Macromolecules **2005,** *38,* 4595−4603

Highly Branched Poly(*N*-isopropylacrylamide)s with Imidazole End Groups Prepared by Radical Polymerization in the Presence of a Styryl Monomer Containing a Dithioester Group

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Received November 3, 2004; Revised Manuscript Received March 23, 2005

ABSTRACT: Highly branched poly(*N*-isopropylacrylamide) (PNIPAM) compounds were prepared by copolymerization of 3*H*-imidazole-4-carbodithioic acid 4-vinylbenzyl ester, **1**, with *N*-isopropylacrylamide (NIPAM) using reversible addition−fragmentation chain transfer (RAFT) polymerization. The polymerizations proceeded well with few side reactions. An increase in the content of **1** in the monomer feed appears to increase the number of branch chains, and at the same time no evidence was obtained for the presence of substituted acrylamide chain ends that may potentially result via elimination of the dithioate group. The polymer products show a clear tendency to increased molecular weight as the extent of conversion of monomer increases, while size exclusion chromatography (SEC) profiles indicate a complex distribution of molecular weights compared to linear polymers obtained with a non-RAFT carboxylate monomer. Both NMR and viscometry indicate that, as expected, increasing the amount of **1** in the feed has the effect of increasing the degree of branching in the final product. This increase in branching reduces the intrinsic viscosity of the solutions of the highly branched polymers compared to similar linear polymers. Poly(*N*-isopropylacrylamide) displays a lower critical solution temperature (LCST) in aqueous solutions, and cloud point data indicate a clear effect of chain architecture on the temperature at which this transition occurs. Thus, a set of linear analogous copolymers have LCST's that, for equivalent mole fractions of imidazole content, are higher than the similar highly branched polymers. However, on complexation of copper by the imidazole groups the LCSTs of the linear and highly branched sets cannot be differentiated.

Introduction

Branched polymers owe much of their utility to the presence of a large number of chain ends per molecule and their chain architecture. The latter can have a profound effect on materials properties, such as rheology and solubility.[1,2] On the other hand, the large number of chain ends can be used to add useful chemical functionality, which may differ from similar functionality added along the main chain.[2−5] These polymers can be produced in chain growth polymerization by using branching monomers, which act as both monomers and transfer agents or as monomers and initiators.[6] Both of these functions are combined in approaches that use addition−fragmentation as the branch forming reaction,[7] and of these, the reversible addition−fragmentation chain transfer (RAFT) methodology introduced by Thang et al.[8,9] also offers the opportunity to modify the end groups. This method has proved to be a useful technique for the synthesis of reactive polymers and polymers with well-defined architectures. The currently accepted mechanism of RAFT polymerization, as documented by other authors, has been formulated so as to proceed by a series of reversible addition−fragmentation steps, as shown in Scheme 1. The process is initiated by the formation of a propagating radical $P_n^\bullet$ which adds to the thiocarbonyl group of the RAFT agent to give a radical adduct which fragments to a polymeric dithioate species and a new radical adduct, $R^\bullet$. This radical then reinitiates polymerization to give a new propagating radical, $P_m^\bullet$. An equilibrium is thus set up between the propagating radicals $P_n^\bullet$ and $P_m^\bullet$ and the dormant polymeric dithioate compound via the formation of an intermediate radical. In this way polymers of low polydispersity can be obtained and a variety of R and Z groups exploited to give polymer chain-end functionality.

RAFT polymerization has been used to prepare block copolymers[10] and star-shaped polymers.[11,12] Yang et al.[13] prepared highly branched polystyrene using a RAFT polymerization by incorporating a polymerizable dithioate ester as the RAFT agent. These branching monomers based on vinyl dithioate esters place the dithioate ester group at the chain ends. Therefore, if the RAFT agent contains a specific chemical functionality, this will also be located at the chain ends. More recently, a dithioate ester was used as a transfer agent aimed at preventing the gelation of a radical polymerization containing a difunctional monomer.[14] Alternatively, the dithioate ester chain ends can be further modified to provide the target functionality.[15]

In the work reported here we describe the use of an imidazole functional RAFT agent, **1**, used to prepare stimuli responsive poly(*N*-isopropylacrylamide) (PNIPAM), highly, branched polymers with imidazole groups at the chain ends. The latter function finds application as a ligand in protein purification[16−20] and potentially in gene and drug delivery.[21−23] The lower critical solution temperature of these polymers was then compared to those of linear analogues produced by copolymerization of NIPAM with **2**. We also describe an initial study using the RAFT agent **3**, which contains the same imidazole functionality as **1** but lacks the styryl double bond. Structures **1**−**3** are shown in Figure 1. PNIPAM is probably the most well-studied stimuli responsive polymer, and it has attracted considerable

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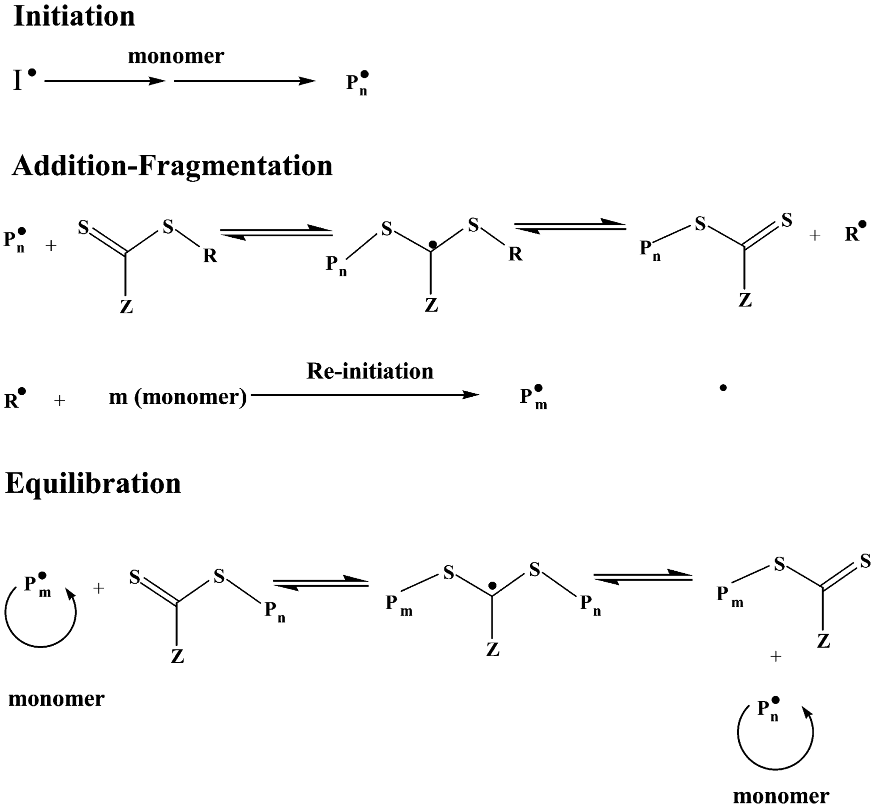
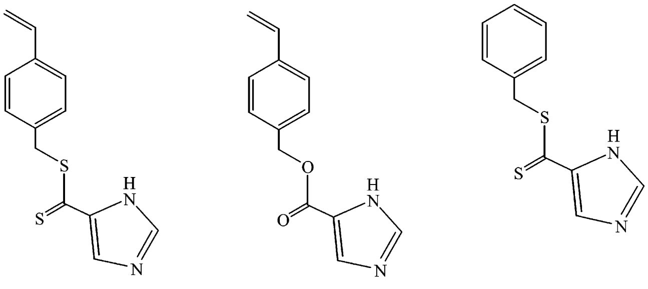
10.1021/ma047742n CCC: \$30.25

Scheme 1. Currently Accepted Mechanism for RAFT Polymerization



attention as the basis of many thermally responsive polymer systems. The behaviors of both the homopolymer[24−30] and its copolymers[31,32] are very well studied due to the narrow temperature range over which the lower critical solution transition occurs in aqueous media.[33] NIPAM has also been successfully polymerized using the RAFT technique.[34,35]



1 2 3

Figure 1. Structures of imidazole species that were incorporated in polymerizations of NIPAM.

Results and Discussion

Linear PNIPAM. The use of RAFT polymerization to synthesize low-polydispersity linear PNIPAM has previously been carried out by other workers using benzyl 1-pyrrolecarbodithioate as the chain-transfer agent in 1,4-dioxane at 60 °C with AIBN as initiator.[35] In a preliminary study designed to investigate the feasibility of using **1** to produce highly branched PNIPAMs, we carried out a similar series of RAFT polymerization reactions using **3** and NIPAM. By reducing the amount of **3**, we were able to selectively synthesize a range of PNIPAMs of increasing molecular weights.

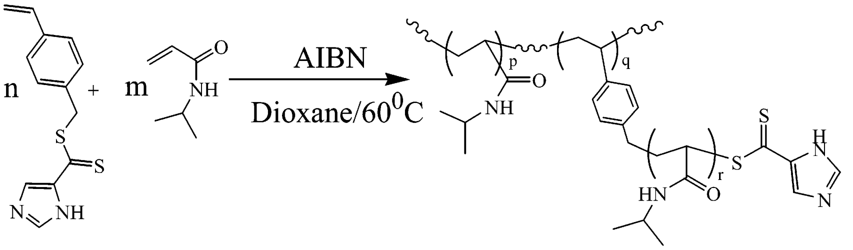
Table 1. Triple Detection SEC Data (Eluant Was THF/TBAB, with Triple Detection) for Linear PNIPAM Generated by Polymerization in the Presence of 3

mole ratio NIPAM/**3**	temp (°C)	conv (mol %)	M_w (g mol^{-1})	PDI
116:1	60	20	7 600	1.12
174:1	60	51	12 000	1.35
232:1	60	45	22 500	1.26
87:1	80	35	31 200	1.43
116:1	80	67	38 500	1.41
174:1	80	56	51 000	1.21
232:1	80	34	58 800	1.21
348:1	80	48	62 600	1.26
1394:1	80	56	69 200	1.29

The latter data (see Table 1) were obtained by triple detection SEC in THF (0.1 wt % tetrabutylammonium bromide). Table 1 shows that the polydispersity (PdI) indexes ranged from 1.2 to 1.45 and were similar to those obtained by Müller.[35] The PdIs are a good indication of the control provided to the radical polymerization by the inclusion of **3**. The data thus suggest that the RAFT mechanism outlined in Scheme 1 is occurring at the two specified temperatures. Further characterization using MALDI−TOF mass spectrometry (using entry 1 from Table 1) showed, as predicted, the presence of the benzyl and 4(5)-imidazole dithioate end groups (see Supporting Information).

Highly Branched PNIPAM. The formation of the PNIPAM highly branched polymers required the synthesis of the imidazole-functionalized RAFT agent, 3*H*-imidazole-4-carbodithioic acid 4-vinylbenzyl ester, **1**. The use of this styryl imidazole−dithioate allowed copolymerization with NIPAM to proceed via the presence of a styryl double bond and chain branching to proceed via RAFT polymerization with the imidazole dithioate. RAFT agent **1** was synthesized in reasonable

Scheme 2. Highly Branched PNIPAM Prepared by RAFT Polymerization



yield via the cesium carbonate-assisted coupling of 4(5)-imidazole dithioic acid to 4-vinylbenzyl chloride.

All of the attempted RAFT polymerizations of NIPAM in the presence of **1** were carried out for 24 h and generated polymeric materials as hard free-flowing powders after reprecipitation. Scheme 2 shows the generalized scheme for the preparation of these highly branched PNIPAMs with imidazole end groups. As can be seen from these structures, the imidazole groups sit at the chain ends and the styryl unit provides a branching point. Evidence for the presence of the imidazole groups at the termini of polymer branches was obtained via ^{1}H NMR as shown in Figure 2, in which broad signals that were derived from the CH imidazole resonances were apparent at δ 7.5−8.0 (see the expanded region of Figure 2). The styryl residues were observed, also as broad peaks, between 6.7 and 7.3 ppm. The results of the calculations derived from these spectra are shown in Table 2. The data show that it was possible to produce average values of degrees of branching (DB) by comparison of the NIPAM isopropyl methine protons at δ 4.0 to the aromatic protons (imidazole + xylyl) at δ 6.7−8.0 to obtain the number of repeat units per branch (RB).

The data also show that the monomer feed and polymer compositions are very similar after polymerization for 24 h and that they are essentially within the experimental error of the NMR technique, which was calculated to be ±5%. These analyses thus suggest that, at least at these low levels of mole fraction of **1** in the feed, the monomer feed can be used to approximate the overall polymer composition.

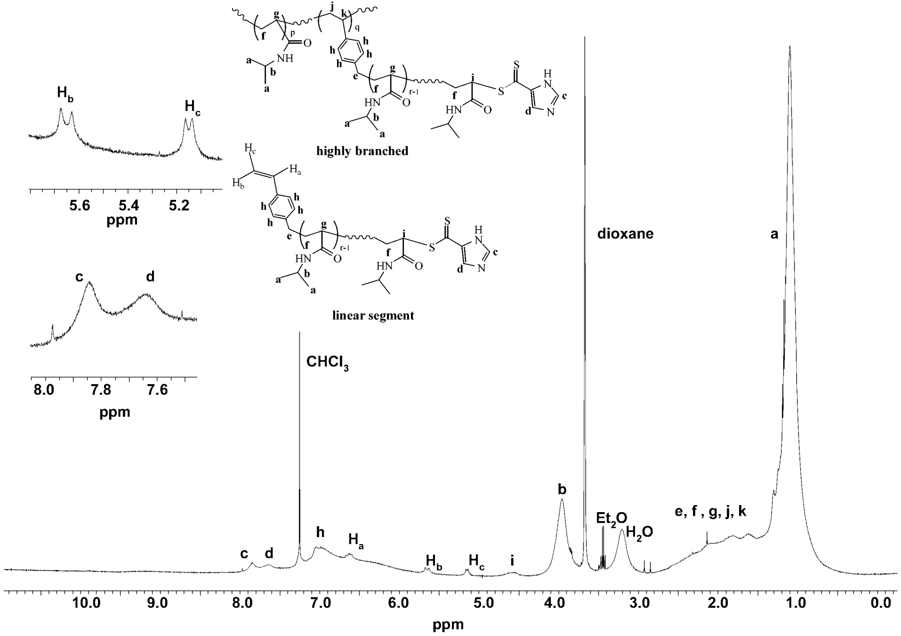


Figure 2. ^{1}H NMR (400 MHz) spectrum of highly branched PNIPAM ($v_1 = 0.042$, $v_1' = 0.039$) at 24 h reaction time.

Table 2. Results of Polymerization Reactions of NIPAM in the Presence of 1 at 60 °C[a]

					yield (%)			*P*	
NIPAM/**1** (feed)	v_1	v_1'	RB	DB	24 h	48 h	M_w (g mol^{-1})	24 h	48 h
15:1	0.063	0.077	5.2	0.19[a]	18	52	61 300	0.6	1.0
23:1	0.042	0.039	8.8	0.12[a]	17	48	60 900	0.8	1.0
25:1	0.039	0.048	5.8	0.17[a]	19	47	19 748	0.9	1.0
28:1	0.035	0.042	6.0	0.16[b]	23	42	25 090	1.0	1.0
30:1	0.033	0.036	6.5	0.15[b]	19	45	24 672	1.0	1.0
33:1	0.029	0.032	12.5	0.08[b]	22	52	22 960	1.0	1.0
46:1	0.021	0.024	13.8	0.07[b]	15	39	53 400	1.0	1.0

[a] v_1 = mole fraction of **1** in the monomer feed; v_1' = mole fraction of **1** in the polymer (from ^{1}H NMR spectra); RB = repeat units per branch; DB = degree of branching (1/RB) as determined by ^{1}H NMR after a = 48 h and b = 24 h and where RB = {area(CH-isopropyl) + [area(CH−Im) + area(CH-aromatic)]/6}/{[area(CH−Im) + area(CH-aromatic)]/6}. *P* = proportion of chain transfer agent in highly branched polymer; at 70 °C/28 h DB = 0.04. The associated error in measuring integrated NMR signals for all polymer samples was estimated to be ±5%.

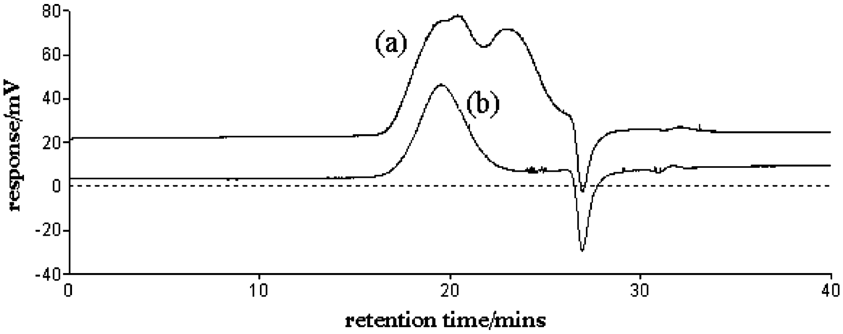


Figure 3. Typical SEC chromatograms derived from (a) NIPAM polymerized in the presence of **1** and (b) linear polymer prepared copolymerization of NIPAM and **2**.

The NMR spectrum in Figure 2 can also be used to determine the proportion of chain transfer agent **1** that has been incorporated into these polymers (P) by examining the ^{1}H NMR spectra at $\delta = 5.15-5.65$ ppm (see expanded region) attributable to the CH_2= (styryl) groups. The ratio of these signals to those of the imidazole end groups ($\delta = 7.5-8.0$ ppm) then gives the proportion of unreacted styryl groups in the polymer. The other vinyl proton (CH_2=C*H*−) of the styryl group is observed at 6.6 ppm and serves to unequivocally assign these resonances as vinyl end groups. They are the result of the incomplete conversion of styryl groups that arise from molecules of **1** that have undergone transfer and reinitiation but have not propagated by copolymerization with NIPAM. The results of the chain end functionality calculations are given in Table 2. As can be seen from these data, significant amounts of alkene (stryryl) end groups were only observed in polymerizations in which the fraction of **1** in the monomer feed exceeded 3.8 mol % and when the reactions were run for 24 h. The resonances due to vinyl peaks were absent from the products obtained from polymerizations that were carried out for 48 h (Table 2). This observation confirms that the vinyl resonances are due to incomplete conversion of the styryl group of **1**. It should also be noted we could not assign any resonances from alkene chain ends produced by base-catalyzed or pyrolytic elimination of the dithioate end group.

Polymerizations in the presence of **1** produced high molecular weight polymer, and as expected in a polymerization containing a branching monomer, the molecular weight distributions were broad and multimodal.[36] The multimodal chromatograms are exemplified, in Figure 3, by the size exclusion chromatography (SEC)-derived molecular weight distributions. The figure also shows data derived from copolymerization of NIPAM with **2**, a nonbranching imidazole-functional comonomer. These SEC results illustrate that the molecular weight distributions of these linear copolymers are unimodal. Therefore, the multimodal distributions observed in polymerizations incorporating **1** appear to be a consequence of the branch producing transfer events. The results from all of the copolymerizations incorporating **2** are given in Table 3. Two aspects are worthy of note from these data. First, over these limited feed ratios, the feed and final polymer compositions are essentially the same. Second, the polydispersities range from 3.3 to 5.1, i.e., values that are typical for radical copolymerizations taken to moderate to high conversions.

We also obtained the SEC profiles of the highly branched polymers prepared at various NIPAM:**1** ratios in accordance with Table 2 which are exemplified by the log(molecular weight) plots in Figure 4. All of the polymers were characterized by high M_w values and high polydispersities, which ranged from 6 to 14. The SEC profiles do not appear to be due to simple mixtures and illustrate the complex nature of these reactions.

Table 3. Results of Copolymerization Reactions of 2 with NIPAM[a]

v_2	v_2'	M_w[b] (g mol^{-1})	PDI	conv (mol %)
0.021	0.019	148 000	5.1	74
0.026	0.022	119 000	4.1	72
0.029	0.027	103 000	3.3	52
0.033	0.026	73 000	3.5	51
0.036	0.028	72 300	3.9	58
0.039	0.034	59 600	5.0	39
0.040	0.044	85 500	4.0	47
0.046	0.049	84 600	4.6	34
0.053	0.049	76 900	4.1	44

[a] v_2 = mole fraction of **2** in the monomer feed; v_2' = mole fraction of **2** in the polymer (from ^{1}H NMR spectra). [b] Determined by SEC (DMF, PEO standards).

We next repeated the polymerization carried out with a feed mole fraction of **1**, $v_1 = 0.063$ (mole fraction **1** in polymer from ^{1}H NMR, $v_1' = 0.077$), which corresponded to a NIPAM:**1** feed ratio of 15:1. The reaction was repeated and sampled in order to enable a study, using SEC, of the development of molecular weight and its distribution during the polymerization. Figure 5 shows the molecular weight distributions determined at various reaction times, as determined using a poly(ethylene oxide) calibration.

To minimize adsorption phenomena, we used an eluant composed of DMF containing 0.1% ammonium acetate at 70 °C. The first observation to be made from these data is that the molecular weight distributions shift to higher values of log(molecular weight) as the polymerization progresses. Unfortunately, the changes in the form of the distribution with reaction time preclude the formation of the molecular weight vs monomer conversion plots that are often associated with studies of living or living-radical chain growth polymerizations. However, it is clear qualitatively from the data illustrated in Figure 5 that an increase in molecular weight occurs as the extent of monomer conversion increases. The branching process produces increasingly broader molecular weight distributions as the polymerization progresses, and a clear shift to higher molecular weights is observed. These observations are in agreement with the predictions of Müller et al.,[36] who have shown that the molecular weight distributions produced by related self-condensing vinyl polymerizations broaden exponentially with the degree of conversion of the vinyl groups. We also noted that while the

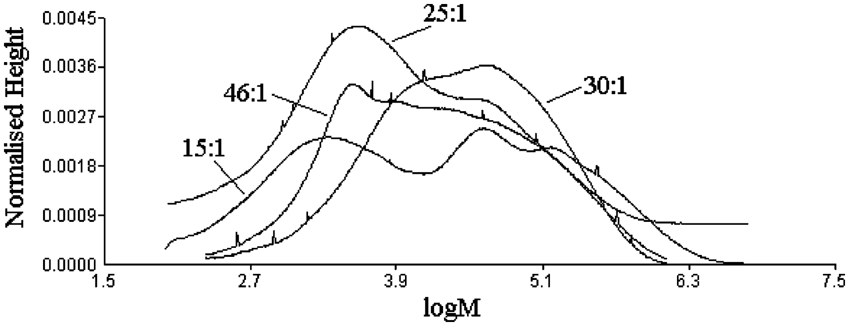


Figure 4. SEC (eluant 0.1% ammonium acetate in DMF at 70 °C) profiles for highly branched polymers (24 h reaction time) showing the effect of NIPAM:**1** feed ratios.

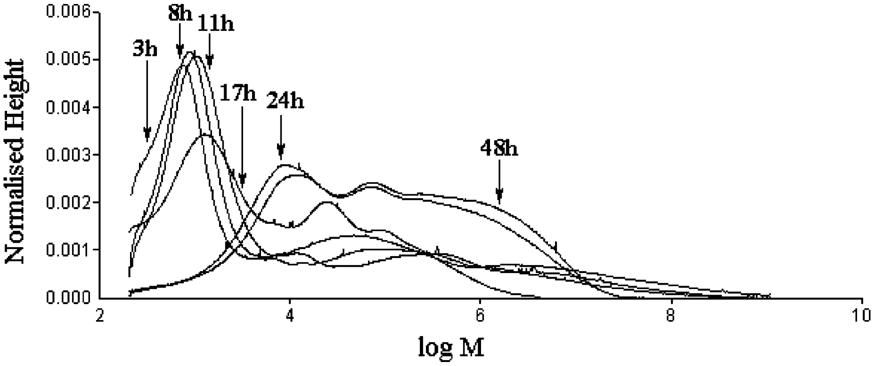


Figure 5. Molecular weight distributions for polymerizations of NIPAM in the presence of **1**, obtained at various reaction times ($\upsilon_1 = 0.063$, $\upsilon_1' = 0.077$).

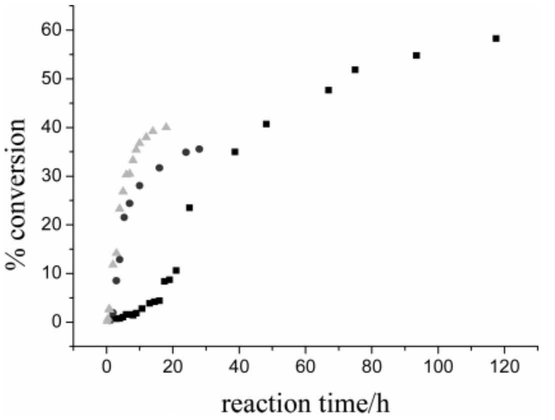


Figure 6. Time−conversion plots for polymerizations of NIPAM/1 at 60 (■), 70 (●), and 80 (▲) °C using a monomer feed ratio of $\upsilon_1 = 0.063$.

yield of polymer could be increased beyond 40% using an extended reaction time of 48 h, the SEC profile did not appear to notably change beyond 24 h.

Next several reactions were performed at a range of temperatures (at 60, 70, and 80 °C).The reaction time vs monomer conversion plots were produced gravimetrically and are shown in Figure 6.

The polymerization carried out at 60 °C gave a strong indication of the induction period that is often associated with RAFT polymerizations.[35,37] In these cases the induction period appears to be completed by ≈16 h reaction time. At elevated temperatures, however, this long induction period is not evident, and to investigate this effect further, we chose to examine the ^{1}H NMR spectrum of the polymer produced at a NIPAM:**1** feed ratio of 15:1 after reaction at 70 °C for 28 h. In this case we found that the imidazole CH signals were still present while there was no evidence for the presence of CH signals at $\delta = 5.15-5.65$ ppm that may have been attributable to end-chain or styryl double bonds. It was also found that the DB value was significantly lower (see Table 2). Thus, it would appear that at these elevated temperatures the copolymerization reaction between the styryl groups of **1** and NIPAM occurs to a greater extent than at 60 °C. SEC results also revealed the presence of a relatively large amount of high molecular weight polymer at 70 °C, and this would suggest that at elevated temperatures highly branched polymer is produced via the RAFT mechanism, albeit after a shorter induction period.

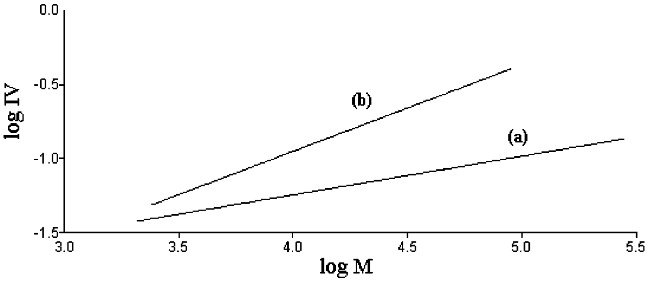


Figure 7. Mark−Houwink plots for linear (b) and branched polymer (a) ($\upsilon_1 = 0.063$, $\upsilon_1' = 0.077$) generated at 60 °C.

SEC Viscometry. Ideally, we would have compared data from SEC with triple detection of the linear copolymers derived from copolymerization of NIPAM and **2** with the branched polymers derived from polymerization of NIPAM in the presence of **1**. However, the latter were only partially soluble in THF and gave generally a two-phase mixture of solution and dispersed polymer. We therefore carried out reversible addition−fragmentation chain transfer (RAFT) polymerization studies using the polymers prepared from polymerization of NIPAM in the presence of **3**. However, these studies were limited by the decrease in solubility of the

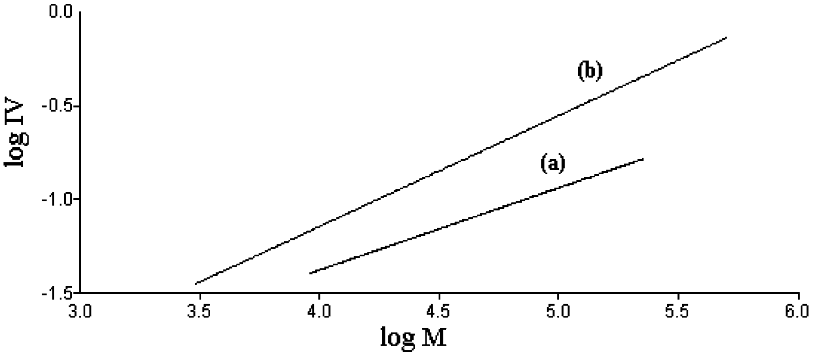


Figure 8. Mark−Houwink plots for linear (b) and branched polymer (a) ($v_1 = 0.021$, $v_1' = 0.024$) generated at 60 °C.

polymers in THF as the amount of **1** was increased. It was not possible to use DMF as the eluant with the viscometric detector because of the high viscosity of this solvent. Within these limitations we were able to extract some useful information using this technique. Mark−Houwink plots were obtained by plotting log[η] vs log(molecular weight) for selected branched polymers generated from the polymerization of NIPAM in the presence of **1** and for the linear PNIPAMs prepared in the presence of **3**. The linear copolymers were produced with the aim of comparing the behavior of the highly branched polymers to linear polymers with imidazole functionality. A highly branched polymer generated from a feed ratio of $v_1 = 0.063$ ($v_1' = 0.077$) at 60 °C gave the Mark−Houwink plot shown in Figure 7a, while a linear polymer (mole ratio NIPAM:**3** = 1394:1), which had a molecular weight distribution that lay within the same range, gave the plot in Figure 7b. It is clear from these data that at all molecular weights the highly branched polymer gave lower values of log[η] and that plot (a) had a considerably lower gradient. The branched polymer was characterized by $\alpha = 0.166$ compared to its linear counterpart, which gave $\alpha = 0.612$.

The effect of decreasing the amount of **1** in the feed is illustrated in Figure 8, which shows the Mark−Houwink plot for a branched polymer generated from a feed of $v_1 = 0.021$ ($v_1' = 0.024$) at 60 °C (a) and the linear analogue (mole ratio NIPAM:**3** = 87:1) (b). These data are similar to those of Figure 7, in that, for all values of log M, log[η] is lower for the branched material than it is in the linear polymer. However, in Figure 8 the slope of the plot for the highly branched polymer, characterized by $\alpha = 0.253$, more closely approaches that of the linear material where $\alpha = 0.555$. Thus, these results support the expectation that increasing the amount of the branching RAFT agent, **1**, increases the degree of branching and that this in turn further decreases solution viscosity.

Cloud Point Analysis of Highly Branched Polymers and Linear Analogues. The highly branched polymers formed from the polymerization of NIPAM in the presence of **1** were ultrafiltered through a cellulose membrane (MWCO 10 000), dissolved in water (10 mg/mL) at 0−1 °C, and the cloud points were determined visually. The range of linear analogous polymers formed from NIPAM and **2** with an equivalent hydrophobe content as the branched versions were also dissolved in water at low temperature and the cloud points determined. For each polymer solution the cloud point was also recorded in the presence of copper(II) ions by the addition of an aliquot of copper(II) sulfate. In Figure 9, the cloud points of all of these polymers are plotted against proportion of imidazole functional polymer. The cloud points for the linear polymers were significantly higher than the cloud points of their branched equivalents. This change in cloud point was unexpected since, if we consider that the system's free volume would be expected to increase as the average number of end groups per chain increases, it might reasonably be expected that the cloud point would increase with branching. These results can only be rationalized if we assume that, in the absence of an added metal ion, the imidazole end groups can aggregate more effectively than the pendant imidazole groups on the linear polymers. The addition of Cu(II) ions substantially raised and sharpened the cloud points for each polymer to an upper limit of 32−36 °C for the branched polymers and 33−36 °C for their linear counterparts. The cloud points of the branched and linear polymers in the presence of copper ions thus appear to be similar. A tentative explanation for this effect would be that in the native form both the linear and branched polymers are present as aggregates in solution, and this may be due to the presence of extensive intermolecular binding interactions occurring between the imidazole groups. The addition of Cu(II) upon binding to the imidazoles has the effect of rendering the chain ends more hydrophilic and at the same time disrupting these interactions so that aggregation is less likely to occur unless the temperature is further raised. Further work is being carried out in our laboratories to study these effects in detail using light scattering, NMR and luminescence techniques and will be reported in due course.

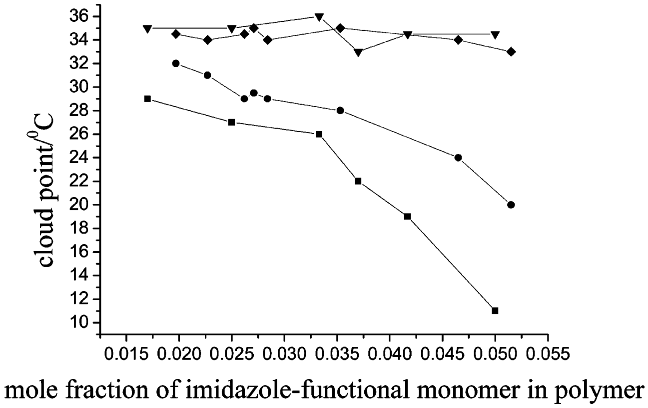


Figure 9. Plots of cloud point vs mole fraction of imidazole for branched (■) and linear PNIPAMs (●) and the cloud points obtained from the branched (▼) and linear (◆) PNIPAMs after the addition of Cu(II) ions.

Summary

In summary we have shown that RAFT controlled radical polymerization can be used to produce highly branched PNIPAMs by incorporation of a styryl dithioate ester in the polymerization mixture. In this case the RAFT agent also carried imidazole functionality, which was placed at the chain ends of the final product. Evidence for the livingness of the procedure was obtained using a RAFT agent which did not have a polymerizable styrenic double bond in its structure, but which produced linear PNIPAMs of low polydispersity. Mark−Houwink plots also showed the highly branched nature of the polymers. Thus, when larger amounts of the branching agent were incorporated in the structure, the viscometry profiles displayed a greater divergence in slope of the plot when compared to a linear PNIPAM. Surprisingly, the highly branched polymers had cloud points that were lower than equivalent linear polymers that were produced by copolymerizing NIPAM with a styryl monomer carrying an ester and imidazole functionality. We tentatively suggest that the decrease in cloud point as the degree of branching increases may be due to aggregation of the imidazole end groups.

Experimental Section

Materials. *N*-Isopropylacrylamide (Aldrich, 97%) was recrystallized (3×) from hexane (Fisher, HPLC grade) via dissolution at 45 °C and then cooling under refrigeration. 4(5)-Imidazoledithiocarboxylic acid (Aldrich, 70%) and 4-imidazolecarboxylic acid (Aldrich, 98%) were used without further purification. Cesium carbonate (Aldrich, 99%) was ground to a fine powder and dried at 200 °C. 4-Vinylbenzyl chloride (Aldrich, 90%) was distilled under reduced pressure, and benzyl bromide (Fluka, 98%) was used without further purification. Triethylamine (BDH, 99%) was distilled prior to use, and α-azoisobutyronitrile (AIBN) (BDH, 97%) was recrystallized from diethyl ether (Fisher, HPLC grade). *N*,*N*-Dimethylformamide (DMF) (Aldrich, sure-seal) and dioxane (Aldrich, sure-seal) were used as purchased; tetrahydrofuran and dichloromethane were distilled from sodium or calcium hydride, respectively, prior to use. Chromatographic media were silica gel (BDH, 40−63 μm) and aluminum oxide (BDH, Brockmann Grade 1). TLC was carried out using Merck silica gel 60 F_{254} (aluminum sheet) plates and Macherey-Nagel (Germany) aluminum oxide/UV_{254}, 0.2 mm (precoated plastic sheet) plates.

Instrumentation. Average molecular weights and molecular weight distributions (measured relative to poly(ethylene oxide) (PEO) standards) of polymers were measured by gel permeation chromatography (GPC) with PL gel mixed B (10 μm particle size, 100−10^6 Å pore size, effective MW range 10^3−10×10^6, 3 × 30 cm + guard columns) (Polymer Laboratories, UK) and a refractive index detector. DMF was used as the eluent at a flow rate of 1.0 $cm^3\ min^{-1}$ at 70 °C. Sample concentrations were approximately 2.0 mg cm^{-3} and were filtered through tissue paper. Triple detection SEC was carried out using a Viscotek VE1121 solvent pump (flow 1.0 $cm^3\ min^{-1}$) and Rheodyne 7725i injector with 100 μL loop. Columns were PL gel mixed C (5 μm particle size, 100−10^5 Å pore size, effective MW range 10^2−2×10^6, 2 × 30 cm + guard column) (Polymer Laboratories, UK) thermostated at 35 °C. Detectors were Viscotek model 250 dual refractometer/viscometer plus Viscotek RALLS detector. Data acquisition and analysis using Polymer Laboratories multidetector software. Eluant was THF (0.1% w/v tetrabutylammonium bromide). For triple detection SEC ca. 10 mg of each polymer was accurately weighed and dissolved in the THF (0.1% TBAB) eluant at ca. 2 mg/mL and then filtered through tissue paper. ^{1}H NMR (250 and 400 MHz) and ^{13}C NMR (62.5 and 100 MHz) spectra were recorded using Bruker AC-250 and AMX2-400 instruments. CHN analysis was performed on a Perkin-Elmer 2400 CHNS/0 series II elemental analyzer. LC-MS analysis was carried out using a Waters 2695 HPLC system coupled to a Waters LCT (TOF) mass spectrometry detection system.

Synthesis of 3*H*-Imidazole-4-carbodithioic Acid 4-Vinylbenzyl Ester, 1. 4(5)-Imidazoledithiocarboxylic acid (22.05 g, 70%, 107 mmol) was dissolved in DMF (450 mL), in which an excess of cesium carbonate (154 g, 471 mmol, 4.4 equiv) was suspended and the mixture stirred rapidly at room temperature under a nitrogen atmosphere for 30 min to form a deep orange coloration. 4-Vinylbenzyl chloride (18.33 g, 16.93 mL, 120 mmol) was added to the suspension in one portion, and stirring continued for 70 h. The suspension was filtered to remove cesium carbonate, and the solids were washed with dichloromethane. The DMF was removed by rotary evaporation (50 °C, high vacuum), and the remaining oil was dissolved in dichloromethane (800 mL) and then washed with saturated sodium hydrogen carbonate solution (2 × 500 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give a dense orange-brown oil.

An initial purification was carried out using flash silica column chromatography (2.5% MeOH/CH_2Cl_2) to give a semipure oily solid. A final purification was carried out by elution down an alumina column (2% MeOH/CH_2Cl_2), and after evaporation of the appropriate fractions the title compound was isolated as bright orange crystals (7.47 g, 26.8%), R_f (silica, 2.5% MeOH/CH_2Cl_2) 0.19. ^{1}H NMR ($CDCl_3$, ca. 5% CD_3OD, RT, 250 MHz): δ/ppm 4.52 (s, 2H, $-S-CH_2-$), 5.15 (d, 1H, $=CH_2$ vinyl, $J = 10.63$ Hz), 5.65 (d, 1H, $=CH_2$ vinyl, $J = 17.51$ Hz), 6.62 (dd, 1H, $=CH$ vinyl, $J_1 = 16.26$ Hz, $J_2 = 9.38$ Hz), 7.25 (s, 4H, $-C_6H_4-$)7.60 (s, 1H, CH-imidazole), 7.78 (s, 1H, CH-imidazole). LC-MS (TOF, ES$^+$): 12.67 min [50% AcN (0.1% formic acid)/50% H_2O (0.1% formic acid)−95% AcN, 20 min], 261 (M^+), 262 (MH^+) [desolvation gas 462 l h^{-1}, capillary 3129 V, sample cone 36 V, extraction cone 3 V, desolvation temperature 150 °C, source temperature 100 °C]. Calculated for $C_{13}H_{12}N_2S_2$: C, 59.97; H, 4.65; N, 10.76; S, 24.63. Found: C, 59.78; H, 4.68; N, 10.72; S, 24.55.

Synthesis of 4(5)-Imidazole-(4-vinylbenzyl carboxylate), 2. 4-Imidazolecarboxylic acid (5.40 g, 48.2 mmol) was suspended in DMF (160 mL) and stirred under a nitrogen atmosphere. 4-Vinylbenzyl chloride (7.36 g, 48.2 mmol) was added to the suspension followed by triethylamine (4.87 g, 48.2 mmol) and water (0.867 g, 48.2 mmol), and then stirring was continued for 24 h at room temperature. The suspension was partitioned between water (150 mL) and ethyl acetate (250 mL) and then separated, and the aqueous layer was further extracted with ethyl acetate (2 × 250 mL). The organic extracts were combined, dried over magnesium sulfate, filtered, and evaporated to give an oil in residual DMF. The excess solvent was removed in vacuo (high vacuum) at 50 °C. The resultant oil was separated using flash column chromatography with 95:5 dichloromethane/methanol on silica to give 1.134 g (10.3%) of the title compound as a white solid, R_f (silica, 95:5 dichloromethane/methanol) 0.15. ^{1}H NMR ($CDCl_3$/ca. 5% CD_3OD, RT, 250 MHz): δ/ppm 5.21 (s, 2H, $-O-CH_2-$), 5.18 (d, 1H, $=CH_2$, vinyl, $J = 10.63$ Hz), 5.68 (d, 1H, $=CH_2$ vinyl, $J = 17.51$ Hz), 6.63 (dd, 1H, $=CH$ vinyl, $J_1 = 16.26$ Hz, $J_2 = 9.38$ Hz), 7.32 (s, 4H, $-C_6H_4-$, 7.60 (s, 1H, CH-imidazole), 7.65 (s, 1H, CH-imidazole). LC-MS (TOF, ES$^+$): 5.70 min [50% AcN (0.1% formic acid)/50% H_2O (0.1% formic acid)−95% AcN, 20 min], 229 (M^+), 230 (MH^+) [desolvation gas 462 l h^{-1}, capillary 3129 V, sample cone 36 V, extraction cone 3 V, desolvation temperature 150 °C, source temperature 100 °C]. Calculated for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27; O, 14.02. Found: C, 68.52; H, 5.05; N, 12.20; O, 14.23.

Synthesis of Benzyl-4(5)-imidazole Dithioate, 3. Cesium carbonate (149 g, 0.458 mmol) was added to 4(5)-imidazoledithiocarboxylic acid (21.43 g, 0.104 mmol) dissolved in DMF (400 mL), and the mixture was rapidly stirred at room temperature under a nitrogen atmosphere for 30 min. To the suspension benzyl bromide (19.57 g, 0.114 mmol) was added as a solution in DMF (50 mL), and stirring continued in a foil-covered flask for 5 days. The suspension was filtered to remove excess cesium carbonate, and the DMF was removed in vacuo (50 °C, high vacuum). The resultant oil was dissolved in dichloromethane (600 mL), then washed with saturated aqueous sodium hydrogen carbonate (2 × 500 mL), dried over anhydrous magnesium sulfate, filtered, and evaporated to give an orange-brown solid. An initial purification was carried out using flash column chromatography on silica (5:4:1 40−60 petroleum ether/dichloromethane/methanol) to give, after removal of solvent in vacuo, an orange-brown solid (ca. 13 g). A second purification was carried out via column chromatography on alumina (50:46:4 40−60 petroleum ether/dichoromethane/methanol) to give after removal of solvent the title compound as a foul smelling bright orange solid (5.50 g, 22.6%). R_f (alumina, 50:46:4 40−60 petroleum ether/dichloromethane/methanol) 0.31. ^{1}H NMR ($CDCl_3$, ca. 5% CD_3OD, RT, 250 MHz): δ/ppm 4.52 (s, 2H, $-S-CH_2-$), 7.21 (m, 5H, $-C_6H_5-$), 7.57 (s, 1H, CH-imidazole), 7.74 (s, 1H, CH-imidazole). LC-MS (TOF, ES$^+$): 12.67 min [50% AcN (0.1% formic acid)/50% H_2O (0.1% formic acid)−95% AcN, 20 min], 234 (M^+), 235 (MH^+) [desolvation gas 462 l h^{-1}, capillary 3129 V, sample cone 36 V, extraction cone 3 V, desolvation temperature 150 °C, source temperature 100 °C]. Calculated for $C_{11}H_{10}N_2S_2$: C, 56.38; H, 4.30; N, 11.95; S, 27.37. Found: C, 55.89; H, 4.04; N, 11.94; S, 27.43.

Synthesis of Highly Branched and Nonbranched Polymers. Polymerization of NIPAM with 1 or 3. *N*-Isopropylacrylamide (3.514 g, 30.9 mmol) was dissolved in dioxane (11 mL) and added to the required amount of **1** or **3** to give an orange solution. The initiator AIBN (0.111 g, 0.68 mmol) was dissolved in the solution, which was then transferred to a 25 mL glass ampule. The ampule was freeze−pump−thawed on a vacuum line (10^{-4} mbar, three cycles), flame-sealed, and heated in a thermostated water bath at 60 °C for 24 h. The polymer was purified by reprecipitation as follows. The polymer−dioxane solution was added dropwise to rapidly stirring ether (500 mL) at room temperature over 20 min. The ether was decanted from the solids, which were then vacuum-oven dried at RT for 16 h and redissolved in dioxane (11 mL), and the reprecipitation/drying procedure was repeated twice more to give the polymer. The solids were dried (vacuum oven, RT/16 h) to give a yellow-orange solid and finally ultrafiltered.

Polymerization of NIPAM with 2. *N*-Isopropylacrylamide (1.00 g, 8.83 mmol) was dissolved in dioxane/DMF mixture (3.4 mL) under a nitrogen atmosphere, and an appropriate amount of **2** was dissolved in the solution. The initiator AIBN was then added, and full dissolution was effected by gentle shaking. The solution was transferred to an ampule and freeze−pump−thawed (10^{-4} mbar, three cycles); the ampule was flame-sealed and then transferred to a water bath at 60 °C and heated for 24 h. The polymer solution was diluted with DMF (2.0 mL) and then precipitated by adding dropwise to rapidly stirring diethyl ether (80 mL). The ether was decanted off, and the solids were washed with ether (3 × 20 mL) and then dried in a vacuum oven at room temperature (16 h). The reprecipitation/washing drying procedure was twice repeated, and then the polymer was ultrafiltered.

Cloud Point Determination for Highly Branched and Linear Polymers. The cloud points of the branched polymers from the polymerization of NIPAM with **1** and of the linear polymers from the polymerization of NIPAM with **2** were determined by eye using a stirrer hot plate/temperature probe. Each polymer (0.010 g) was dissolved in distilled/deionized water (1.0 mL) at 0−1 °C (ice bath) and then immersed in a magnetically stirred ice bath (100 mL) which was slowly warmed from 0 °C to beyond 35 °C over ca. 15 min. The cloud point range was determined as the temperature interval at which the solution became cloudy and before which any significant agglomerization occurred. Upon recooling to 0−1 °C (ice bath) a 100 μL aliquot of aqueous 0.1 M copper(II) sulfate was added and the cloud point recorded by reimmersing in a magnetically stirred ice bath and warming beyond 35 °C.

Purification of Highly Branched and Linear Polymers by Ultrafiltration. The polymer (500 mg) was dissolved in 10% ethanol/acetone (300 mL) and concentrated by ultrafiltration through a 10 000 MWCO cellulose filter in a 350 mL Millipore filtration unit at 4 atm nitrogen pressure. The procedure was carried out over ca. 45 min to give a final volume of ≈50 mL. The procedure was twice repeated by the addition of more solvent (≈300 mL), and the solvent was removed from the concentrate by rotary evaporation at 40 °C. To allow for ease of handling, the solids were redissolved in DMF (10 mL) and then reprecipitated into diethyl ether (400 mL). The ether was decanted off, the solids were washed with ether (3 × 20 mL), and then the polymer was dried in a vacuum oven at RT for 16 h. Final recoveries of polymer were in the range 80−90%.

Supporting Information Available: MALDI TOF mass spectrum of a PNIPAM produced in the presence of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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MA047742N