Grafting of Poly(*N*-isopropylacrylamide) with Poly(ethylene oxide) under Various Reaction Conditions

Janne Virtanen,[†] Caroline Baron,[‡] and Heikki Tenhu*,[†]

Laboratory of Polymer Chemistry, University of Helsinki, PB 55, FIN-00014 HY, Finland, and INSA de Rouen, Place Emile Blondel, 76130 Mont Saint Aignan, France

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ABSTRACT: Poly(*N*-isopropylacrylamides) grafted with varying amounts of poly(ethylene oxide) (PNIPA-*g*-PEO) were synthesized and studied with differential refractometry, differential scanning calorimetry, and dynamic light scattering. By free radical reaction between *N*-isopropylacrylamide (NIPA) and either *N*-acryloylsuccinimide (NASI) or glycidyl methacrylate (GMA), two functional copolymers, PNIPA-*co*-NASI ($M_w = 1.9 \times 10^5$) and PNIPA-*co*-GMA ($M_w = 1.8 \times 10^5$), were synthesized. Various amounts of PEO ($M_w = 6000$) were attached to the functionalized backbones either in dioxane or in water. Thermal behavior of PNIPA-*g*-PEO copolymers in aqueous solutions both below and above LCST depends on the amount of PEO grafts and on the polymer concentration. Above the LCST, the size of the aggregates of the graft copolymers sterically stabilized by a low number of PEO grafts is dependent on these two factors. Factors determining the shrinking and collapse of PNIPA-*g*-PEO include hydrophobic interactions, intra- and interchain interactions, and the solubilizing effect of PEO on the shrinking backbone.

Introduction

Polymeric micelles are a class of self-assembling materials that have been intensively studied.[1] Also, much attention has been paid to amphiphilic block and graft copolymers owing to their capability to build up aggregates with a core−shell structure in solution.[2,3] Amphiphilic graft copolymers having poly(ethylene oxide) as a hydrophilic segment have been the issue of interest from the viewpoints of their preparation methods and physicochemical properties such as low protein and cell adhesion in aqueous systems.[4] Polymeric micelles may have several applications. From the medical point of view, they are potential drug carriers in corresponding delivery systems.

Responsive polymers, i.e., polymers that respond to external chemical and physical stimuli like temperature, pH, ionic strengh, solvent composition, electric field, and light, have recently attracted noticeable attention.[5−9] Poly(*N*-isopropylacrylamide) (PNIPA) is one of the most studied responsive polymers that exhibits a lower critical solution temperature (LCST) in water around 32 °C. This paper describes the syntheses of linear graft copolymers, for which PNIPA was chosen as a hydrophobic core because of its thermosensitivity. For a hydrophilic shell, poly(ethylene oxide) was chosen because of its high solubility in water in a wide temperature range, also above the LCST of PNIPA.

A widely used procedure to synthesize graft copolymers starts from the preparation of a functional backbone.[3,10−12] For instance, Wesslen and Wesslen employed the method to prepare polymeric precursors for further PEO substitution, obtaining comb-shaped graft polymers.[10] One of the aims of this work was to explore a proper synthetic route for a well-defined PEO-grafted PNIPA. The first stage was the preparation of a functionalized backbone polymer. Second, various amounts of PEO were connected to the backbone under different conditions. The competition between hydrophobic interactions in PNIPA and the solubilizing effect of PEO on the shrinking backbone was studied by differential scanning calorimetry and dynamic light scattering to find out the effects of the number and distribution of the PEO grafts on the properties of the polymers.

The purpose of carring out the grafting reaction in water at two different temperatures was to explore how the conformation of PNIPA affects the chemical composition and thermal properties of the product graft copolymer. The hydrodynamic volume of the backbone was expected to affect the localization of the PEO chains in the graft copolymer. A concept on "proteinlike copolymers" has recently been introduced by Khokhlov et al.[13,14] According to the theoretical model by these authors, a copolymer consisting of structural units with different solubilities may remember the conformation in which it has been synthesized and under favorable conditions tends to readopt this conformation.

In this study, the number of PEO chains bound to PNIPA was varied in a wide range. The purpose was to find out the effect of the grafts on the LCST, as well as on the aggregate formation of the copolymers. Of special interest has been to see whether the polymers grafted in water at different temperatures show any differences in their chemical composition and thermal behavior.

Experimental Section

Materials. The monomer *N*-isopropylacrylamide (NIPA, Polysciences, Ins.) was used as received. *N*-Acryloylsuccinimide (NASI) was obtained through the reaction of *N*-hydroxysuccinimide (Fluka) and acryloyl chloride (Fluka) in chloroform, catalyzed by triethylamine (Fluka).[15] Glycidyl methacrylate (GMA, Aldrich) was distilled in vacuo and stored in a freezer. Amino-terminated poly(ethylene oxide) (NH_2-PEO, Shearwater Polymers) with $M_w = 6000$ g/mol was used as received. Azobis(isobutyronitrile) (AIBN) was recrystallized twice from methanol. Isopropylamine (IPA, Fluka) and diethylamine (DEA, Riedel-de Haën) were used as received. Dioxane (Lab-Scan, Analytical Sc.) was distilled. The water used for all the mearurements was purified and deionized in an Elgastat UHQ-PS purification system.

[†] University of Helsinki.
[‡] INSA de Rouen.
* Correspondence author.

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Table 1. Summary of Reaction Conditions and Compositions of Linear and Graft Polymers

sample	T (°C)	t (h)	AIBN (mg)	conc (g/L)/ a solvent	DEA or IPA (g/L)	comonomer (mol %) PEO (mol %) in feed	comonomer (mol %) PEO (mol %) in polymer[a]	no. of PEO grafts[b]	mass % of PEO (wt %)	M_w (g/mol)
PNIPA-*co*-GMA	70	7	10	176/dioxane		5.0	1.5			1.80×10^5 [c]
PNIPA-*g*-PEO-6/15	15	120		10/water		2.3	0.38	6	17	2.16×10^5 [d]
PNIPA-*g*-PEO-7/29	29	120		10/water		2.3	0.44	7	19	2.22×10^5 [d]
PNIPA-*g*-PEO-10	reflux	72		126/dioxane	140	3.0	0.6	10	25	2.40×10^5 [d]
PNIPA-*co*-NASI	70	18	10	207/dioxane		2.5	4.0			1.90×10^5 [c]
PNIPA-*g*-PEO-43	35	18		177/dioxane	21	5.3	2.5	43	57	4.48×10^5 [d]
PNIPA-*g*-PEO-51	reflux	5		177/dioxane	21	5.3	3.0	51	61	4.96×10^5 [d]
PNIPA-*g*-PEO-57	reflux	18		177/dioxane	21	5.3	3.3	57	65	5.32×10^5 [d]
PNIPA-*g*-PEO-79	reflux	66		177/dioxane	21	5.3	4.0	79	72	6.64×10^5 [d]

[a] Determined by ^{1}H NMR or ^{13}C NMR. [b] Determined by ^{13}C NMR. [c] Measured by static laser light scattering. [d] Calculated by M_w(backbone polymer) + number of PEO grafts × M_w(PEO).

Table 2. Thermal Behavior of Polymers by Differential Scanning Calorimetry

sample	concn (wt %)	onset T (°C)	ΔH (J/g)	reduction in ΔH (%)[a,b]
PNIPA-*co*-GMA	26.3	28.4	44.8	
PNIPA-*g*-PEO-6/15	29.2	26.8	34.9	−22
PNIPA-*g*-PEO-7/29	28.5	27.6	31.8	−29
PNIPA-*g*-PEO-10	28.8	27.7	29.5	−34
PNIPA-*co*-NASI	30.3	26.5	33.2	
PNIPA-*g*-PEO-43	34.7	47.9	1.5	−95
PNIPA-*g*-PEO-51	30.0	49.6	0.6	−98
PNIPA-*g*-PEO-57	35.4	48.4	2.8	−92
PNIPA-*g*-PEO-79	30.9	47.8	1.7	−95

[a] For PNIPA-*g*-PEO-6/15, -7/29, and -10: $-[(\Delta H_{\text{PNIPA-}co\text{-GMA}} - \Delta H_{\text{PNIPA-}g\text{-PEO}})/\Delta H_{\text{PNIPA-}co\text{-GMA}}] \times 100\%$. [b] For PNIPA-*g*-PEO-43, -51, -57, and -71: $-[(\Delta H_{\text{PNIPA-}co\text{-NASI}} - \Delta H_{\text{PNIPA-}g\text{-PEO}})/\Delta H_{\text{PNIPA-}co\text{-NASI}}] \times 100\%$.

Syntheses (Table 1). *PNIPA-co-GMA.* NIPA was dissolved in dry dioxane and flushed with nitrogen for 30 min. AIBN was added when the mixture reached 70 °C. GMA was added dropwise in a period of the first 2 h of polymerization. The copolymer was precipitated twice into diethyl ether and dried in vacuo for 24 h. M_w/M_n measured by GPC calibrated with polystyrene standards was 3.4.

PNIPA-g-PEO-6/15 and PNIPA-g-PEO-7/29 were synthesized by grafting PNIPA-*co*-GMA in aqueous solutions in a double-wall reaction vessel at two different temperatures, 15 and 29 °C. The stability of temperatures was ensured for 48 h before the actual reactions. NH_2-PEO was added after dissolving PNIPA-*co*-GMA in pure water, and the mixture was stirred for a week. The graft copolymers were purified in dialysis and dried in vacuo.

PNIPA-g-PEO-10 was prepared from PNIPA-*co*-GMA and NH_2-PEO in dioxane with stirring at refluxing temperature for 3 days (72 h). The reaction mixture was cooled at room temperature, and DEA was added to quench the excess epoxide groups. The mixture was stirred for 2 h. The grafted polymer was isolated by precipitation into diethyl ether. The graft copolymer was finally purified by dialysis.

PNIPA-co-NASI. NIPA and NASI were dissolved in dry dioxane and flushed with nitrogen for 30 min. The reaction mixture was heated to 70 °C, and AIBN was added. After 18 h the polymer was precipitated in diethyl ether. The reprecipitation was carried out from acetone into diethyl ether. The copolymer was dried in vacuo for 24 h at room temperature.

PNIPA-g-PEO-79, -57, -51, and -43. PNIPA-*co*-NASI and NH_2-PEO were dissolved in dry dioxane, and the reaction was carried out at elevated temperature. After the reaction the mixture was cooled at room temperature. Isopropylamine was added to consume unreacted NASI in a period of 2 h (see Table 1). The purification of the graft polymers was carried out by dialysis.

Instrumentation and Characterization. *NMR Spectroscopy.* ^{1}H and ^{13}C NMR spectra of the synthesized polymers were measured with a 200 MHz Varian Gemini 2000 spectrometer using $CDCl_3$ as a solvent. The compositions of the copolymers PNIPA-*co*-GMA and PNIPA-*co*-NASI were determined by ^{1}H NMR from the characteristic peaks of the monomers. PNIPA-*co*-GMA: ^{1}H NMR ($CDCl_3$) [200 MHz] δ ppm: 3.95 (br, 1H, −NH−C*H*−Me_2) for NIPA, 3.25 (br, 1H, −O−CH_2−C*H*−Epox) for GMA. PNIPA-*co*-NASI: ^{1}H NMR ($CDCl_3$) [200 MHz] δ ppm: 4.03 (br, 1H, −NH−C*H*−Me_2) for NIPA, 3.18 (br, 4H, COCH_2CH_2CO) for NASI. The compositions of the graft copolymers were calculated using the characteristic peaks of PEO and NIPA in the ^{13}C NMR spectra. ^{13}C NMR ($CDCl_3$) [200 MHz] δ ppm: 70.6 for PEO (−CH_2−, EO-homosequence), 22.7 for NIPA (CH_3−).

Light Scattering. Static light scattering (SLS) and dynamic light scattering (DLS) measurements were conducted with a Brookhaven Instruments BI-200SM goniometer and a BI-9000AT digital correlator. The light source was Spectra Physics model 127 helium/neon laser (633 nm, 35 mW). Time correlation functions were analyzed with a Laplace inversion program (CONTIN). The range of polymer concentrations was 0.1−5.0 mg/mL. The solutions were filtered through Millipore membranes (0.22 μm pore size). Experiments were carried out in a temperature range from 20 to 60 °C, at the scattering angle of 90°. At each temperature the samples were equilibrated from 20 to 60 min.

Differential Scanning Calorimetry. Phase transition temperatures and the corresponding enthalpy changes of the copolymers were measured with a Perkin-Elmer DSC7. Polymer concentrations varied from 26 to 35 wt %. The samples were heated with the rates of 3 and 5 °C/min. The onset temperature was taken as the transition temperature. The enthalpy change is given per mass of the polymers.

Refractive Index Increment Measurements. The determination of the refractive index increment of a graft copolymer was conducted with a KMX-16 laser differential refractometer using a He−Ne light source with a wavelength 633 nm. dn/dc was also calculated using the equation[16]

$$dn/dc = w_A(dn/dc)_A + w_B(dn/dc)_B \quad (1)$$

in which w_A and w_B are the mass fractions of pure polymers PNIPA and PEO and $(dn/dc)_A$ and $(dn/dc)_B$ their refractive index increments, respectively.

Results and Discussion

Grafting of PNIPA with PEO. Several amphiphilic polymers with poly(ethylene oxide) as a hydrophilic segment have been synthesized and studied so far.[10,17−19] Various monomers have been copolymerized by radical polymerization with methacrylate functionalized poly(ethylene oxides) of varying chain lengths. In many cases, however, the focus has been on the kinetic aspects during the early stage of polymerization.[20,21] Qiu et al. managed to prepare a high molecular weight copolymer of NIPA and PEO methacrylate and also were able to study the coil-to-globule transition of a single chain.[22]

Several studies have also been concentrated on the preparation of a functional polymer and its subsequent reaction with a reactive substituent.[11,12,26] In this way a graft copolymer is obtained in a reasonable reaction time without side reactions. In this work, a graft polymer was attempted to be synthesized by a free radical reaction of NIPA and PEO methacrylate. The reaction, however, ended up to gel formation. The occurrence of unwanted cross-linking was independent of the reaction conditions. In the early stage of polymerization, neither the gel formation nor the polymerization of PEO methacrylate occurred, which was verified by ^{1}H NMR. The ethylene oxide repeating unit in PEO and its derivatives has a chain transfer constant of the order of $10^{-3}-10^{-4}$ in the polymerization of vinyl acetate,[23] methacrylates,[24] and acrylonitrile.[25] The cross-linking reaction has also been observed by Bo et al.[3] According to these authors, the presence of long poly(ethylene oxide) chains in the copolymers gives a high probability for the chain transfer to polymer. The prevention of cross-linking of any kind in the graft polymer was one of the aims in this work. Monomers NASI and GMA were chosen as functional groups because their reactivity toward primary amine groups is reasonably high.[11,12,26-28] However, the longer is the PEO chain, the longer the reaction time needed. This may be understood by the probability of a long PEO chain to shield the functional amine end group.[20] Because of this effect, PEO was used in excess. The graft copolymers with varying amounts of PEO chains were synthesized in an organic solvent, except PNIPA-*g*-PEO-6/15 and PNIPA-*g*-PEO-7/29. Both PNIPA and NH_2-PEO are well soluble in dioxane whereas in water the solubilities of the polymers depend strongly on temperature.

The monomer ratios in the feed and in the final copolymers PNIPA-*co*-GMA and PNIPA-*co*-NASI are summarized in Table 1. Since preliminary experiments had shown GMA to be more reactive than NIPA in a radical polymerization, GMA was slowly added in drops into the polymerization mixture. This method was expected to produce a copolymer with a random distribution of GMA units in the backbone. The high reactivity of GMA has also been observed and studied in the copolymerization with *N*-vinylpyrrolidone.[3,29]

The reaction of NH_2-PEO with NASI proceeded quickly, but for that with GMA, longer reaction time was needed. The latter reaction is known to be fast in an alkaline solution;[30] in the present case, however, it was necessary to conduct the reactions in pure solvents. The adjustment of the number of PEO grafts on the PNIPA-*co*-NASI turned out to be more difficult than expected. Owing to the difference in the reactivities of GMA and NASI, the attachment of only a low number of PEO chains was relatively easy in the case of PNIPA-*co*-GMA. The grafting of PNIPA-*co*-GMA in aqueous solutions at 15 and 29 °C was allowed to proceed for 5 days to ensure that all the epoxy groups available have reacted. It turned out that the product copolymers contained slightly different amounts of PEO, this most probably being due to different conformations of the parent polymer during the reaction.

Because the active ester of NASI was reacted with isopropylamine after the grafting, it may well be assumed that the differences in the behavior of polymers derived from PNIPA-*co*-GMA and PNIPA-*co*-NASI are due to a considerable difference in the number of PEO grafts but not to the choice of the reactive comonomer.

Refractive Index Increment. Upon heating of an aqueous solution of PNIPA-*g*-PEO, PNIPA collapses at the vicinity of its LCST due to hydrophobic interactions whereas PEO chains face mostly outward on the surface of the PNIPA globules. Thus, PEO forms a hydrophilic outer shell which sterically stabilizes the globular aggregates; the aggregates may be regarded as nanoparticles. The collapse of the PNIPA chains was studied by measuring the refractive index increment of one of the copolymers at two temperatures. The polymer used in this measurement was PNIPA-*g*-PEO-7/29, the one grafted in an aqueous solution at a temperature very close to the LCST. Owing to the compression of the polymer backbone during the grafting reaction, this polymer is expected to show a strong tendency to form micellar like structures at $T >$ LCST of PNIPA. At 20 °C, PNIPA-*g*-PEO-7/29 is well soluble in water, and its measured dn/dc was 0.154 mL/g. The value calculated using eq 1 is 0.161 mL/g. To measure the dn/dc at 45 °C, low concentrations (0.07−1.17 mg/mL) were used in order to avoid a disturbing turbidity of solutions. The dn/dc at this temperature was 0.142 mL/g. Richtering et al. prepared polysurfactants from alkylated PEO and defined their dn/dc at different temperatures in water.[37] They also observed a decrease in dn/dc with increasing temperature, of the same order of magnitude as in the present case. The measured dn/dc at 20 °C is below that calculated with the additivity rule (eq 1); this indicates that even at room temperature the PEO chains tend to concentrate onto the surface of the polymer coil. It is not possible to judge whether the change in dn/dc upon heating owes to an increased amount of PEO on the surface of PNIPA. However, it seems clear that at both temperatures PNIPA entities are covered with PEO. The dn/dc value for PNIPA used in the calculations is 0.167 mL/g (20 °C, 488 nm).[32] The literature values for PEO ($M_w = 5000$ g/mol) are 0.132 mL/g (40 °C, 633 nm) and 0.129 mL/g (50 °C, 633 nm).[34]

Differential Scanning Calorimetry. The differences in the graft copolymers may be detected by studying calorimetrically the collapse of the PNIPA backbone. In water PNIPA is surrounded by highly organized water molecules which dissociate with increasing temperature to free water molecules due to enhanced hydrophobic interactions of the PNIPA segments.[31] The dissociation of the water clusters is an endothermic process and can be detected by DSC. The graft copolymers show interesting differences in their thermal behavior. The effect of the number of PEO chains on the LCST and on the corresponding enthalpy change is clearly seen in Figures 1 and 2. PEO tends to solubilize PNIPA segments even at temperatures below the critical, and thus, an increase of the amount of PEO results in a decrease in ΔH associated with the collapse of PNIPA. In other words, PNIPA is partially mixed with PEO, and thus, not all of the PNIPA segments take part in the thermal transition. For instance, the enthalpy change for PNIPA-*g*-PEO-10 containing 25 wt % of PEO was ∼ 34% less than that of PNIPA-*co*-GMA. Differences between the LCSTs of the graft copolymers derived from PNIPA-*co*-GMA are small and may be due to slightly different polymer concentrations. When the mass fraction of PEO was high enough (∼57 wt % in our experiments), ΔH reached a constant value. The enthalpy change of the graft copolymers prepared from PNIPA-*co*-NASI that contain high amounts of PEO is

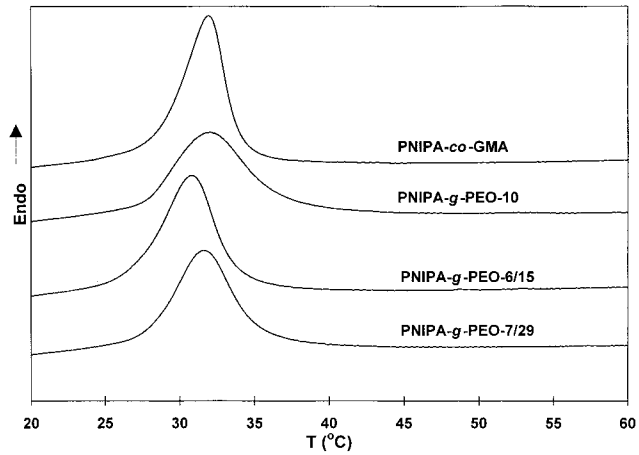

Figure 1. Thermograms of PNIPA-*co*-GMA and the graft copolymers.

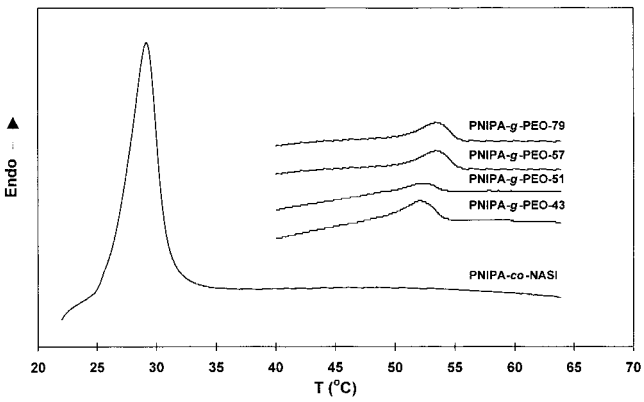

Figure 2. Thermograms of PNIPA-*co*-NASI and the graft copolymers.

very low, ≤3 J/g. The solubilization of PNIPA by the PEO chains is also observed as an increase of the LCST. The critical temperatures of the graft copolymers prepared from PNIPA-*co*-NASI with high PEO contents are shifted to ∼50 °C while PNIPA-*co*-NASI has the LCST at ∼26 °C. This indicates that, at high polymer concentrations needed in the DSC measurements, PNIPA and PEO phases are mixed with each other. Yoshioka et al.[17] have concluded that the critical temperature is dependent on the length of the PNIPA segment in a copolymer. In the present case, however, PNIPA-*co*-NASI and the graft copolymers prepared from it have equal lengths of the PNIPA segments, and it is pertinent to conclude that the sequence length is not the only factor determining the LCST. In addition, the solubility of the comonomer plays a role.

Light Scattering. In the thermal measurements using a conventional DSC as described above, the polymer concentration needs to be kept high to detect the enthalpy change at the LCST. The collapse of PNIPA in a dilute aqueous solution proceeds in two stages.[22] When approaching the LCST, intrachain interactions dominate and water gradually becomes a poor solvent for PNIPA, and the polymer shrinks. Close to the critical temperature, interchain aggregation affects simultaneously with the intrachain interactions, resulting in the phase separation of PNIPA from water, i.e., the polymer collapses. The backbone polymers PNIPA-*co*-GMA and PNIPA-*co*-NASI with a concentration 1.0 mg/mL have the critical aggregation temperatures at 31.0 and 31.8 °C, respectively. This is in a good agreement with the studies where the length of the PNIPA sequences was varied by different amounts of comonomers.[17]

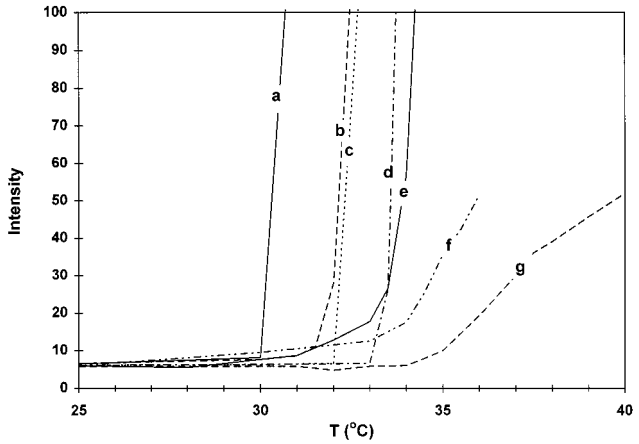

Figure 3. Dependence of the scattered light intensity of the aqueous copolymer solution on temperature. Polymer concentration 1.0 mg/mL. (a) PNIPA-*co*-GMA; (b) PNIPA-*co*-NASI; (c) PNIPA-*g*-PEO-6/15; (d) PNIPA-*g*-PEO-7/29; (e) PNIPA-*g*-PEO-10; (f) PNIPA-*g*-PEO-43; (g) PNIPA-*g*-PEO-51.

The intensity of light scattered from the aqueous polymer solutions with a constant concentration (1.0 mg/mL) is plotted against temperature in Figure 3. The intensity of PNIPA-*g*-PEO-10 slowly increases with temperature, and at ∼33.8 °C, a sharp increase indicates the formation of aggregates. With varying the number of the PEO chains, the LCST was found for PNIPA-*g*-PEO-6/15, -7/29, -43, and -51 to be 32.5, 33.5, 33.7, and 34.7 °C, respectively; see Figure 3.

The amount of PEO has been shown to have an influence on the LCST. This has been observed also in an investigation on PNIPA microgels.[18] The length of the PNIPA sequence also affects the critical temperature. In addition, the hydrophobic or hydrophilic nature of the comonomer strongly affects the solution behavior of polymers.[33,35,36] The intensity curves in Figure 3 reflect the competition between the hydrophobic interactions and the solubilizing effect of PEO on the shrinking PNIPA. In addition to the increasing critical temperature, it may be seen that also the sharpness of the intensity curves close to LCST is smoothed in the course of increasing the amount of PEO. The shift in the LCST with increasing amount of PEO shows that although the polymers are covered with a PEO shell, PNIPA and PEO are not totally phase separated but mix with each other.

Figure 4 shows the dependence of the LCST on concentration. As concentration increases, the critical temperature of aggregation slightly decreases. The dilution of the polymer solutions increases interparticle distances, which favors intramolecular interactions over the intermolecular attraction. Also, the stabilization of the surfaces of the polymer particles by PEO is expected to be more pronounced at high dilution. The exact value of LCST should be found in extreme dilution which was not possible to monitor with the light source used but will be a subject for further studies. An increase of the concentration of PNIPA-*g*-PEO-10 from 0.1 to 5.0 mg/mL caused merely a ∼1.4 °C decrease in the LCST. In the case of PNIPA-*g*-PEO-43 a smaller variation in concentration, from 0.1 to 1.0 mg/mL, induced a difference in the LCST higher than 2 °C.

The sizes of the aggregates of the graft copolymers were measured by dynamic light scattering at 45 °C

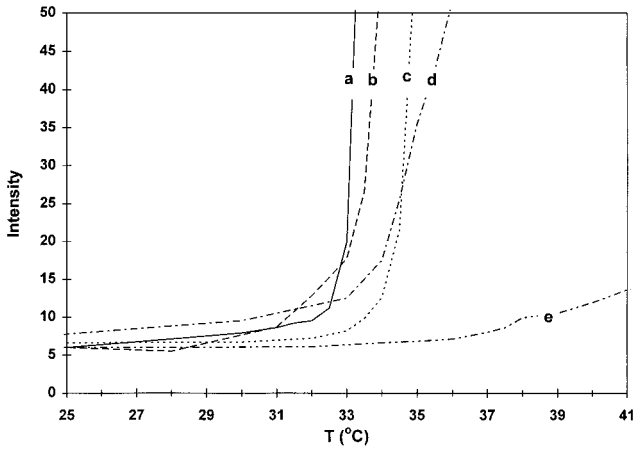

Figure 4. Dependence of the scattered light intensity of PNIPA-*g*-PEO-10 and PNIPA-*g*-PEO-43 on concentration. PNIPA-*g*-PEO-10: (a) 5.0 mg/mL; (b) 1.0 mg/mL; (c) 0.1 mg/mL. PNIPA-*g*-PEO-43: (d) 1.0 mg/mL; (e) 0.1 mg/mL.

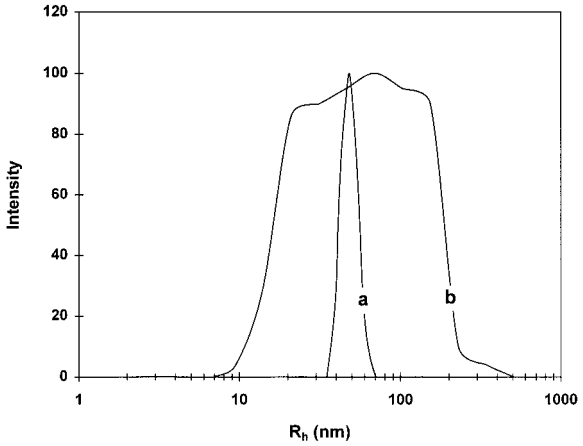

Figure 5. Size distribution of the aggregates at 45 °C. Polymer concentration 1.0 mg/mL. (a) PNIPA-*g*-PEO-6/15; (b) PNIPA-*g*-PEO-79.

using solutions with the polymer concentration 1.0 mg/mL. It turned out that in every case the average radius of the particles was almost the same, but the size distribution of the aggregates broadened with increasing amount of PEO (see Figure 5). With increasing PEO content of the polymers, the intensity of the light scattered by the aggregates decreased, which indicates that the density of the particles decreased. The decrease of the intensity was more than 1 order of magnitude through the whole sample series. This owes to the capability of PEO to partially prevent the collapse of the PNIPA chains. It is also possible that through the whole sample series the aggregation number decreases as PEO content increases, as will be shown to be the case with two polymers with the lowest number of PEO grafts.

Above the LCST, the size of the aggregates slightly decreased upon dilution. At 45 °C, the effect of dilution was only observed with the polymers having a low amount of PEO. For example, the average hydrodynamic radii $\langle R_h \rangle$ of the PNIPA-*g*-PEO-7/29 aggregates at concentrations 1.0 and 0.33 mg/mL were 42 and 36 nm, respectively. A similar 3-fold dilution did not change the size of the aggregates of the polymers with high PEO contents at 45 °C. However, at 60 °C a clear change was observed. $\langle R_h \rangle$ of PNIPA-*g*-PEO-79 decreased from 57 to 47 nm, and that of PNIPA-*g*-PEO-43 decreased from

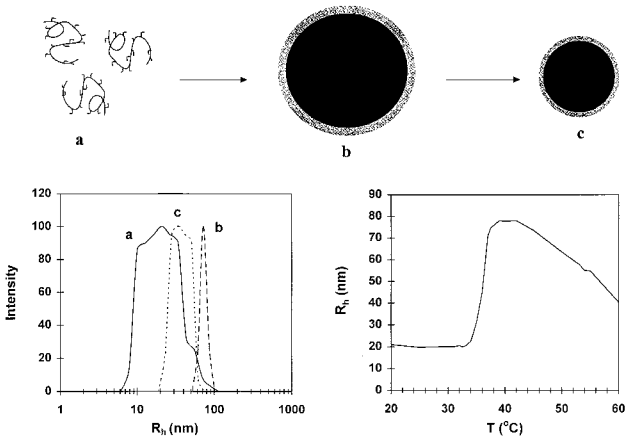

Figure 6. Formation of an aggregate and the dependence of its hydrodynamic radius (R_h) on temperature. The studied polymer was PNIPA-*g*-PEO-51 with $c = 1.0$ mg/mL. Above, a model describes steps of the formation of the aggregate and its shrinking upon slow heating from 20 °C (a) to 45 °C (b) and to 60 °C (c).

42 to 36 nm. It may be concluded that dilution enhances the surface stabilization of the shrinking chain, thus leading to smaller aggregates.

The aggregation number of PNIPA-*g*-PEO-6/15 and PNIPA-*g*-PEO-7/29 at 45 °C was measured using static light scattering. At the polymer concentration 1.0 mg/mL, the aggregate numbers were 610 and 210 for PNIPA-*g*-PEO-6/15 and PNIPA-*g*-PEO-7/29, respectively. The difference between these two polymers is noticeable. The aggregates formed by various copolymers need to be studied at high dilution to find out whether the difference owes to the slightly different number of PEO chains solely or also to the capability of the polymers to remember their conformation during the synthesis.

With a gradual raise in temperature it is possible to detect the aggregate formation followed by the shrinking of the aggregates. According to Qiu et al., for short PNIPA-*g*-PEO chains (as the polymers in this work) the interchain aggregation is prior to the intrachain "coil-to-globule" transition.[22] In other words, the individual PNIPA chains inside the aggregates gradually start to shrink after the aggregates are stabilized with a sufficient amount of PEO. Figure 6 illustrates a model of the aggregate formation of PNIPA-*g*-PEO-51 based on the measurements.

Conclusions

In this work, graft copolymers were synthesized using two different linear functional backbones as precursors. Polymers with varying degree of grafting were prepared in water and dioxane.

Evidence for the micelle formation of PNIPA-*g*-PEO upon increasing temperature could not be obtained by measuring the d*n*/d*c* of the soluble graft copolymer at different temperatures. However, the difference in the measured and calculated values of d*n*/d*c* implies that PNIPA coils and aggregates are covered with PEO at temperatures below and above the LCST of PNIPA.

In dilute solutions of the graft copolymers, hydrophobic interactions compete with the solubilizing effect and the surface stabilization of PEO. At $T <$ LCST the PNIPA chains gradually shrink when temperature approaches the critical, and flexible PEO chains with high hydrophilicity turn outward pointing out to the water phase and sustain the polymer aggregates soluble.

PEO and PNIPA partially mix with each other, and the collapsed aggregates may be concluded to consist of a PNIPA/PEO core sterically stabilized by a PEO shell. The stabilizing effect is more pronounced with increasing number of the PEO grafts. Also, the dilution of the solutions has been shown to stabilize the collapsed polymers. An increase in the number of the PEO grafts as well as the dilution of the solutions increases the LCST of the copolymers.

Because PNIPA and PEO mix to a certain extent, the LCST increases with an increasing number of the PEO grafts. Also, with an increasing amount of PEO, the density of the aggregates formed at $T >$ LCST decreases and their size distribution broadens. Above the LCST, the loosely packed aggregates shrink with increasing temperature.

The size of the aggregates and the LCST are determined by the net effect of various factors such as intra- and interchain interactions of PNIPA and the solubilizing effect and the surface stabilization of PEO.

The graft copolymers show lower enthalpy changes upon the phase transition than pure PNIPA. Thus, PEO grafts solubilize the PNIPA segments to which they are attached. At high concentrations, with an increasing number of the PEO chains the collapse of PNIPA is almost totally prevented because of the mixing of PNIPA and PEO.

The graft copolymers synthesized in water at two different temperatures showed a remarkable difference in their thermal behavior when compared to the other copolymers. The properties of these two polymers will be studied further.

References and Notes

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