group functionalized polymers can be isolated and employed as a macromolecular chain transfer agent in a second polymerization reaction, using a different monomer to obtain block copolymers.[30] Due to the inertness of the process to protic solvents such as water, and due to its efficiency even in diluted monomer solutions, the RAFT process is very

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promising for the synthesis of even complex hydrophilic block copolymers, as exemplified recently.[33,34]

A good control of polymerization of the first block is essential for the synthesis of block copolymers. For the block copolymer poly(methyl methacrylate-*b*-styrene) for instance, the right choice of the first block was crucial for its efficient synthesis; the methacrylate block should be prepared first.[35] Similarly in our case, the choice of the first block was essential when performing the controlled free radical polymerization in the presence of the simple compound, in particular as the very simple RAFT agent benzyl dithiobenzoate (BDTB) was employed. Studies in our laboratory demonstrated that BDTB does not control the reaction of methacrylic monomers,[36] whereas it controls the polymerization of acrylates and acrylamides in agreement with the reports of Rizzardo et al.[30] Therefore, the poly-NIPA block was synthesized first, and the polymethacrylamide block second, as outlined in Scheme 1, although such a sequence has not been recommended for other RAFT agents.[35] To minimize the increasing risk of incomplete end group functionalization with the RAFT moiety of the first block—as needed to attach the second block—with ongoing reaction, the polymerization of the first block was stopped at the moderate conversion of 27%. We want to emphasize that our strategy successfully provided block copolymers, but it implies neither that blocks with low polydispersities are made nor that the efficiency of grafting of the second block is close to quantitative. However, the RAFT approach is experimentally much simpler to implement than classical living cationic or anionic polymerization procedures,[1] and enables the use of functional monomers such as SPP that for multiple reasons are not suited for these methods.

Capillary viscometry was used to determine the viscosity average molar mass (M_η) of the poly-NIPA block by applying the standard Mark−Houwink−Sakurada relation with the reported parameters of $K = 0.1.12$ mL/g and $\alpha = 0.51$.[37,38] The measured intrinsic viscosity of poly-NIPA of 12.8 mL/g provides thus a value of $M_\eta = 10\,800$ g/mol for the average molar mass. This value is somewhat lower than the theoretical value of 15300 g/mol, calculated for a (pseudo)living system according to the relation for the number average molar mass M_n = conversion $\times$ [monomer]/[RAFT agent], assuming a low polydispersity so that $M_n \sim M_\eta$.

Alternatively, we estimated the number average molar mass by end group analysis, exploiting the $n-\pi^*$ absorbance band of the dithioester RAFT moieties at about 500 nm. Assuming that the extinction coefficient of the chromophore is identical for BDTB (determined as 106 $L \cdot mol^{-1} \cdot cm^{-1}$ in ethanol) and for the polymer, and that the poly-NIPA blocks are fully end group functionalized, we obtained $M_n = 19\,800$ g/mol. This value is somewhat higher than the theoretical one, but nevertheless close to it, suggesting a high degree of end-group functionalization.

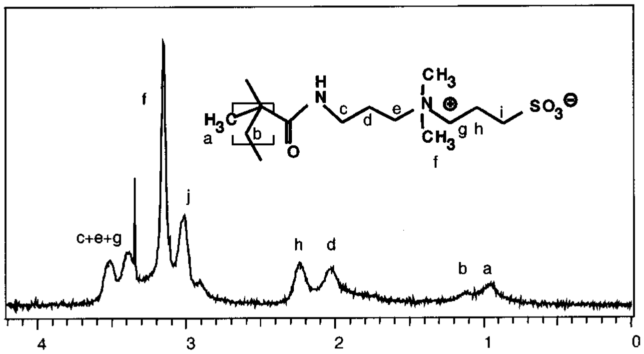

Figure 1. ^1H NMR spectra of poly-SPP in D_2O at 25 °C.

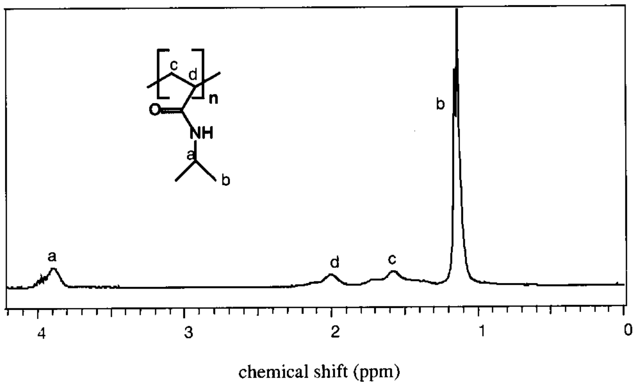

Figure 2. ^1H NMR spectra of poly-NIPA in D_2O at 25 °C.

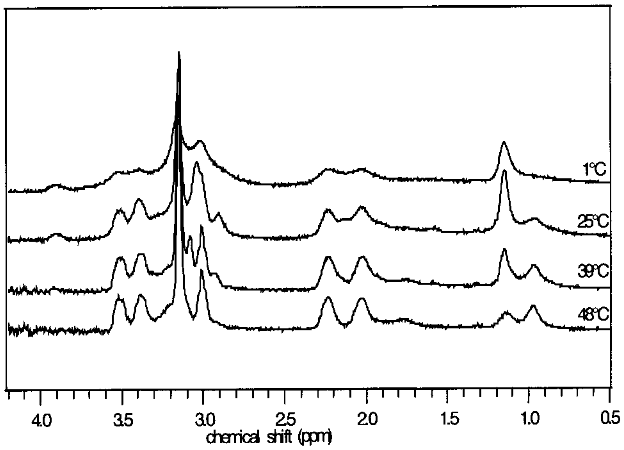

Figure 3. Evolution of ^1H NMR chemical shift δ of a solution of block copolymer CP180 in D_2O with temperature.

The block copolymers were synthesized in methanol. The solution became turbid after 2 h of polymerization, but no precipitate was observed during the whole reaction. The isolation and purification of the block copolymers were complicated. To separate the block copolymers from eventual homopolymer contaminations, the products were repeatedly precipitated from different solvents. No clean poly-NIPA could be recovered during the purification steps of the block copolymers, but a small amount of poly-SPP was recovered. Finally, the block copolymers were separated from residual amounts of monomer SPP by dialysis. The ^1H NMR spectrum of the block copolymer taken at 25 °C superposes the characteristic peaks of poly-SPP (Figure 1) and of poly-NIPA (Figure 2), as shown in Figure 3. In the spectra, the signal at 3.8−4.0 ppm is typical for poly-NIPA

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Table 1. Characteristic Data of Block Copolymers CP33 and CP180

	poly-NIPA block		poly-SPP block	
sample	monomers units[a]	M_n (g/mol)[a]	monomers units[b]	M_n (g/mol)[b]
CP33	95	10 800	33	9 700
CP180	95	10 800	180	52 800

[a] Determined by viscometry before use in copolymerization, assuming no changes during copolymerization and workup. [b] Calculated from relative signal intensities of characteristic peaks in ^{1}H NMR, assuming conditions as footnote *a*.

Table 2. Cloud Points of Aqueous Solutions of Poly-NIPA and Poly-SPP and Their Block Copolymers CP33 and CP180 Determined by Turbidimetry during Heating and Cooling Cycles

	upper cloud point (°C)			lower cloud point (°C)		
sample	cooling	heating	OD max	cooling	heating	OD max
poly-SPP	12.5	12.5	0.8			
poly-NIPA				29.8	32.3	2.3
CP33	8.6	8.6	0.45	31.5	33.4	1.4
CP180	18.4	19.9	1.1	31.4	34.3	0.3

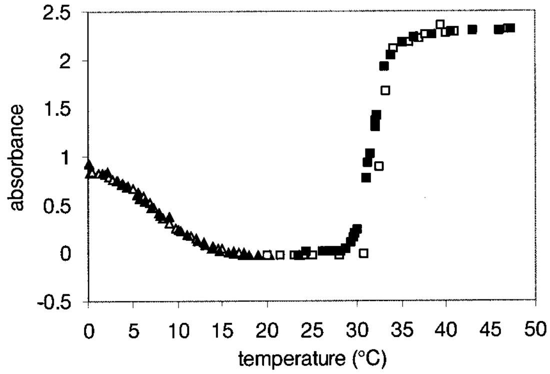

Figure 4. Optical density (at $\lambda = 550$ nm) of an aqueous solution (1 g/L) of homopolymers depending on the temperature: (a) poly-SPP, heating (Δ) and cooling (▲); (b) poly-NIPA, heating (□) and cooling (■).

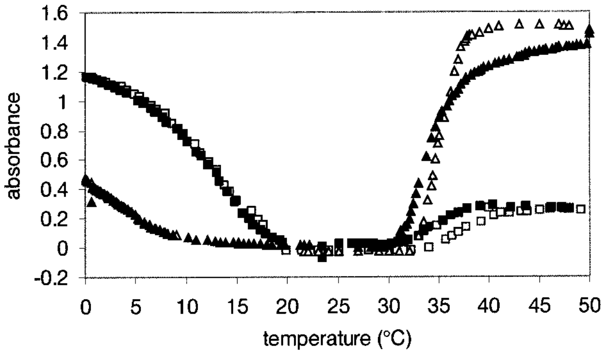

Figure 5. Optical density ($\lambda = 550$ nm) of an aqueous solution (1 g/L) of block copolymers depending on the temperature: (a) polymer CP180, heating (□) and cooling (■); (b) polymer CP33, heating (Δ) and cooling (▲).

(signal **a** in Figure 2) corresponding to one proton. This signal is well resolved from the broad signal complex at 2.8−3.6 ppm that is characteristic for poly-SPP (signals **c** + **e** + **g** + **f** + **j** in Figure 1) and that corresponds to 14 protons. By comparing the relative intensities of these peaks in the block copolymer spectrum, the degree of polymerization of the SPP blocks was estimated, as listed in Table 1. The estimation assumes that the average molar mass of the poly-NIPA blocks incorporated in the copolymer does not differ significantly from the average molar mass of the poly-NIPA block engaged in the copolymerization. The block copolymers were denoted as CP33 and CP180 according to the estimated degree of polymerization of the SPP blocks (cf. Table 1).

(b) Phase Transition Temperatures. Like other polyzwitterions, poly-SPP has the ability to exhibit an upper critical solution temperature (UCST) in water that notably increases with the molar mass. This is attributed to the strong mutual intermolecular attraction of the zwitterionic groups.[39,40] By cooling a transparent solution of 1 g/L of poly-SPP in water, the solution becomes increasingly turbid below a characteristic temperature (Figure 4), indicating the collapse of the polymer coils. Eventually with waiting, the polymer precipitates out. By heating the freshly cooled solution from 0 °C to 20 °C, the solution becomes increasingly clear again, with the curves of the optical density overlapping the cooling curve and no notable hysteresis. The upper cloud point, i.e., the temperature for the given concentration above which the solution becomes clear, was established at 12.5 °C (Table 2). Apparently the range of temperature in which the phase transition occurs is rather broad.

Analogously, at 20 °C, a solution of 1 g/L of the poly-NIPA block used for the synthesis of the block copolymers in water is transparent (Figure 4). With heating above 32 °C, the solution becomes opaque due to the collapse of the poly-NIPA coils and the slow precipitation of the polymer. The phase transition occurs in a very narrow temperature range, different from the thermal transition of poly-SPP. The optical density of poly-NIPA used for the synthesis of block copolymers indicates a lower cloud point (i.e. the temperature for the given concentration below which the solution is clear) of 32.3 °C by heating and of 29.8 °C by cooling (Table 2). Similar values and a similar small hysteresis in the heating and cooling cycles was previously observed in the coil-to-globule transition of individual NIPA chains in water.[41] The effect was explained by the formation of associative intrachain structures. The demixing temperatures of poly-NIPA have been reported to be independent of heating/cooling rates in a wide range of concentrations.[28,42]

As for the homopolymers, the turbidity of aqueous solutions of 1 g/L of block copolymers CP33 and CP180 was studied in the dependence on the temperature (Figure 5). As expected, such solutions are turbid at low as well as high temperatures, while being transparent under ambient conditions. But different from the behavior of the two parent homopolymers, even extended annealing of block copolymer solutions in the temperature ranges where they are turbid does not lead to precipitation. This means that these solutions are at least metastable, the block copolymers being soluble in the whole temperature range, even after collapse of one of the two blocks (cf. Scheme 2).

As for the homopolymer of SPP, no thermal hysteresis was observed at low temperatures for block copolymer CP33, but a small thermal hysteresis was observed for CP180 (Table 2). CP33 presents a phase transition temperature of 8.6 °C whereas the value for CP180 is about 19 °C. These differences are consistent with the general tendency of molar mass dependence

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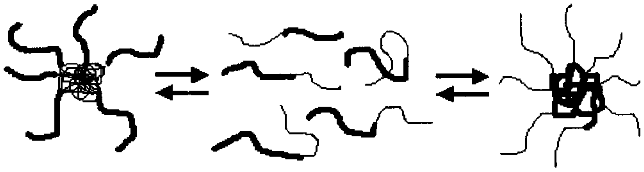
Scheme 2. Simplified Model of the Changing Association of Poly(NIPA-*b*-SPP) Block Copolymers with Temperature



of the UCST of poly-SPP. Obviously, the cloud points of these block copolymers can be tuned via the length of the SPP block.

The lower cloud point temperatures of the block copolymers, due to the collapse of the poly-NIPA block, are listed in Table 2 as well. These temperatures are slightly higher than for the starting poly-NIPA block, and the phase transitions occur in a larger temperature range. Obviously, the poly-SPP block only slightly affects the thermal behavior of the poly-NIPA block. This behavior differs markedly from the effect of similar zwitterionic monomers incorporated in statistical copolymers of poly-NIPA, increasing the LCST dramatically already in small amounts.[43] But our observations agree well with other studies on double-hydrophilic block copolymers containing poly-NIPA, for which only small increases or decreases of the LCST were reported.[44−46] Interestingly, similar small increases of the collapse temperature for poly-NIPA in water were reported recently for adsorbed samples, attributing the delay of the collapse to a hindered conformational rearrangement of the macromolecules by anchoring points.[47] One may assume a similar effect due to the covalent attachment of the poly-SPP block.

There is another interesting point in the turbidimetric studies. The curves in Figure 5 show that the block copolymer that presents a high turbidity at low temperatures, namely CP180, gives a low turbidity at high temperatures, and vice versa. Both copolymers are studied at the same mass concentration, at 1 g/L. So, while the length of the poly-NIPA block is the same in both block copolymers, the relative content of poly-NIPA is higher in copolymer CP33 than in CP180. Presumably, solutions of CP180 are less turbid above the lower cloud point because the longer hydrophilic block can stabilize smaller poly-NIPA aggregates. Inversely, below the upper cloud point, solutions of CP33 are less turbid because the higher content of poly-NIPA can stabilize smaller poly-SPP aggregates.

Figure 3 presents the ^{1}H NMR spectra of CP180 in water at different temperatures. In the intermediate temperature range, i.e., above the UCST and below the LCST, the relative intensities of the various NMR signals are constant, but beyond this range, the shape of the spectra varies with the temperature. Already qualitatively one can see that the signals characteristic for the poly-NIPA block (cf. Figure 2) diminish at high temperatures, whereas many signals characteristic for the poly-SPP block (cf. Figure 1) diminish at low temperatures (Figure 6). The changes of the signals of the poly-NIPA block happen rather suddenly upon heating to about 34 °C, i.e., basically at the same transition temperature as the onset of turbidity. In contrast, the changes of the signals of the poly-SPP block occur more gradually when cooling the solutions below around 21 °C, again in parallel to the gradual onset of turbidity. Figure 6 presents the relative intensities of four different characteristic proton signals of CP180. The signal at 3.15 ppm belongs to the methylammonium groups in the zwitterionic side chains of poly-SPP (6H, **f** in Figure 1), while the signal at 1.05 ppm belongs to the methyl group of its polymer backbone (3H, **a** of Figure 1). Typical for the poly-NIPA block is the signal at 3.90 ppm as discussed above (cf. Figure 2). The signal at 1.15 ppm derives from both blocks, namely from the methyl groups of the isopropyl fragment of the poly-NIPA block (6H, **b** in Figure 2) as well as of the methylene group in the polymer backbone of poly-SPP (2H, **b** in Figure 1). This signal may contain also small contributions of the methyl group in the polymer backbone of poly-SPP (signal **a** in Figure 1), as the chemical shift of these protons varies markedly for the isotactic, syndiotactic, and atactic triades.[48]

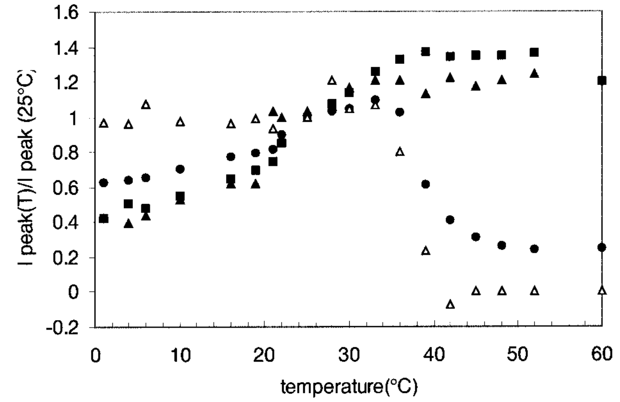


Figure 6. Relative intensities of ^{1}H NMR peaks normalized to the intensity at 25 °C at 1.05 (□), 1.15 (●), 3.15 (■), and 3.90 ppm (Δ) for copolymer CP180 in aqueous solution (1 g/L), depending on the temperature.

Above the LCST, the intensities of the peaks at 1.05 and 3.15 ppm, both indicative of the poly-SPP block, remain stable, and show that the backbone as well as the zwitterionic side chains maintain their “normal” mobility and aqueous environment. In fact, the spectra of the block copolymers look at 40 °C very much like that of homopolymer poly-SPP. In contrast, the signal at 3.90 ppm that is due to the poly-NIPA block drastically decreases in intensity above 34 °C and finally disappears. This loss can be explained by the collapse of the poly-NIPA block, resulting in the formation of a dense hydrophobic core and the expulsion of the hydration water.[47] Similarly, the NMR signal at 1.15 ppm that has a strong contribution from the poly-NIPA block drastically decreases in intensity. But different from the signal at 3.90 ppm, it does not vanish completely but keeps about 25% of the intensity observed at 25 °C. This is attributed to the contribution of protons of the poly-SPP backbone (cf. Figure 1).

Below the UCST, the intensity of the peak at 3.90 ppm stays constant, but the intensities of the signals at 3.15, 1.15, and 1.05 ppm (Figure 6) decrease. The peak at 1.05 ppm that is indicative of the methyl fragment on the backbone of the poly-SPP block disappears completely at 1 °C. In contrast, residual

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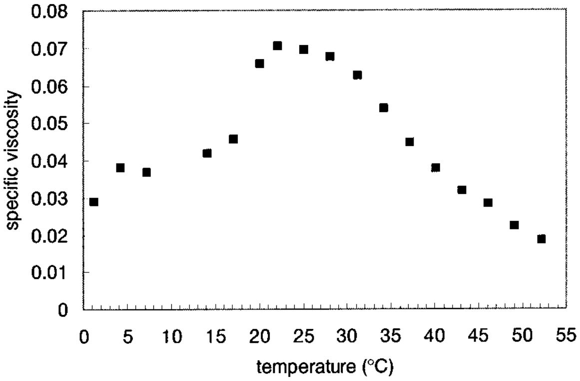

Figure 7. Evolution of the specific viscosity of an aqueous solution of block copolymer CP180 in aqueous solution (5.5 g/L) depending on the temperature.

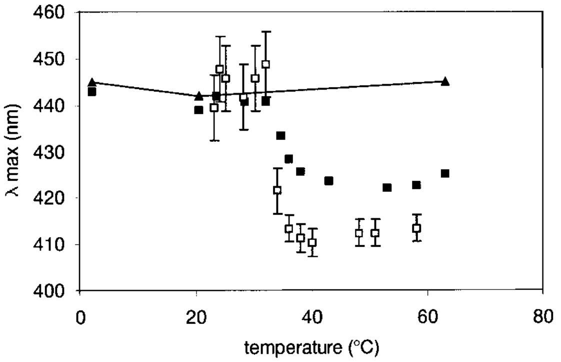

Figure 8. Wavelength of the absorbance maximum (λ_{max}) of 2-anilinonaphthalene (2-AN) in aqueous solutions, depending on the temperature, λ_{exc} = 294 nm: (a) without polymer (▲); (b) for 1 g/L of copolymer CP180 (■); and (c) for 1 g/L of copolymer CP33 (□).

signals at 3.15 and 1.15 ppm are still visible. Their relative intensities seem to be similar, with about half of the original value at 25 °C. Presumably in the case of the signal at 1.15 ppm the observed loss of intensity results from the disappearance of the proton signal of the methylene fragment in the backbone of the poly-SPP block, while the contribution from the poly-NIPA block persists. The situation is different for the peak at 3.15 ppm. The complete group of signals in the range of 2.8 to 3.6 ppm, which is exclusively attributed to poly-SPP, namely to the zwitterionic side chains, is still visible even at 1 °C, though reduced in intensity. We therefore conclude that at low temperatures, the fragments of the polymer backbone and of the zwitterionic side chains behave differently. The backbone seems to be completely dehydrated and strongly immobilized while the hydration of zwitterionic side chain remains important as does their mobility even after the polymer coil has collapsed.

The thermal transitions are seen in the viscometric measurements also. Figure 7 shows the specific viscosity of aqueous solutions of block copolymer CP180 depending on the temperature. This measurement indicates how the hydrodynamic radius of the block copolymer evolves with the temperature. The shape of the curve shows a sharp increase of viscosity, and thus of the hydrodynamic radius, at about 20 °C, corresponding to the upper cloud point. The specific viscosity passes a maximum upon further heating and then slowly decreases until 33 °C, i.e., until reaching the lower cloud point of the poly-NIPA block. For higher temperatures, the viscosifying effect is markedly reduced.

Between the two cloud points, the polymer exists as an extended coil in dilute aqueous solution. For higher or lower temperatures, one of the blocks is collapsed. As the collapsed chains form aggregates, it is not self-evident whether the viscosifying effect should decrease due to the reduced dimensions of the individual polymer chains or whether it should increase due to the polymer association. In the case of poly(NIPA-*g*-ethylene oxide), Tenhu and co-workers[49] observed the formation of aggregates by light scattering above the LCST. Simultaneously, the viscosity decreased because the dynamic flow tends to break the aggregates through the capillary. The case here of CP180 seems similar. The reduction in viscosity indicates the shrink from an extended conformation to a collapsed one, thus reducing the hydrodynamic radius. Below the upper cloud point, a similar rheological behavior is observed due to the collapse of the poly-SPP block.

(c) Selective Solubilization of a Fluorescence Probe. The fluorescence probe 2-anilinonaphthalene (2-AN) was used to investigate whether the aggregates formed above the lower cloud point or below the upper cloud point, respectively, were able to solubilize hydrophobic molecules in water. 2-AN is very sensitive to its surrounding polarity, the emission wavelength decreasing with the polarity.[50]

Figure 8 presents the maximum emission wavelength of 2-AN in aqueous solutions of the block copolymers as a function of temperature. A pure aqueous solution saturated with 2-AN emits at 445 nm in the temperature range studied. Similarly, solutions of CP33 and CP180 emit at about 444−445 nm when below the LCST. This observation suggests that there is no particular interaction between the probe and the block copolymers when dissolved. This is even true when the temperature goes below the UCST, where the poly-SPP block forms aggregates (Scheme 2). The latter contains apparently a polar core that is not suited for the solubilization of a hydrophobic probe such as 2-AN.

However, when the thermal transition of the poly-NIPA block occurs, the emission wavelength decreases sharply in the temperature interval between 34 and 40 °C (Figure 8). For higher temperatures, the value becomes nearly constant. According to the data of solvatochromism reported for 2-AN,[50] the spectral shift indicates a transfer of the probe from a hydrophilic environment to a more hydrophobic surrounding. This can be explained by the formation of hydrophobic microdomains in the aggregates formed by poly-NIPA which can solubilize the probe.

Above the lower cloud point, the emission wavelength of the probe is about 10 nm lower in the presence of CP33 than in the presence of CP180 (Figure 8), indicating a more hydrophobic environment. However, in both block copolymers, the poly-NIPA block has the same size. Therefore, the difference between the two polymers must be due to the different lengths of the poly-SPP block. Possibly, when aggregates are formed, this block acts as a barrier to the diffusion of 2-AN into the newly formed hydrophobic domains, so that the access is more hindered for CP180 having the longer poly-SPP block. Alternatively, the longer poly-SPP block might hamper efficient

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packing of the hydrophobic block, leading to smaller or less dense micellar cores. A possibly related observation was discussed above already concerning the temperature-dependent turbidities of CP33 and CP180 (cf. Figure 5).

Conclusions

The use of a simple RAFT agent allows the synthesis of a block copolymer containing two different hydrophilic blocks. Each block is thermosensitive, exhibiting an UCST and a LCST for one or the other of the blocks. The block copolymers could be purified from residual monomer and homopolymers, and show some intriguing properties.

First of all, thermal transitions occur in aqueous solution at low and at high temperatures, very close to the transition temperatures observed for the homopolymers. The transition temperature at low temperatures depends on the length of the zwitterionic poly-SPP block and can thus be adapted according to the needs. Different from the parent homopolymers, the diblock copolymers stay in solution throughout the full temperature range studied. This implies that, while the soluble second block keeps the aggregates in solution, micellar domains with very different polarities are formed at low and high temperatures from the block, which is collapsed under the given conditions. The microdomains formed at low temperatures are rather polar and not able to solubilize hydrophobic probes, whereas the microdomains formed at high temperatures are unpolar and able to do so. Heating or cooling allows a reversible switch between the different forms of aggregation, without requiring any external additive (such as salt, acid, or base). This variation of the polarity of the micellar cores opens the possibility of solubilizing different compounds in a given solution just by varying the temperature.

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Supporting Information Available: Details of the synthesis and purification of the block copolymers and of the analytical methods (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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