Synthesis of Thermally Switchable Poly(*N*-isopropylacrylamide-*block*-dendronized methacrylate)s

Caixia Cheng,[†] Manfred Schmidt,[§] Afang Zhang,*[,†,‡] and A. Dieter Schlüter[†]

Laboratory for Polymer Chemistry, Department of Materials, ETH-Zurich, HCI J 541, 8093 Zurich, Switzerland; Institut für Physikalische Chemie, Johannes Gutenberg-Universität, Jakob-Welder-Weg 11, 55128 Mainz, Germany; and School of Materials Science and Engineering, Zhengzhou University, Daxue Beilu 75, Zhengzhou 450052, China

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ABSTRACT: A series of water-soluble linear diblock copolymers were synthesized, and their thermally switchable behavior under aqueous conditions was investigated. One block of these copolymers consists of poly(*N*-isopropylacrylamide) [poly(*N*iPAM)] and the other of positively charged first- and second-generation dendronized polymethacrylates [**PG1** and **PG2**]. The copolymers were prepared via reversible addition−fragmentation chain transfer (RAFT) polymerization and the block lengths varied. The thermally switchable aggregation behavior of the copolymers was investigated by ^{1}H NMR and fluorescence spectroscopy, and the lower critical aggregation temperatures (LCATs) were determined by turbidity measurements using UV/vis spectroscopy. Some of these block copolymers at elevated temperature formed supramolecular assemblies in the size range of 50−400 nm whose structures were investigated by transmission electron microscopy (TEM).

1. Introduction

Self-assembly of block copolymers (BCPs) is a powerful tool to form ordered supramolecular structures[1] at various length scales in solution,[2] in the bulk,[3] at interfaces,[4] and in the thin films.[5] Research in this direction is spurred not only by fascinating applications of these ordered structures in areas such as biosensors,[6] microreactors,[7] encapsulation/drug delivery,[8] and information technology[9] but also by the fact that little or no synthetic effort is required to create a whole variety of different morphologies. An additional plus of certain BCPs is the fact that their modes of assembly and phase transformation can be triggered by external stimuli[10] which are commonly based on pH values[11] and temperature variation[12] as well as irradiation with UV light.[13] A prominent case of stimuli responsive BCPs are those which have a poly(*N*iPAM) block. They have a lower critical solution temperature (LCST) in the range of ∼32 °C, which is especially attractive for bioapplications.[14] Dendronized polymers are a well-established class of comb polymers in which each repeat unit carries a dendron.[15] This dendronization reduces the attainable backbone conformations and in the extreme case can render a random coil polymer into a cylindrically shaped, rigid molecular object with a more or less stretched backbone in the interior. Several homologous series of such polymers which differ in the dendrons' generation have been prepared.[16] When going from first- (G1) to fourth-generation (G4) representatives both the backbone rigidity and the number of peripheral functional groups per repeat unit are altered systematically. Dendronized polymers were therefore considered unique candidates for a systematic approach to engineer novel ordered assemblies. It is of interest in this regard that positively charged third- and fourth-generation dendronized polymers with polystyrene backbone were recently found to spontaneously form networks in aqueous media whereby the net segments comprise of loosely braided double helices.[17] Considering both the potential of dendronized polymers for a systematic exploration of superstructure formation and the considerable body of knowledge on poly(*N*iPAM) homopolymers and block copolymers in the same matter, it was an obvious task to try to combine both polymers into BCPs and investigate their properties. It should be mentioned at this point that two different kinds of BCPs with dendronized blocks have already been reported. The first one has a polymethacrylate block decorated with Frèchet-type dendrons which combined with either linear PEO or PMMA block.[18] The second one has a polyisoprene block to which mesogen decorated dendron were attached. This block is combined with linear polystyrene block.[19] Both these BCPs do not carry charges and are not water-soluble. For the first the self-assembly behaviors were studied in interfaces as well as in solvent mixtures and led to defined supramolecular aggregates with different morphologies. The other was spin-coated on substrates, and the surface topologies were investigated by SFM. Microphase separation on large scale with periodic dome structures was observed.

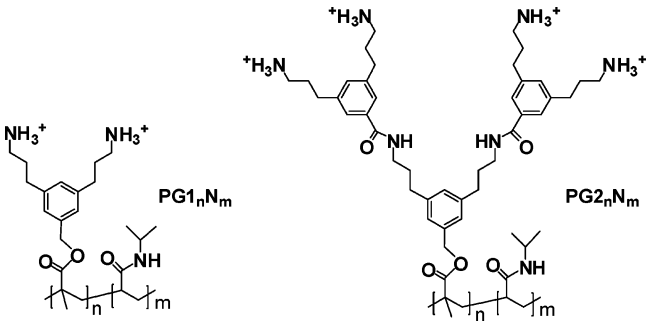

Figure 1. Chemical structures of $\mathbf{PG1}_n\mathbf{N}_m$ (n = 14−450, m = 74−602) and $\mathbf{PG2}_n\mathbf{N}_m$ (n = 22−74, m = 177−1280). The polymer end groups and the $CF_3CO_2^-$ counterions are not shown.

Here we report on the synthesis of the water-soluble BCPs $\mathbf{PG1}_n\mathbf{N}_m$ and $\mathbf{PG2}_n\mathbf{N}_m$ with polymethacrylate block decorated with G1 and G2 dendrons and a poly(*N*iPAM) block (**N**), as shown in Figure 1. The dendrons carry two and four peripheral ammonium groups which mediate the water solubility of the corresponding block. Both polymers were synthesized with

* Corresponding author: Fax (+41) 44- 633 1390; e-mail afang.zhang@mat.ethz.ch or azhang@zzu.edu.cn.
† ETH Zurich.
§ Johannes Gutenberg-Universität.
‡ Zhengzhou University.

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different block lengths *n* and *m*, and their thermally induced aggregation behavior in aqueous medium was studied in some detail.

2. Experimental Section

Materials. Macromonomers **1**[16b] and **3**[16b] as well as the dendronized macro-chain-transfer reagents **2**[20] and **4**[20] were synthesized according to previous reports. *N*-Isopropylacrylamide (*N*iPAM) was purchased from Aldrich and purified by recrystallization from a mixture of benzene and hexane (3/7, v/v). Azobis(isobutyronitrile) (AIBN) was purchased from Fluka and recrystallized twice from methanol. Water was purified with a Millipore Mill-Q system. A citric acid based buffer (Sigma-Aldrich, No. 82566) was used to maintain a pH = 4.0 at 20 °C. Other reagents and solvents were used as received.

Measurements. ^{1}H NMR spectroscopy was carried out on a Bruker 300 MHz spectrometer in either $CDCl_3$ or D_2O solution. The spectra in D_2O were referenced to sodium 3-(trimethylsilyl)-propionate-*2,2,3,3-d*$_4$ as an internal standard. Gel permeation chromatography (GPC) measurements were carried out by using a PL-GPC 220 instrument with a 2 × PL-Gel Mix-B LS column set (2 × 30 cm) equipped with refractive index (RI), viscosity, and light scattering (LS; 15° and 90° angles) detectors and DMF containing LiBr (1 g/L) as eluent at 80 °C. Universal calibration was performed with poly(methyl methacrylate) standards in the range of M_p = 2680−3 900 000 (Polymer Laboratories Ltd., UK). Transmission electron microscopy (TEM) measurements were performed on a FEI Morgagni 286 instrument operated in the zero-loss bright-field mode and an acceleration voltage of 100 kV. Digital images were recorded with CCD camera systems. The samples were prepared by placing a drop of an aqueous solution of the respective diblock copolymer at 20 or 50 °C onto a carbon-coated copper grid. This grid as well as all equipment used for the preparation was kept at either of these temperatures prior to use. The preparations were completed in less than 1 min for the sample preparation at 50 °C, which ensured a high reproducibility of the measurements. The samples were measured without staining. The fluorescence spectra were recorded with a Spex Fluorolog 2 luminescence spectrometer from jobin Yvon (U.K.). The temperature of the water-jacketed cell holder was controlled by a programmed circulation bath, and the polymer solutions in a 1 cm quartz cell were slowly heated at a rate of 0.5 °C/min. The critical aggregation concentrations (CACs) were determined at 35 °C as described previously for pyrene as a hydrophobic fluorescence probe.[21] A pyrene solution in acetone (1.28×10^{-6} M, 1 mL) was added to a series of volumetric flasks which were kept at 50 °C for a complete evaporation of acetone. Then 10 mL of the respective 0.3% (w/v) aqueous **PG1**$_n$**N**$_m$ or **PG2**$_n$**N**$_m$ solutions was added. These solutions were kept for 24 h prior to the measurement to allow an equilibration of the system. The final pyrene concentration for every solution was fixed at 1.28×10^{-7} M. The excitation was done at λ = 390 nm, and the emissions were recorded (see Supporting Information). Both excitation and emission bandwidths were 10 nm. From the pyrene excitation spectra, the intensities (peak height) of the first (I_{333}) and the second band (I_{338}) were analyzed as a function of the polymer concentrations. A CAC value was determined from the intersection of the tangent to the curve at the inflection with the horizontal tangent through the points at low copolymer concentration (see Supporting Information). For UV/vis turbidity measurements, the lower critical aggregation temperatures (LCATs) were determined on a Varian Cary 1E (Australia) UV/vis spectrophotometer, equipped with a thermostatically regulated bath. A solution of the respective diblock copolymer (3 mg) in pure water (3 mL) was put into a cell (path length 1 cm) which was placed in the spectrophotometer and heated at a rate of 0.5 °C/min. The temperature of the phase transition was considered the one at which the transmittance at λ = 500 nm had reached 50% of its initial value.

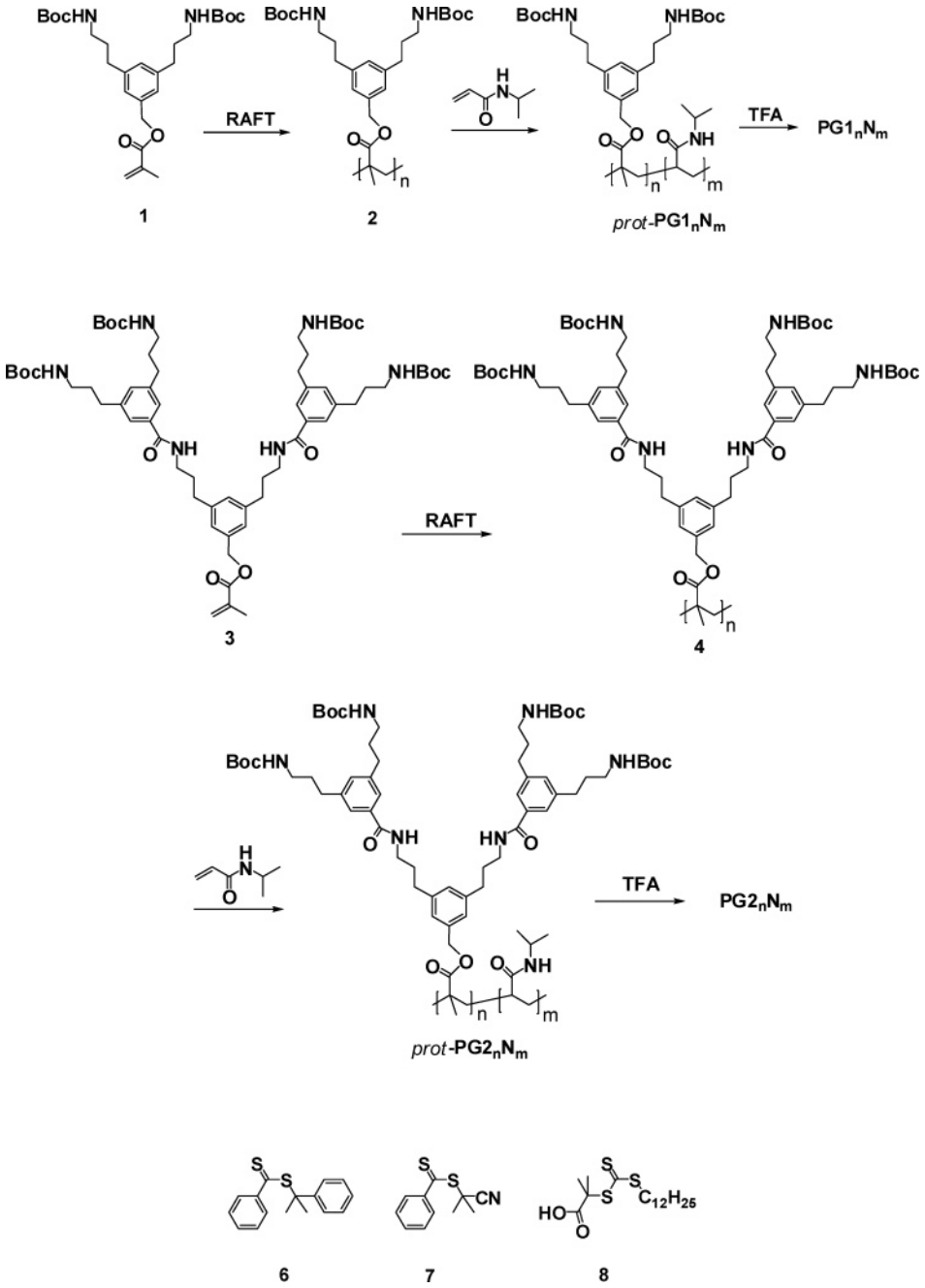
Synthesis of Diblock Copolymers. A typical procedure is as follows (for details see Table 1): The required amounts of *N*iPAM,

Table 1. Conditions and RAFT Polymerization Results for *prot*-PG1$_n$N$_m$ (Entries 1−6 and 11, 12) and *prot*-PG2$_n$N$_m$ (Entries 7−10 and 13) as Well as LCAT and CAC Data for the Corresponding Deprotected Copolymers PG1$_n$N$_m$ (Entries 1−6, 11, and 12) and PG2$_n$N$_m$ (Entries 7−10)[a]

	first block									second block									
	polymerization conditions					GPC results[b]				polymerization conditions[c]						block length ratio r^d			
entry	1st monomer	RAFT reagent	[A]:[R]:[M][g]	time (h)	yield (%)	$M_n \times 10^{-4}$	DP	PDI	2nd monomer	[A]:[R]:[M]	time (h)	yield (%)	$M_n{}^f \times 10^{-4}$	DP	PDI	NMR[e]	GPC	CMC (mg/L)	LCAT (°C)
1	**1**	**7**	1:2:20	4	87	0.69	14	1.12	*N*iPAM	1:3:100	16	86	0.93	82	1.24	6.0	5.9	1.2	33.3
2	**1**	**7**	1:2:20	6	92	1.08	22	1.10	*N*iPAM	1:3:100	16	81	1.51	134	1.18	6.2	6.1	1.6	33.3
3	**1**	**7**	1:2:40	11	83	2.21	45	1.32	*N*iPAM	1:3:400	36	92	4.80	425	1.28	9.6	9.4	3.6	33.7
4	**1**	**6**	1:2:100	10	90	4.81	98	1.29	*N*iPAM	1:3:600	36	78	6.80	602	1.30	6.2	6.1	6.0	33.9
5	**1**	**8**	1:2:100	2	68	5.49	112	1.29	*N*iPAM	1:3:100	12	58	0.90	80	1.32	0.8	0.7	5.7	42.5
6	**1**	**6**	1:2:300	8	88	22.1	450	1.28	*N*iPAM	1:3:100	32	65	0.84	74	1.65	0.2	0.2	–[k]	–[k]
7	**3**	**6**	1:2:50	16	88	2.82	25	1.59	*N*iPAM	1:2:500	48	84	6.01	532	1.79	21.6	21.3	6.9	42.7
8	**3**	**6**	1:2:100	15	84	8.34	74	1.34	*N*iPAM	1:3:200	15	80	2.00	177	1.55	2.4	2.4	6.5	41.0
9	**3**	**6**	1:2:100	15	84	8.34	74	1.34	*N*iPAM	1:3:400	48	86	5.08	450	2.44	6.1	6.1	5.6	42.6
10	**3**	**6**	1:2:100	15	84	8.34	74	1.34	*N*iPAM	1:3:1800	48	82	14.40	1280	2.86	17.5	17.3	5.2	42.8
11	*N*iPAM[h]	**7**	1:2:260	16	74	2.97	263	1.23	1	1:3:60	42	84	2.21	45	1.52	6.1	5.8	2.0	33.5
12	*N*iPAM[i]	**7**	1:2:380	40	89	3.89	344	1.24	1	1:3:60	40	81	2.21	45	1.73	7.7	7.6	2.8	33.6
13	*N*iPAM[h]	**7**	1:2:260	16	74	2.97	263	1.23	3	1:3:60	60	21	2.48	22	3.47[j]	12.2	11.9		

[a] Polymerization in DMF at 90 °C with [**1**] = 1.36 mol/L or [**3**] = 0.6 mol/L. [b] Calibrated with a polystyrene standard. [c] Copolymerization in DMF at 90 °C with [*N*iPAM] = 2.5 mol/L or [**1**] = 1.36 mol/L, [**3**] = 0.6 mol/L. [d] r = DP[poly(*N*iPAM)]/DP(PG1 or PG2). [e] Calculated based on the ^{1}H NMR integration (see text). [f] Calculated by subtracting the molar mass of the first block from that of the corresponding BCP. [g] [A]:[R]:[M] is to be understood as [AIBN]:[RAFT mediator]:[monomer]. [h] [*N*iPAM] = 14.8 mol/L. [i] [*N*iPAM] = 9.5 mol/L. [j] Bimodal molar mass distribution. [k] Could not be experimentally observed.

Scheme 1. Synthesis of the G1 and G2 Diblock Copolymers *prot*-PG1$_n$N$_m$ and *prot*-PG2$_n$N$_m$ via RAFT Polymerization Starting from the Dendronized Polymethacrylate Block with RAFT-Active End Group (Not Shown) and the Structures of the RAFT Reagents 6−8 Used in This Study



dendronized macro-CTA (PG1 or PG2),[20] and AIBN were dissolved in DMF (80 wt % to the total mass added) inside a Schlenk tube. The solution was thoroughly deoxygenated by several freeze−pump−thaw cycles and heated to 90 °C under N_2 for 12 h. After cooling to room temperature, the polymer was dissolved in dichloromethane and purified by column chromatographic workup with dichloromethane as eluent followed by its precipitation from a methanol solution into redistilled water. The obtained precipitate was recovered by filtration and characterized.

prot-**PG1$_{45}$N$_{263}$**. ^{1}H NMR ($CDCl_3$): δ = 0.72−0.93 (br, CH_2 + CH_3), 1.12 [br, CH_3 (*N*iPAM)], 1.38 (br, CH_3), 1.58 [br, CH_2 (*N*iPAM)], 1.70 (br, CH_2), 1.85 [br, CH (*N*iPAM)], 2.49 (br, CH_2-Ph), 3.02 (br, CH_2NH), 3.98 [br, CH (*N*iPAM)], 4.79 (br, NH), 5.27 (br, CH_2O), 6.87 (br, Ph).

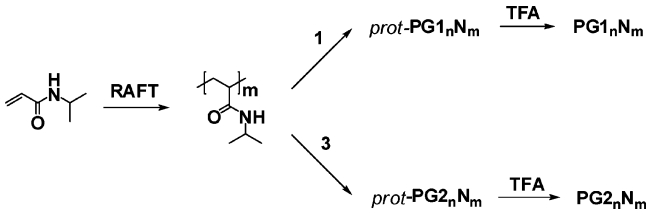
prot-**PG2$_{74}$N$_{177}$**. ^{1}H NMR ($CDCl_3$): δ = 0.65 (br, CH_2), 0.78 (br, CH_3), 1.12 [br, CH_3 (*N*iPAM)],1.30 (br, CH_3), 1.59 [br, CH_2 + CH_2 (*N*iPAM)], 1.70 (br, CH_2), 1.85 [br, CH (*N*iPAM)], 2.37 (br, CH_2Ph), 2.88 (br, CH_2NH), 3.20 (br, CH_2NH), 3.98 [br, CH (*N*iPAM)], 4.65 (br, CH_2O), 5.30 (br, NH), 6.82 (br, Ph), 6.94 (br, Ph), 7.43 ppm (br, Ph).

The target diblock copolymers were also prepared from an inverse sequence by using poly(*N*iPAM) as macro-CTA to which the dendronized macromonomers **1** and **3** were copolymerized. The workup of those samples was identical to that of the ones described above.

Deprotection of the Block Copolymers. The respective diblock copolymer (0.5 g) was dissolved in an excess of TFA (5 mL) at 0 °C. After stirring for 4 h at room temperature, excess amount of methanol was added, and the solvents were evaporated in vacuum. The solid product was dried under high vacuum for 10 h (yield: 98%).

PG1$_{45}$N$_{263}$. ^{1}H NMR (D_2O): δ = 0.55−75 (br, CH_2 + CH_3), 1.12 [br, CH_3 (*N*iPAM)], 1.53−1.85 [br, CH_2, CH2 (*N*iPAM), CH (*N*iPAM)], 2.44 (br, CH_2Ph), 2.80 (br, CH_2NH), 3.86 [br, CH

Scheme 2. Synthesis of the First- and Second-Generation Diblock Copolymers *prot*-PG1$_n$N$_m$ and *prot*-PG2$_n$N$_m$ via RAFT Polymerization Starting from the Poly(*N*iPAM) Block with RAFT-Active End Group (Not Shown)



(*N*iPAM)], 4.79 (br, NH), 5.80 (br, CH_2O), 6.90−7.00 (br, Ph).

PG2$_{74}$N$_{177}$. ^{1}H NMR (D_2O): δ = 0.90 (br, CH_2 + CH3), 1.12 [br, CH_3 (*N*iPAM)], 1.30 [br, CH_3(*N*iPAM)], 1.59−1.80 [br, CH_2 + CH_2 (*N*iPAM)], 2.50 (br, CH_2Ph), 2.88 (br, CH_2NH), 3.20 (br, CH_2NH), 3.86 [br, CH (*N*iPAM)], 4.80 (br, CH_2O), 6.82 (br, Ph), 6.94 (br, Ph), 7.43 ppm (br, Ph).

Self-Assembly. The respective diblock copolymer was dissolved in deionized water at a concentration of 0.4 mg/mL and the citric acid buffer solution (pH ≈ 4.0) added. This reduced the copolymer concentration to ∼0.3 mg/mL. This solution was equilibrated for 1 day at room temperature in a closed vial under slow stirring and then put into an isothermal bath at 50 °C. The solution became turbid within a few minutes and was equilibrated for at least 2 days at this temperature before taking samples for the TEM measurements.

3. Results and Discussion

Block Copolymer Synthesis. The synthetic sequences to both series of *tert*-butyloxycarbonyl (Boc)-protected and -deprotected (and then charged) BCPs, *prot*-**PG1$_n$N$_m$**/*prot*-**PG2$_n$N$_m$** and **PG1$_n$N$_m$**/**PG2$_n$N$_m$**, respectively, are shown in Scheme 1. They are based on the RAFT methodology[22] which was considered attractive because both *N*iPAM and the dendronized macromonomers **1** and **3** have already been successfully polymerized by this method into their homopolymers poly(*N*iPAM)[23] as well as **2** and **4**,[20] respectively. Also, BCPs with poly(*N*iPAM) block have been synthesized.[24] Compounds **6** and **7** were used as RAFT mediators. Compound **8** was also tried but gave inferior results because of gelation during polymerization. Polymers **2** and **4** carry RAFT active end groups (not shown) and are therefore to be considered macro-chain-transfer agents (CTAs) capable of letting another block grow off their active termini. Upon addition of *N*iPAM they, in fact, underwent further growth, and the corresponding BCPs *prot*-**PG1$_n$N$_m$** and *prot*-**PG2$_n$N$_m$**, respectively, were obtained. Details on the polymerization conditions and a representative overview of the results are compiled in Table 1 (entries 1−10). This table also contains the results which were obtained for the same diblock copolymers synthesized in the reverse order, i.e., by adding dendronized macromonomer **1** or **3** to poly(*N*iPAM) block (Scheme 2 and Table 1, entries 11−13). As can be seen from all entries except entry 13, the yields of all polymerization steps are high (∼80 ± 10%). For *prot*-**PG1$_n$N$_m$** the block lengths n and m were varied between $14 < n < 450$ and $74 < m < 602$ and for *prot*-**PG2$_n$N$_m$** between $22 < n < 74$ and $177 < m < 1280$. The molar masses and mass distributions were determined by GPC. The molar masses of the second block were obtained by subtracting that of the first one from the total BCP molar masses. The block length ratios r were varied between $0.2 < r < 9.5$ for *prot*-**PG1$_n$N$_m$** and $2.4 < r < 21.5$ for *prot*-**PG2$_n$N$_m$**. They were determined using the GPC data and also, independently, by ^{1}H NMR integration. For this purpose the intensity of the aromatic signals of the dendronized blocks at δ = 6.87 for *prot*-**PG1$_n$N$_m$** and at δ = 7.43 ppm for *prot*-**PG2$_n$N$_m$** were compared

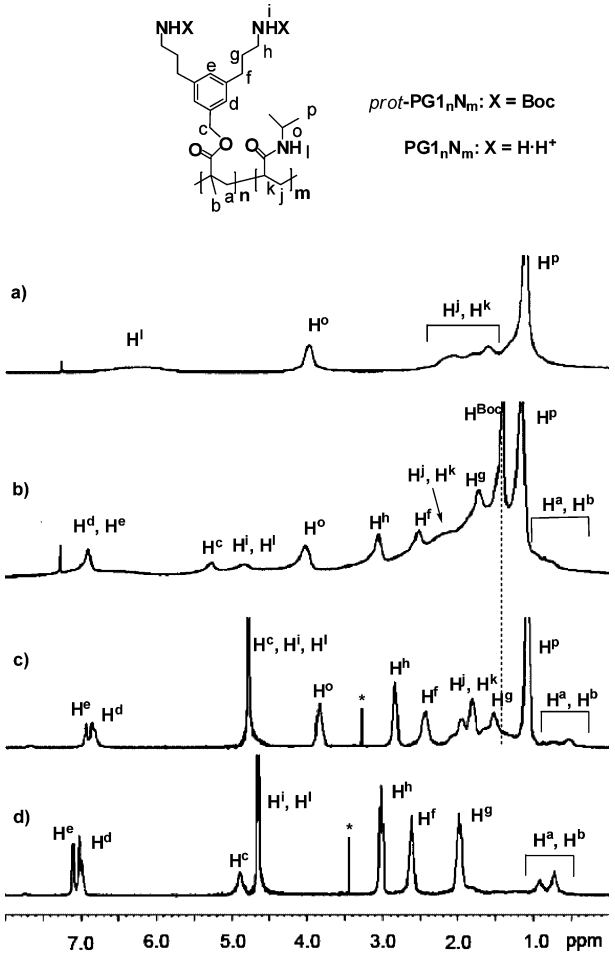


Figure 2. ^{1}H NMR spectra of poly(*N*iPAM) in $CDCl_3$ (a), *prot*-**PG1$_{45}$N$_{263}$** in $CDCl_3$ (b), and the positively charged **PG1$_{45}$N$_{263}$** in D_2O at 25 (c) and 50 °C (d). Solvent signals are marked (∗).

with the −CH signal of the *N*iPAM block at δ = 3.98. Figure 2b shows a typical NMR spectrum of *prot*-**PG1$_n$N$_m$** as it was used for this determination. Despite the uncertainty of the integration caused by the relatively broad signals, the match between the results from both methods is satisfactory. All BCPs in which the dendronized block was synthesized first (entries 1−10) gave monomodal GPC elution curves and did not contain any eventual traces of homopolymers. Figure 3 shows typical GPC elution curves to illustrate this point. The block copolymer structure was also confirmed by comparison of the ^{1}H NMR spectra of poly(*N*iPAM) (Figure 2a) with *prot*-**PG1$_n$N$_m$** (Figure 2b). A full signal assignment is provided. The PDIs for the first block were the narrowest when compound **7** was used as RAFT mediator and are in a reasonable range for this method. The degrees of polymerization for the first block were larger throughout than the calculated ones (not shown) by a factor of roughly 1.5−2. Similar observations have already been reported.[20] The PDIs of *prot*-**PG1$_n$N$_m$** are also in a reasonable range (entries 1−5) with the exception when a high molar mass first block was used (entry 6). The PDIs of the higher generation analog *prot*-**PG2$_n$N$_m$** are significantly larger, however, seemingly irrespective of the molar mass. The reason for this is not yet understood. Some of the *prot*-**PG2$_n$N$_m$** samples were prepared with an identical dendronized block and different poly(*N*iPAM) block lengths by starting from the same batch of **3** (entries 8−10). This was done to study the effect of this systematic structural change on the aggregation behavior of the corresponding charged samples **PG2$_n$N$_m$** (see below). Entries

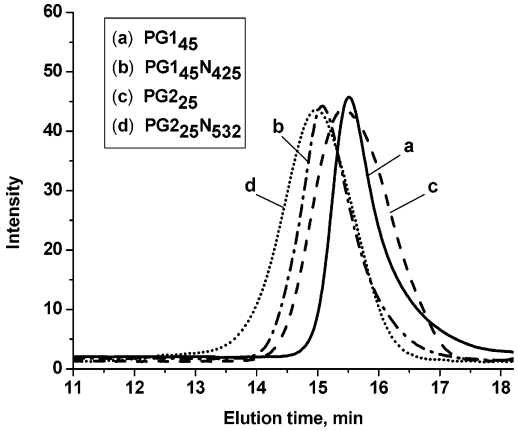


Figure 3. Typical GPC elution curves of (a) G1 macro-chain-transfer agent **2**, the diblock copolymer *prot*-**PG1$_{45}$N$_{425}$** synthesized from it (b), the G2 macro-chain-transfer agent **4** (c), and the diblock copolymer *prot*-**PG2$_{25}$N$_{532}$** synthesized from it (d). The elution curves refer to the entries 3 and 7 in Table 1.

11−13, finally, show that the reversed order of synthesis seems to be inferior. First, the PDIs are larger; only the best values obtained in several experiments are given in Table 1 (entries 11 and 12). Second, for the G2 monomer **3** bimodal molar mass distributions were observed in several experiments (for example, see entry 13).

For the aggregation studies all BCPs were deprotected so as to render them fully water-soluble in both parts. The deprotection was done with trifluoroacetic acid (TFA) and afforded cleanly the BCPs **PG1$_n$N$_m$** and **PG2$_n$N$_m$** under conditions for which it is known that the Boc protecting groups are quantitatively removed from dendronized polymers.[25] Figure 2b,c illustrates this point. The signal due to the Boc groups in *prot*-**PG1$_n$N$_m$** can be clearly seen at approximately $\delta = 1.38$ ppm (Figure 2b). Upon deprotection it disappeared completely (Figure 2c).

Thermally Switchable Aggregation Behavior of PG1$_n$N$_m$ and PG2$_n$N$_m$. First indication that the BCPs prepared above show thermally switchable aggregation behavior came from ^{1}H NMR spectroscopy. The spectra of the **PG1$_n$N$_m$** samples with relatively long *N*iPAM block (Table 1, entries 1−4 and 11−12) in aqueous medium showed a reversible disappearance of the *N*iPAM signals upon raising the temperature from 25 to 50 °C. Similar phenomena have already been observed for *N*iPAM homo- and copolymers[26] and were interpreted in terms of a reversible collapse of the *N*iPAM part almost simultaneously followed by its aggregation.[27] As a representative case, Figure 2 shows the spectra of **PG1$_{45}$N$_{263}$** (Table 1, entry 11) at both these temperatures which were recorded for a concentration of ~40 mg/mL. The signals due to the *N*iPAM block (H^p, H^j, H^k, and H°) (Figure 2c) disappeared completely in Figure 2d while the ones of the dendronized block remained as they were, except for slight changes in chemical shift. Upon cooling, Figure 2c was fully recovered. The **PG1$_n$N$_m$** samples with shorter *N*iPAM block (Table 1, entries 5 and 6) behaved differently. At the higher temperature the signals due to the *N*iPAM block did not disappear completely (see Figure 4). Finally, the NMR spectra of all **PG2$_n$N$_m$** samples (Table 1, entries 7−10) resembled very much that of the **PG1$_n$N$_m$** samples with short *N*iPAM block even when the temperature was further raised to 70 °C (see Supporting Information). In accordance with the accepted interpretation for the behavior of poly(*N*iPAM), the NMR results lead to the following conclusions for the three different cases described:

The complete disappearance of the *N*iPAM signals for the BCPs with long *N*iPAM block is caused by the collapse of this very block at the higher temperature and followed by the formation of compact aggregates. Because the NMR solutions at 50 °C were turbid by visual inspection, it is concluded that these aggregates are large and compact enough to scatter the light. At this stage it cannot be assessed whether both processes, collapse and aggregate formation, occur at the same temperature

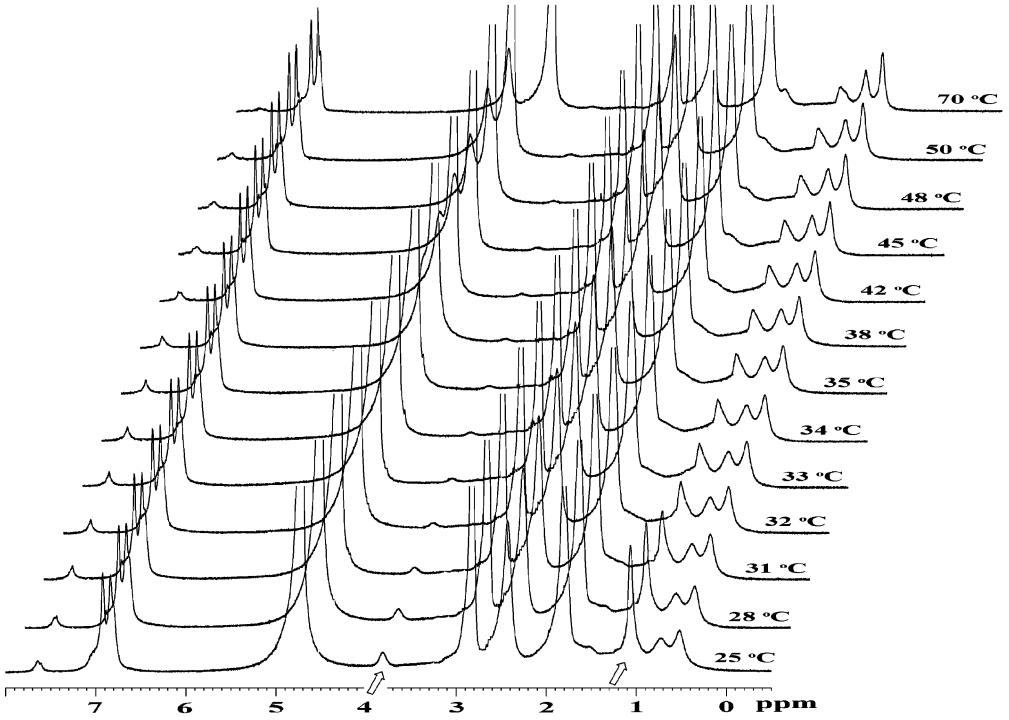


Figure 4. Temperature-dependent NMR spectroscopies of **PG$_{112}$N$_{80}$** in D_2O. All spectra were oriented according to the same intensity of the peak at 3.0 ppm. The two arrows indicate the poly(NiPAM) signals whose intensities decrease with increasing temperature.

(see below). In the second case, it seems that the BCPs with longer G1 dendronized block form less compact aggregates at higher temperatures in which the *N*iPAM block has sufficient mobility to be visible by NMR spectroscopy, although their NMR solutions were also turbid. Since *N*iPAM homopolymers of comparable lengths under these conditions form tight aggregates,[28] the dendronized block obviously influences the BCPs' aggregation/solution behavior. It seems to "protect" the collapsed *N*iPAM part against tight aggregation. The third case in which the BCPs carry a G2 dendronized block behave very much like the BCPs with long G1 block. Obviously, also here the dendronized block dominates over *N*iPAM at least for the block length ratios tested.

In order to find out whether the *N*iPAM collapse in the BCPs described here and the aggregation of the collapsed chains are simultaneous processes as is proposed for poly(*N*iPAM), the collapse temperature was determined by temperature-dependent NMR spectroscopic studies on $\mathbf{PG_{112}N_{80}}$. Comparison of this temperature with the LCAT described below would then allow answering this question. Figure 4 shows a series of NMR spectra in a temperature range from 25 to 70 °C. In spite of the concentration decreasing effect because of the increase of the solution volume with the increase of NMR measurement temperature, one can easily observe the intensity of *N*iPAM signals (indicated with arrays) has started decreasing obviously from 31 °C, but kept nearly constant above 33 °C. This should be a clear indication that *N*iPAM block collapse around 32 ± 1 °C, which is nearly the same as for the *N*iPAM homopolymers.

After these findings the aggregation behavior was investigated more systematically. Critical micelle concentrations (CMCs) of small amphiphiles are usually determined for a certain temperature by monitoring the entrapment of the fluorophore pyrene into the micelle's nonpolar regions in dependence of the amphiphile concentration.[29] The same method is commonly also applied for amphiphilic BCPs even though for those compounds it is often only assumed that regular micelles are formed. Because of the structural ambiguity, the method is therefore sometimes referred to as critical aggregation concentration (CAC).[30] In the case of BCPs with a block which can collapse into a nonpolar globule this method can also be applied. Here the characteristic intensity changes of the pyrene emission spectrum upon entering into a nonpolar environment, however, cannot even be associated with aggregate formation. For long enough collapsible blocks it may well be that the fluorophore is just taken up by the globular part of otherwise molecularly dispersed chains. All values reported in the present paper have therefore to be considered with care. Though structural proposals cannot be made at the present stage of research, we refer to the obtained values as CACs. All BCPs of Table 1 were investigated. The experiments were done at 35 °C (see Experimental Section), and the results are given in Table 1. Please note that the observed concentration is in the range of 1−7 mg/L and, thus, ∼1000 times lower than that applied for the NMR studies.

In the next step, the aggregation phenomenon was investigated by turbidity measurements aiming at the determination of LCAT. These measurements were done for all samples of Table 1 (entries 1−12) in buffered aqueous media and in concentrations of ∼10 mg/mL. This concentration is in a similar though somewhat lower range than that used in the NMR experiments. The corresponding transmittance curves are shown in Figure 5, and the results are compiled in Table 1. As can be seen from entries 1−6, 11, and 12 of Table 1, all LCATs for $\mathbf{PG1}_n\mathbf{N}_m$ lie between 33 and 43 °C. As expected, for high block lengths ratios (r = 5−9) the *N*iPAM block dominates and the values are

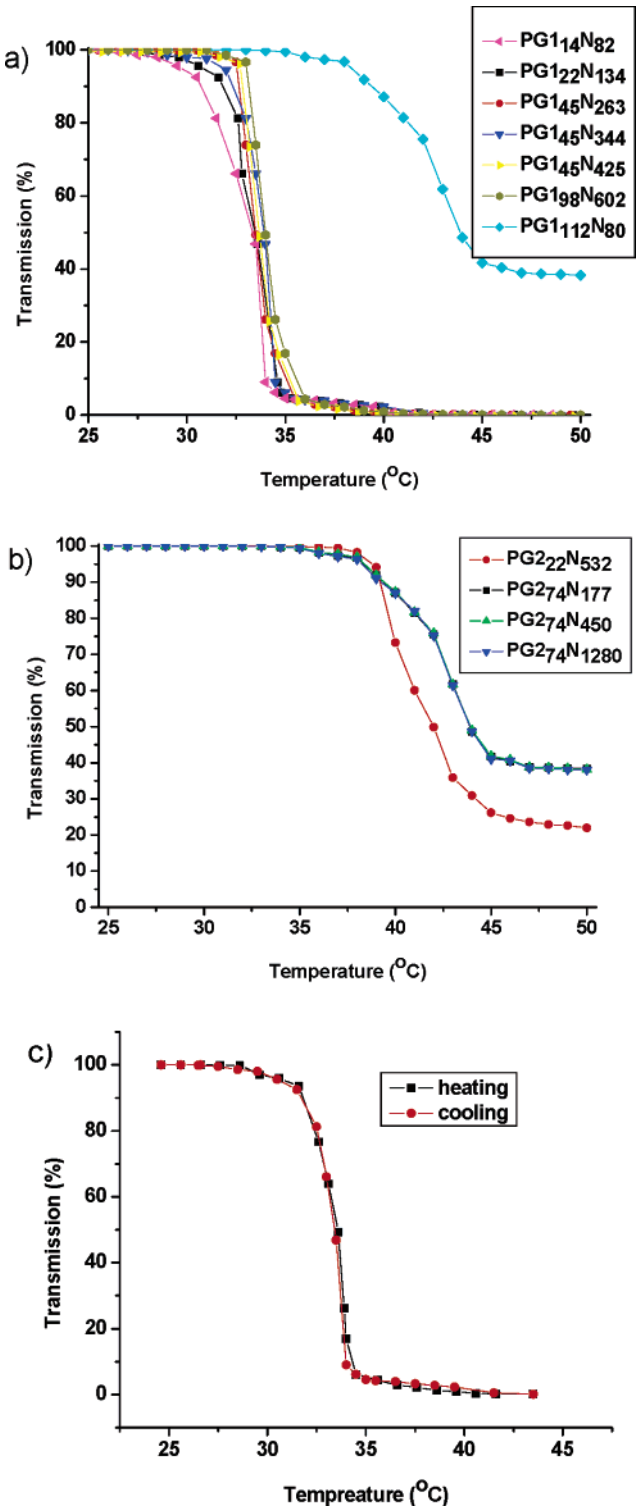


Figure 5. Transmittance vs increased temperature curves for 1 wt % buffered aqueous solutions (pH = 4.0) of block copolymers $\mathbf{PG1}_n\mathbf{N}_m$ (a) and $\mathbf{PG2}_n\mathbf{N}_m$ (b) with different block length ratios. Transmittance vs increased and then decreased temperature curves for $\mathbf{PG1_{45}N_{263}}$ to illustrate the degree of reversibility (c). Heating and cooling rate = 0.5 °C/min.

around 33 °C, a temperature which is close to the one reported for poly(*N*iPAM) homopolymers.[14a,27] If the absolute block lengths are increased while the block length ratios are kept similar, however, the values increase slightly (entries 1, 2, 4, and 11). With small block length ratios (r = 0.7) as in entry 5, the LCAT increases to 42.5 °C, with even lower ratios (r = 0.2, entry 6) no LCAT is found anymore. For the higher

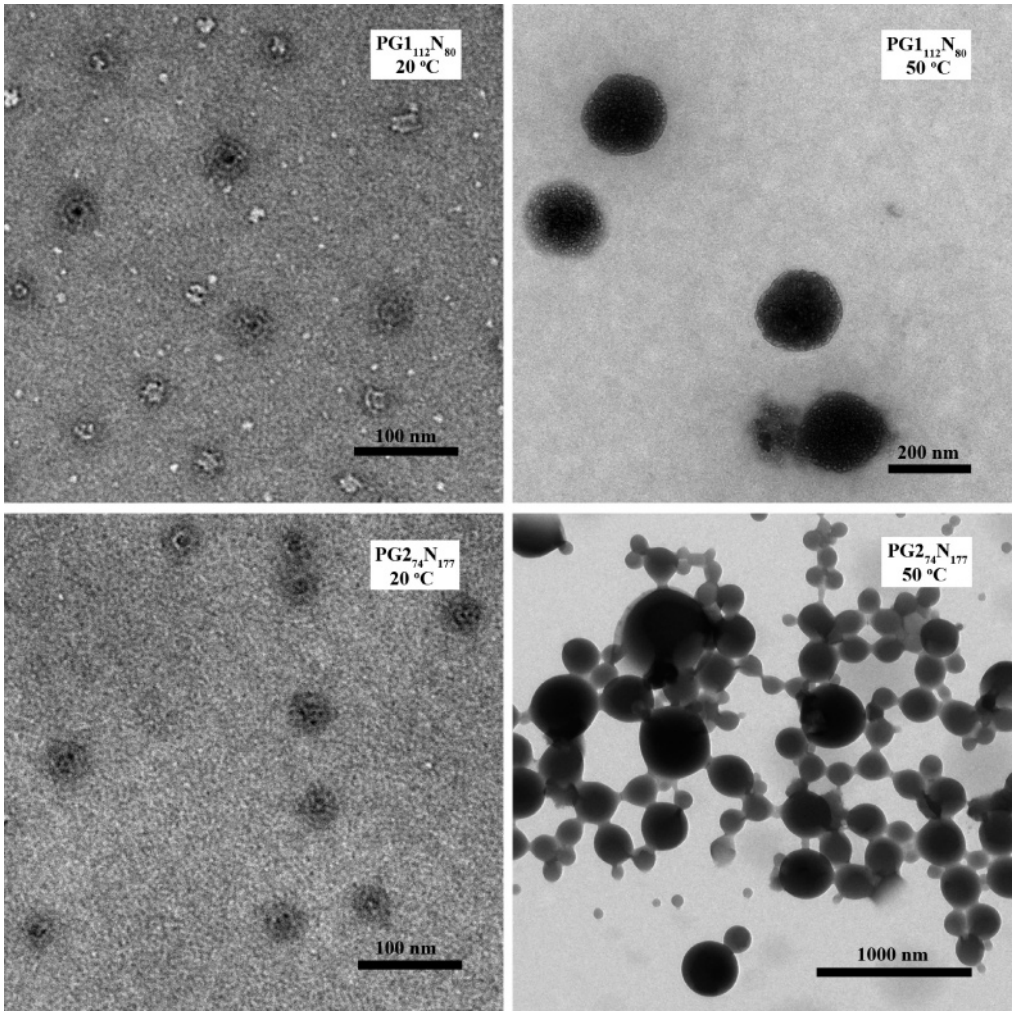


Figure 6. TEM images for $\mathbf{PG1_{112}N_{80}}$ and $\mathbf{PG2_{74}N_{177}}$ cast from buffered aqueous solution of pH 4.0 at 20 and 50 °C, respectively.

generation samples of $\mathbf{PG2}_n\mathbf{N}_m$, the values are higher than those of $\mathbf{PG1}_n\mathbf{N}_m$. For example, whereas $\mathbf{PG1_{98}N_{602}}$ has a LCAT of 33.9 °C, that of $\mathbf{PG2_{74}N_{450}}$ is 42.6 °C, even though the latter has shorter absolute block lengths.

From the curves in Figure 5a,b it can be seen that the transitions are especially sharp for those $\mathbf{PG1}_n\mathbf{N}_m$ samples which have low LCATs. For those also the remaining transmittance at high temperature is rather low (few percent). This indicates that basically all material is involved in aggregation and that the aggregates are large and tight enough to scatter light. For a sample with low block length ratio (Table 1, entry 5), the transmittance curve differs markedly in that not only the LCAT is shifted to higher values but also the residual transmittance is much larger (∼40%). Additionally, the transition is broader which may indicate a more complex aggregation process. For the second-generation BCPs $\mathbf{PG2}_n\mathbf{N}_m$, the transitions are generally broader, and the behavior is quite similar to that of the first generation BCPs with long dendronized block (Figure 5b). Also, the residual transmittance is considerable throughout (20−40%). The heating and cooling curves for all samples did not show any sizable hysteresis. A concrete example is shown in Figure 5c.

Self-Assembly. On the basis of the ^{1}H NMR evidence and results of the turbidity measurements, it is firm to conclude that block copolymers reported here undergo fully reversible aggregation at their LCATs. In order to further investigate the structures of aggregates formed in solution, TEM measurements were performed on samples of $\mathbf{PG1_{112}N_{80}}$ and $\mathbf{PG2_{74}N_{177}}$ at both 20 and 50 °C so as to provide some insight into the aggregates' nature below and above their LCATs. All preparations were done from buffered aqueous solutions of pH 4.0. Figure 6 shows representative TEM images obtained. At 20 °C, which is below the LCATs of the BCPs, both clear aqueous solution of $\mathbf{PG1_{112}N_{80}}$ and $\mathbf{PG2_{74}N_{177}}$ give loosely packed small aggregates with size up to ∼20 nm. In contrast, when the TEM sample was prepared at 50 °C, which is above the LCATs, $\mathbf{PG1_{112}N_{80}}$ gives round objects with diameters of ∼200 nm. The contrast within these objects is not homogeneous and has a maximum toward the center. This may point toward spherical compound micelles.[31] For $\mathbf{PG2_{74}N_{177}}$ at 50 °C also round objects are observed, but their size distribution is larger than for $\mathbf{PG1_{112}N_{80}}$. The diameters vary between approximately 50 and 400 nm. Again the contrast is strongest in the center of the objects. Also, the objects are partially interconnected with one another.

4. Conclusions

A series of water-soluble diblock copolymers, the poly(*N*iPAM)-*b*-dendronized polymethacrylates $\mathbf{PG1}_n\mathbf{N}_m$ and $\mathbf{PG2}_n\mathbf{N}_m$, were synthesized by RAFT polymerization with broadly varied block lengths. They have two and four positive charges at every repeat unit of the dendronized block, respectively. The PDI values obtained are in a reasonable range though no values below PDI = 1.15 could be obtained. The aggregation behavior of all samples was studied by temperature-dependent NMR spectroscopy as well as CAC and LCAT determinations.

Though no concrete structural proposals can be made, it can nevertheless be concluded that the aggregation process is shifted to higher temperatures when either the length of the dendronized block relative to *N*iPAM is increased or second-generation dendronized blocks are involved. In those cases the dendronized block dominates over *N*iPAM which is underlined by the observation that for $\mathbf{PG1_{112}N_{80}}$ the temperature of the *N*iPAM coil started to collapse (31−32 °C) differs from that at which aggregation occurs (around 42 °C) by 10 deg. The LCAT curves are also broad in the cases the dendronized blocks dominate, indicating a more complex aggregation behavior which may be interpreted in terms of "protection" of the collapsed *N*iPAM block against aggregation by the dendronized block. First TEM measurements show that large, so-called compound micelles are formed at elevated temperatures. Their diameters are in the range 50−400 nm. Further investigations on the thermally induced self-assembly of the copolymers and the morphologies of their aggregates by light scattering and TEM are in progress.

The polymers $\mathbf{PG1}_n\mathbf{N}_m$ and $\mathbf{PG2}_n\mathbf{N}_m$ are novel BCPs where both blocks are water-soluble. Using the synthetic instruments developed for dendronized homopolymers, it would be easy to increase both the thickness of their dendronized blocks and the linear charge density by systematically increasing the dendrons' generations. This makes them interesting candidates not only for aspects discussed in this paper but also for the generation of hybrid materials with biopolymers, biomineralization, and the generation of hierarchically structured matter using polyelectrolytes.

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Supporting Information Available: Fluoroscence spectra for CAC determination and ^{1}H NMR spectra of $\mathbf{PG2_{74}N_{177}}$ at 25 and 70 °C. This material is available free of charge via the Internet at http://pubs.acs.org.

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