Effects of End Group Polarity and Molecular Weight on the Lower Critical Solution Temperature of Poly(*N*-isopropylacrylamide)

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ABSTRACT: The lower critical solution temperatures (LCSTs) for mass fractionated samples of poly(*N*-isopropylacrylamide) (PNIPAM) were studied to determine the effect of polymer molecular weight on the LCST using a high throughput temperature gradient apparatus. PNIPAM fractions prepared by a conventional radical polymerization using azoisobutyronitrile (AIBN) as the initiator had LCSTs that were largely invariant with molecular weight or dispersity. Only slight deviations were noted with lower molecular weight samples. An 18-kDa sample had a 0.6 °C higher LCST. A 56-kDa sample had a 0.2 °C higher LCST. PNIPAM derivatives prepared with a triphenylmethyl (trityl) functionalized azo initiator were also prepared and mass fractionated. These samples' LCSTs were identical to those of PNIPAM samples prepared using AIBN initiation when higher molecular weight samples were compared. The trityl-containing PNIPAM fractions' LCSTs varied when the molecular weight decreased below 100 kDa. Acidolysis of the trityl end groups provided a third set of PNIPAM derivatives whose LCST differed only with samples with M_w values < 60 kDa. These results show there is no effect of molecular weight on LCST until the degree of polymerization is such that end group structure becomes significant. J Polym Sci Part A: Polym Chem 44: 1492–1501, 2006
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INTRODUCTION

Thermoresponsive polymers are widely used in many applications.[1–3] However, the effect of polymer structure on lower critical solution temperatures (LCSTs) is only qualitatively understood. Studies of poly(*N*-isopropylacrylamide) (PNIPAM), a common polymer that has been studied for almost 40 years as an example of thermoresponsiveness, illustrate this.[4] It is known that the general notion advanced by Taylor and Cerankowski that incorporation of more hydrophobic groups will lead to a lower LCST is still a useful qualitative guideline to understand structural effects on LCSTs for polymers including PNIPAM.[5] It is also known that PNIPAM's tacticity has a major influence on PNIPAM's LCST.[6,7] Other solution components can exert a significant and predictable effect on a PNIPAM's LCST. Our recent work has probed these effects in detail, using a high throughput temperature gradient apparatus.[8–11] However, the effect of end groups on LCSTs and the effect of degree of polymerization on LCST is less clear. In the case of PNIPAM, reports variously say that LCSTs increase, decrease, or remain unchanged with molecular weight. Works by Fujishige et al.,[12]

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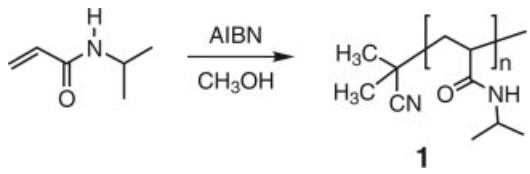
Tiktopulo et al.,[13] Takei et al.,[14] and Ding et al.,[15] report no appreciable change in LCST with changes in the molecular weight of PNIPAM. In contrast, reports by Tong and co-workers[16,17] suggest that LCSTs increase with increasing molecular weight. Finally, Baltes et al.[18] and Schild and Tirrell[19] reported that LCSTs decrease with increasing molecular weight. A very recent report by Xia et al., using PNIPAM samples prepared by atom transfer radical polymerization, suggests that a combination of polymer–solvent interactions and end-group effects are both important.[20] The origin of the differences in these reports is unclear. These different results may reflect the nature of the substrates studied or the fact that different studies used different polymer concentrations or polymers of different purity. For example, sometimes only low-molecular-weight samples of PNIPAM were studied. The paucity of studies directly comparing similar PNIPAM samples with M_n values of 10,000 or less (a degree of polymerization of ~90 or less) with PNIPAM samples having 10-fold larger M_n values (e.g., $M_n > 100{,}000$) presumably could account for some of the differing conclusions about the effects of polymer degree of polymerization and dispersity on LCST. In other cases, low concentrations of additives or impurities or varying polymer concentrations could have affected an LCST either in a positive or negative direction. In any case, the differences in reports about how molecular weights affect LCSTs are confusing. We here have sought to clarify this issue using our experience in PNIPAM synthesis and our ability to measure very subtle differences in LCST with a great precision to provide more definitive results as to how changes in molecular weight of PNIPAM affect LCSTs. The results described here show that LCSTs of high-molecular-weight PNIPAM samples are not affected by molecular weight, end-group structure, or polydispersity until low-molecular-weight samples are examined. In cases where changes in LCST for PNIPAM samples begin to be observed, we have been able to show that these effects are most simply ascribed to the effect of the polymers' end group structure.

RESULTS AND DISCUSSION

To study the effect of molecular weight on LCSTs, we first prepared a large (10 g) batch of PNIPAM via azoisobutyronitrile (AIBN)-initiated polymerization of *N*-isopropylacrylamide in methanol (eq 1).



(1)

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This product was then fractionated into several samples with different molecular weights by a selective precipitation of high-molecular-weight PNIPAM fractions from an acetone solution, using hexane as a "poor" solvent.[21,22] This process afforded us five samples—the starting polymer and the four isolated PNIPAM fractions. All the polymers' molecular weights were characterized by light scattering. Table 1 lists the weight–average molecular weight and LCST data for the starting polymer and the fractionated samples 1–4. A calculation showed that the weighted average (based on the mass of each fraction recovered) of the M_w for fractions 1–4 was 2×10^5 g/mol, a value that is essentially the same as the M_w for the starting polymer. Analyses of these polymers by GPC showed that the fractionated samples generally had a relatively low polydispersity. While the polydispersity index of these fractions could be decreased by further precipitations, the initial fractionated samples were used as isolated.

The LCSTs for the fractions of PNIPAM prepared by the above procedure were then ana-

Table 1. LCST and M_w Data for Unfractionated (Starting Polymer) and Fractionated PNIPAM Samples

	M_w (g/mol)[a]	Polydispersity[b]	LCST (°C)
Starting polymer	2.13×10^5	2.31	30.22
Fraction 1	4.75×10^5	1.32	30.18
Fraction 2	1.70×10^5	1.40	30.21
Fraction 3	5.58×10^4	1.82	30.40
Fraction 4	1.78×10^4	2.55	30.83

[a] Molecular weights were all measured by light scattering in methanol.

[b] Polydispersities were measured by GPC in THF and are based on a comparison to polystyrene standards. The weight–average molecular weight measured by GPC differed from that measured by light scattering (the GPC M_w values were 8.00×10^4, 1.61×10^5, 6.54×10^4, 2.13×10^4, and 1.02×10^4 for the starting polymer and fractions 1–4, respectively).

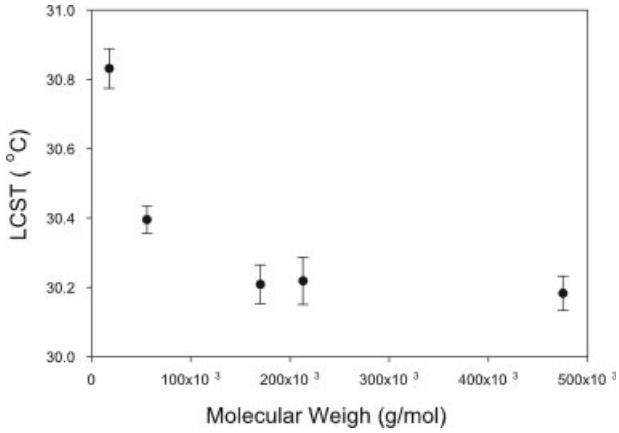


Figure 1. The variation of LCST with M_w of PNIPAM for PNIPAM prepared using AIBN initiation in CH_3OH. The individual polymer sample's M_w values were determined by light scattering.

lyzed using the temperature gradient apparatus we previously described.[8–11] These data are plotted in Figure 1. These data show a small change in the LCST with M_w of the PNIPAM. The maximum change was 0.6 °C with the 17.8-kDa sample. The 55.8-kDa sample had a smaller 0.2 °C change in the LCST. This gradual change in LCST is analogous to what Zhou et al. observed in their study of the effect of M_n on the LCST of poly(*N*,*N*-diethylacrylamide) in water.[23]

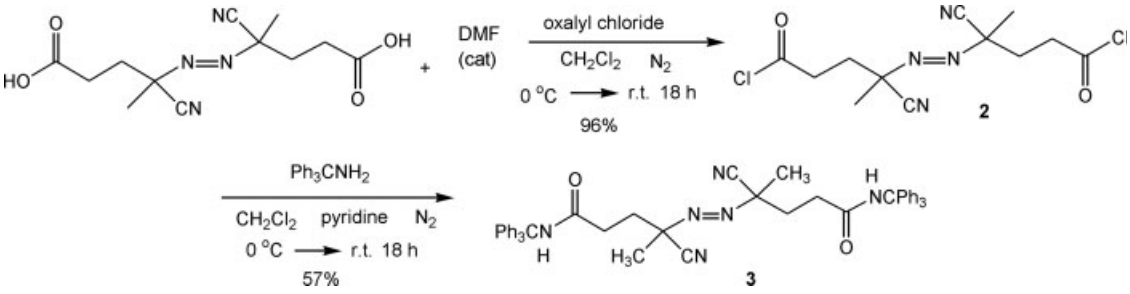
Explanations of the LCST phenomena vary. In general, entropic changes associated with solvation of the macromolecule are presumed to be involved.[11] However, most explanations do not predict the effect of molecular weight on LCST. An exception to this is the qualitative explanation to generally explain the LCSTs that are noted for all polymers that was advanced by Patterson using Flory–Huggins theory.[24]

$$\chi_c = 1/2(1 + r^{-1/2})^2 \qquad (2)$$

In this explanation, the magnitude of χ_c, the critical value of the Flory–Huggins parameter, was used to explain the effect of molecular weight on LCST. This polymer–solvent interaction parameter, χ_c, changes as the size of the polymer changes, since r in eq 2, the ratio of molar volumes of polymer over solvent, decreases as the degree of polymerization decreases, causing χ_c to increase. This increase will result in a higher LCST for polymers with lower molecular weight and this effect would be most noticeable with low-molecular-weight samples in which the macromolecule dimensions change most significantly with the molecular weight.

An alternative explanation for the change in LCST with M_w seen in Figure 1 is that the higher LCST for the lowest molecular weight sample is being determined by polymer end group effects because the importance of the polymer end group increases, as the polymer molecular weight decreases. This explanation was previously considered, but the results are inconsistent. Ding et al.[15] and Baltes et al.[18] prepared carboxyl-terminated PNIPAM oligomers with molecular weights ranging from 2 to 50 $\times$ 10^3 g/mol and did not see any changes in LCST. It was even noted in the work of Freitag et al. that the ionization state of this carboxylic acid end group did not affect the LCST of a polyacrylamide.[25] Takei et al. examined similar carboxyl-terminated PNIPAM derivatives and noted that there was no observable effect on the LCST for solutions of $<$ 1 wt %, but that solutions with 5 wt % PNIPAM had higher LCSTs.[14] A more recent paper by Xia et al. suggests that using different end groups might more predictably affect LCSTs.[20]

Chung et al. prepared a number of other polar and nonpolar end-modified PNIPAMs. They prepared amine and hydroxyl-terminated PNIPAM oligomers (M_w = 7300 Da) and found that the hydroxyl group increased the PNIPAM oligomers' LCST more than the amino group.[26] They also examined the effects of adding hydrophobic end groups onto PNIPAM. They found that the position of the hydrophobic groups on the polymer chain played a crucial role in the ability of the group to alter the polymer's LCST—effects that were complicated by micellarization of the hydrophobically modified PNIPAM polymers. However, when they prepared PNIPAM oligomers of similar molecular weight that were terminated with $C_{18}H_{37}$ chains as well as random copolymers containing $C_{18}H_{37}$ pendant groups, they found that solutions of the PNIPAM oligomers below the critical micelle concentration with hydrophobic end groups had lower LCSTs. The hydrophobic contribution for a single $C_{18}H_{37}$ end group was larger than similar polymers with $C_{18}H_{37}$ groups randomly incorporated as copolymers.[27] They also went on to compare the ability of different carbon chain lengths to alter the LCST of terminally modified PNIPAM oligomers.[27] They prepared PNIPAM oligomers (M_w = 7300 g/mol) with terminal propyl, hexyl, octyl, dodecyl, and octadecyl chains.



Scheme 1

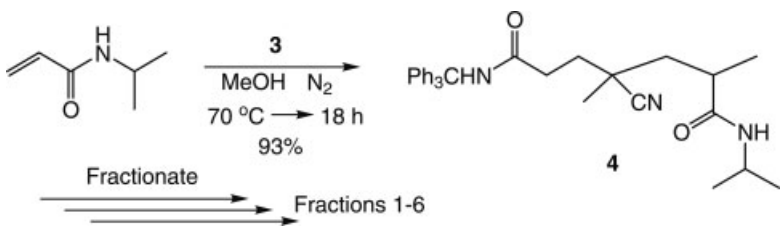
They found that the effects of terminal hydrophobic groups on PNIPAM's LCST were more complex. The propyl, hexyl, and octyl groups of terminally functionalized PNIPAM oligomers progressively lowered the LCST with increasing alkyl chain length, but the trend reversed and the LCST increased for the dodecyl and octadecyl chains. Yamazaki et al. have also shown that PNIPAM with M_n values in the 2000–10,000 range with hydrophobic end groups aggregate to form oligomeric micelles.[28]

Our results shown in Figure 1 combined with the divergent conclusions about the effect of polar and nonpolar end groups on LCSTs of PNIPAM samples led us to carry out our own studies of the significance of end-group hydrophobicity on the LCST of PNIPAM. To eliminate as many variables as possible, we decided that the ideal approach would be to analyze LCSTs of polymers with identical polydispersity and hydrophobicity at the same polymer concentration (10 mg/mL), varying only the hydrophilicity and hydrophobicity of the end groups. We could then use the thermal gradient device we have used previously to look for the variation, if any, in LCST with the polymer's M_w. This was accomplished by preparing a PNIPAM derivative with a triphenylmethylamido (trityl) end group. Such hydrophobic trityl groups can be quantitatively converted to more hydrophilic amido end groups using acidolysis.[29]

A low-molecular-weight model compound *N*-triphenylmethylhexanamide was first prepared by reaction of hexanoyl chloride with triphenylmethylamine. We showed that the triphenylmethyl group of this model amide was quantitatively removed in neat TFA based on ^{1}H and ^{13}C-NMR spectroscopy as well as by the complete disappearance of a spot for the trityl amide in TLC analysis and the concomitant appearance of a spot for the product.

Next, a functionalized initiator, 4,4′-azobis(*N*-triphenylmethyl-4-cyanovaleramide), (**3**) was synthesized. This was accomplished by first converting the commercially available 4,4′-azobis(4-cyanovaleric acid) to the moisture-, heat-, and light-sensitive 4,4′-azobis(4-cyanovaleroyl chloride) (**2**) (Scheme 1). Subsequent treatment of **2** with triphenylmethylamine as shown led to **3**.

Polymerization of *N*-isopropylacrylamide initiated with **3** led to a triphenylmethyl-terminated poly(*N*-isopropylacrylamide) (PNIPAM-CONH-Tr) derivative (Scheme 2). The resulting polymer was fractionated in the same manner as mentioned earlier to produce six fractions of trityl end group-labeled PNIPAM-CONH-Tr (**4**) whose weight-average molecular weight was measured by light scattering. Detection of the end group



Scheme 2

Table 2. LCST and M_w Data for Unfractionated (Starting Polymer) and Fractionated Trityl-Labeled PNIPAM-CONH-Tr (4) Samples

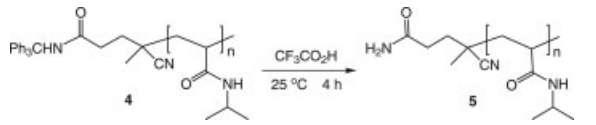
	M_w (g/mol)[a]	Polydispersity[b]	LCST (°C)
Starting Polymer	2.02×10^5	1.56	30.19
Fraction 1	3.84×10^5	1.09	30.27
Fraction 2	1.95×10^5	1.28	30.21
Fraction 3	1.70×10^5	1.17	30.18
Fraction 4	1.44×10^5	1.18	29.95
Fraction 5	9.32×10^4	1.22 (1.13)[c]	29.94
Fraction 6	4.58×10^4	2.18	29.74

[a] Molecular weights were all measured by light scattering in methanol.
[b] Polydispersities were measured by GPC in THF and are based on a comparison to polystyrene standards. The weight–average molecular weight measured by GPC differed from that measured by light scattering (the GPC M_w values were 7.23×10^4, 1.57×10^5, 7.18×10^4, 6.02×10^4, 5.20×10^4, 4.20×10^4, and 1.56×10^4 for the starting polymer and fractions 1–6, respectively).
[c] The polydispersity of the sample after detritylation.

was possible only by ^{1}H-NMR spectroscopy for the lowest molecular weight samples. LCST data (Table 2) for the starting trityl-labeled polymer and the fractionated samples 1–6 were then obtained.

The LCST data for the fractionated samples of **4** are plotted in Figure 2. This figure shows that the LCST of PNIPAM samples with these hydrophobic end groups again hardly varies as long as the M_w is greater than 200 kDa. Indeed, the LCST for the tritylated PNIPAM samples (the starting polymer and fractions 1–3) averaged 30.21 °C while the unfractionated and two highest molecular weight samples of the polymer described in Table 1 had an average LCST of 30.20 °C. However, a decrease in LCST is seen when the M_w of the PNIPAM containing the hydrophobically modified end groups is less than 150 kDa. Presumably, the difference in the effect of M_w on the LCST in Figure 2 *versus* Figure 1 reflects the greater hydrophobicity of the triphenylmethyl *versus* dimethylcyanopropyl end groups in **1** and **4**, respectively.

To confirm that the effects seen in Figure 2 are due to end-group hydrophobicity/hydrophilicity, the hydrophobic end groups of fractions 4, 5, and 6 of PNIPAM-CONH-Tr (**4**) were converted to the more hydrophilic end groups of PNIPAM-$CONH_2$ (**5**) using neat TFA (eq 3). The LCSTs of polymers without the triphenylmethyl end groups were then analyzed. In these experiments, >90% end-group conversion shown in eq 3 was verifiable for the lowest molecular weight fraction using ^{1}H-NMR spectroscopy. The LCST values for the resulting —$CONH_2$-terminated PNIPAM fractions formed in this detritylation are shown in Figure 2. The increase in these LCSTs for polymers of identical degree of polymerization and dispersity and lower degrees of polymerization and the lack of difference in LCSTs for polymers in Tables 1 and 2 with different end groups but with higher molecular weights is clear evidence that the differences in LCSTs for the lower molecular weight fractions of PNIPAMs **1**, **4**, and **5** are due to the hydrophobicity/hydrophilicity of the polymer's end groups.



(3)

Polymer concentration is known to affect LCST values. The results in Figures 1 and 2 were all obtained with solutions containing the same polymer concentration, 10 mg/mL. Studies with an unfractionated PNIPAM sample having a 350,000 M_w value shown in Figure 3 show that this polymer sample's LCST varies slightly with concentration, decreasing ~0.2 °C as the concentration of the polymer changes from 10 to 100 mg/mL. The effects of temperature on fractionated samples' LCSTs were also studied. In Figures 4 and 5, we show that the effects of polymer concentration varying from 2 to 50 mg/mL for fractionated samples of polymer prepared with AIBN- or trityl-derived end groups (i.e., the

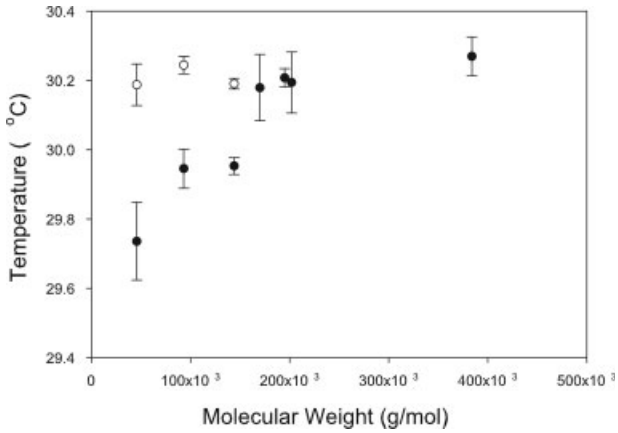


Figure 2. The variation of LCST with the M_w of PNIPAM-CONH-Tr (●) and PNIPAM-$CONH_2$ (○).

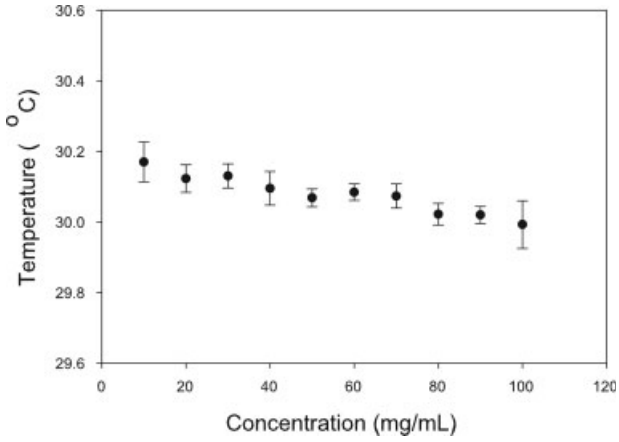


Figure 3. Effects of polymer concentration on LCST for an unfractionated PNIPAM polymer sample with M_w 350,000.

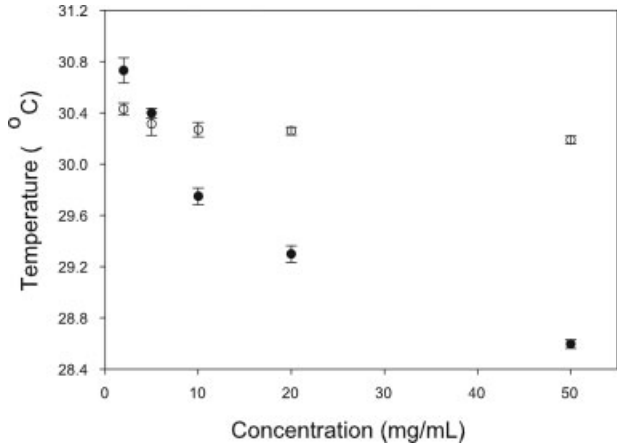


Figure 5. The variation of LCST with concentration of fractionated PNIPAM-CONH-Tr polymer samples having M_w 45,800 (●) and M_w 384,000 (○).

polymers discussed in Figs. 1 and 2, respectively) are also small for higher molecular weight polymers. The effects of polymer concentration on LCST are more marked with a lower molecular weight polymer sample. Such effects seem even more important with a more hydrophobic end group (e.g., with the 45,800 M_w trityl-containing polymer) shown in Figure 5 and presumably reflect aggregation or micellarization induced by this hydrophobic end group, an effect noted by others.[26,27]

The tacticity of the PNIPAM can affect PNIPAM's LCST. To be certain that the trityl end group effects we noted were not due to tacticity changes in the polymer, we used ^{1}H-NMR spectroscopy in DMSO-d_6 at 130 °C to verify that the polymers we studied in these experiments all had the same stereochemistry. The stereoregularity of some of the polymers used in this study could be evaluated because at 130 °C the peaks corresponding to the dyads for the meso (m) and racemic (r) configurations are well resolved. This is shown in the ^{1}H-NMR spectrum in Figure 6 where a ^{1}H-NMR spectrum for a typical polymer studied here is compared with that of a largely isotactic polymer prepared using other chemistry. The tacticity data for the polymers whose LCST values were studied in this article are given in Table 3. These results show that the polymers studied in this article all have the same tacticity within experimental error regardless of the end group.

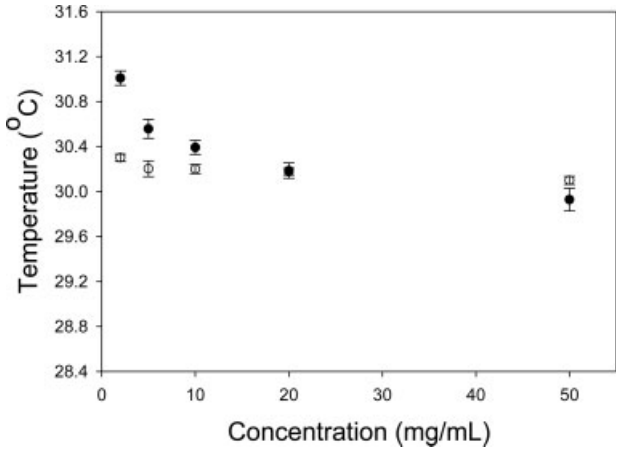


Figure 4. Effects on LCST for varying concentrations of PNIPAM for fractionated PNIPAM samples prepared using AIBN having M_w 55,800 (●) and M_w 475,000 (○).

CONCLUSIONS

The linear temperature gradient apparatus for combinatorial temperature measurements described here coupled with studies of fractionated samples of poly(*N*-alkylacrylamide)s with varying end groups has been used to determine the effect of polymer dispersity, M_w, and end-group structure on the LCST of thermoresponsive polymers. The results shown here clearly demonstrate that at least with a thermoresponsive polymer like PNIPAM, polydispersity and molecular weight have little effect on this polymer's LCST as long as the polymer M_w is $>$ 50,000 Da. For lower molecular weight samples, small (about 1 °C) changes in LCST were observed and were correlated with changes in end-group structure and polarity.

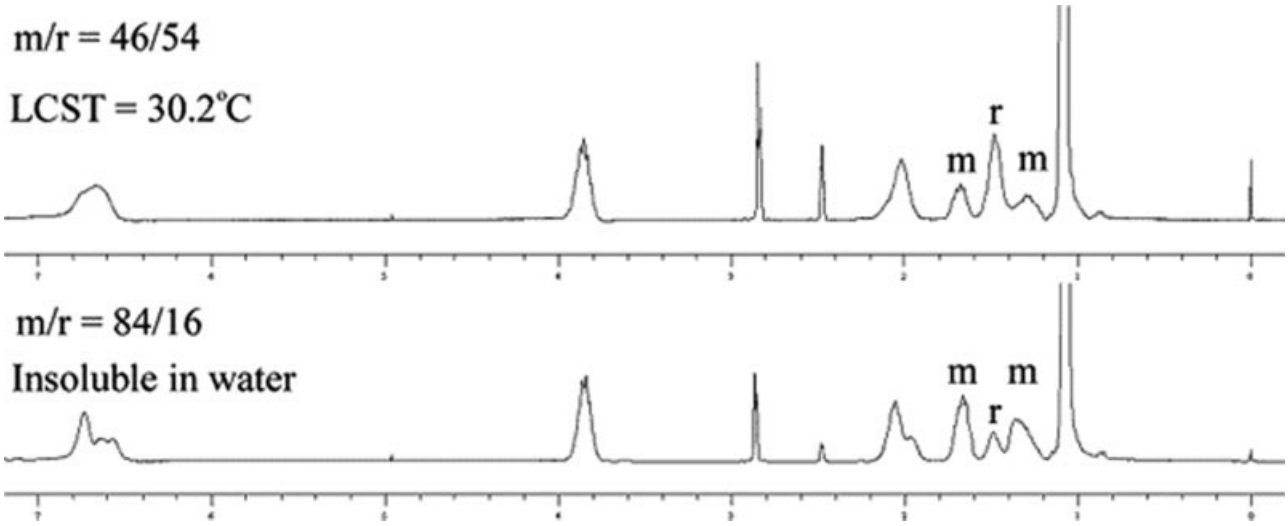


Figure 6. Determination of PNIPAM tacticity by ^{1}H-NMR (DMSO-d_6,130 °C) analysis.

EXPERIMENTAL

Materials and General Methods

All reagents and solvents were obtained from commercial sources and used without further purification unless specified. ^{1}H-NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 300 or 500 MHz. ^{13}C-NMR spectra were obtained on Varian Inova 300, Mercury 300, or Inova 500 spectrometers at 75 or 125 MHz. ^{1}H- and ^{13}C-NMR spectroscopy chemical shifts are reported in ppm referenced to tetramethylsilane. Light scattering experiments were carried out using a Brookhaven Instruments BI-200SM goniometer, BI-9000AT digital correlator, and a Melles Griot HeNe laser. M_w analysis of light scattering data was performed using Brookhaven Instruments Zimm Plot Software. The PNIPAM polymers were also analyzed by gel permeation chromatography in THF. In a typical analysis, 3.48 mg of the PNIPAM fraction with $M_w = 1.7 \times 10^5$ Da was dissolved in degassed THF and the analysis was carried out using a Viscotek I-MBMMW-3078 mixed bed column using a Viscotek GPC instrument. This GPC analysis used multiple detectors, including a Model VE 3580 RI detector and OmniSEC software.

Fabrication of Temperature Gradient Device

Fabrication of the temperature gradient device has been previously decribed.[8–11] Briefly, two hollow square brass tubes (of 1/8th of inch wide) (K&S Engineering, Chicago, IL) were laid in parallel and separated by ~5-mm stints made of glass slides. The temperature gradient apparatus was then placed under a darkfield condenser in an inverted microscope (Nikon, Eclipse TE 2000-U). To establish the temperature gradient, hot and cold antifreeze solutions were circulated through individual brass tubes using standard water bath circulators (Fisher Scientific, Pittsburgh, PA). A coverglass was laid on top of two brass tubes by applying vacuum grease and the linear temperature gradient was confirmed by taking temperature measurements at various points perpendicular to the copper tubes with a type E thermocouple.

LCST Measurement of Thermoresponsive Polymers

To measure the LCSTs of thermoresponsive polymers, rectangular-shaped borosilicate capillary

Table 3. Tacticity Data for LCST Polymers[a]

Polymer	Remarks	m/r
PNIPAM	AIBN/*t*BuOH	45/55
PNIPAM-CONH-Tr	Unfractionated	48/52
PNIPAM-CONH-Tr	Fraction 1	47/53
PNIPAM-CONH-Tr	Fraction 6	48/52
PNIPAM-$CONH_2$	Fraction 6	47/53

[a] ^{1}H-NMR spectra of a representative atactic poly(*N*-isopropylacrylamide) and of a more isotactic poly(*N*-isopropylacrylamide) prepared in the presence of a Lewis acid are provided in the supporting information. An isotactic PNIPAM sample was also prepared to confirm that the NMR analysis worked, but the LCST of the isotactic polymer was not studied in this article, as it was insoluble in water.

tubes (Vitrocom, Mountain Lakes, NJ) with a high aspect ratio (100 μm $\times$1 mm $\times$2 cm) were used as sample containers. Polymer solutions were introduced into the tubes through capillary action and were subsequently sealed with vacuum grease before being laid parallel to the temperature gradient. Polymer clouding was imaged through a darkfield condenser using a CCD camera. Two standard polymer solutions, PNIPAM 10 mg/mL in water (LCST 30.2 °C) and PNIPAM 10 mg/mL in 0.7 M KCl (LCST 26.0 °C), were used as internal temperature standards to determine the temperature gradient for every experiment. Clouding curves of polymers were plotted from linescans of scattering intensity drawn along the temperature gradient where pixel positions were converted to temperatures according to the gradient obtained in the reference samples. The LCST was defined as the onset point of the clouding curve. The absolute value for the LCSTs measured with our temperature gradient device was compared with the onset of the LCST for the same polymer sample in a cuvette in a macroscopic experiment. The onset of the LCST in the macroscopic experiment was no greater than 0.6 °C higher than that measured with the microfluidics device. The measurement of the LCST for each data point was repeated at least eight times in the microfluidics device and the mean value was taken. The measurements had a typical standard error of $\pm$ 0.05 °C.

Preparation and Fractionation of PNIPAM (1)

PNIPAM was prepared by free-radical polymerization. A solution of *N*-isopropylacrylamide and AIBN in methanol was degassed and lowered into a preheated oil bath at 70 °C under positive pressure of N_2. After stirring for 25 h, the solvent was removed and the resulting solid was dried under vacuum. The polymer product **1** was purified from any remaining monomer by first dissolving it in THF and then precipitating the polymer into hexanes three times.

Fractional Precipitation of PNIPAM (1)

PNIPAM was fractionated using a literature procedure.[21]

Synthesis of *N*-Triphenylmethylhexanamide

A solution of hexanoyl chloride (507 mg, 3.8 mmol) in 10 mL of dry CH_2Cl_2 was slowly added to a solution of tritylamine (963 mg, 3.7 mmol) and TEA (0.8 mL, 6.0 mmol) in 20 mL of dry CH_2Cl_2. The system was flushed with N_2 and then allowed to stir at 25 °C under positive pressure of N_2 for 21 h. The clear solution was washed with deionized water (3 $\times$ 20 mL) and brine (1 $\times$ 20 mL) and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting yellow solid was dried under vacuum. The crude product was purified via column chromatography (silica, hexanes:EtOAc 10:90) to yield 290 mg (22%) of the pure product *N*-triphenylmethylhexanamide.

^{1}H-NMR ($CDCl_3$) δ 0.90 (t, 3H), 1.30 (m, 4H), 1.61 (q, 2H), 2.25 (t, 2H), 6.55 (s, 1H), 7.18–7.35 (m, 15H); ^{13}C-NMR ($CDCl_3$) δ 13.94, 22.39, 25.30, 31.43, 37.76, 126.95, 127.90, 128.66, 144.80, 171.90; IR (KBr) 3257, 3060, 3034, 2955, 2929, 2857, 1649, 1535, 1489, 1443, 1391, 697 cm^{-1}.

Removal of Triphenylmethyl Group from *N*-Triphenylmethylhexanamide

N-Triphenylmethylhexanamide (50 mg, 140 μmol) was dissolved in 10 mL of trifluroacetic acid (the solution immediately turned bright yellow) and was allowed to stir at 25 °C for 4 h. The yellow solution was then added to 100 mL of anhydrous ethanol and the solvent was then removed under reduced pressure. Fresh ethanol (100 mL) was then added and this process was repeated three more times to remove all of the trifluroacetic acid. The oil was then dried under vacuum to yield 0.1 g of the crude primary amide. The product was not separated from the triphenylcarbinol by-product. The efficiency of the cleavage was determined by the shift of the —CH_2— group adjacent to the carbonyl from δ 2.25 to 2.23 ppm in the ^{1}H-NMR ($CDCl_3$) spectrum of the secondary *versus* the primary amide, respectively. The cleavage was also confirmed by TLC analysis on silica gel (ethyl acetate:hexanes 1:4). *N*-Triphenylmethylhexanamide had an R_f of 0.45 and was visible only under short-wavelength (λ_{254}) UV light whereas the product and triphenylcarbinol had the same R_f of 0.61 and were visible under both short- and long-wavelenght (λ_{365}) UV light.

Synthesis of 4,4′-Azobis(4-cyanovaleroyl chloride (2)

All glasswares were flame dried before synthesis. Three drops of DMF were added to a sus-

pension of 4,4′-azobis(4-cyanovaleric acid) (1.00 g, 3.6 mmol) in 20 mL of dry CH_2Cl_2. The system was fitted with an air condenser, sealed with septa, and flushed with N_2 for 5 min. The suspension was then cooled to 0 °C, and oxalyl chloride (1.0 mL, 11.6 mmol) was added via syringe and the reaction mixture was protected from light and allowed to stir at 25 °C under a slow stream of N_2 for 3 h. The solid dissolved as the reaction proceeded. The solvent was removed under reduced pressure, by keeping the flask below 30 °C at all times. The resulting yellow oil was then dried under vacuum in the dark yielding 1.09 g (96%) of the yellow solid **2**.

^{1}H-NMR ($CDCl_3$) d 170 (s, 3H), 1.75 (s, 3H), 2.41–2.65 (m, 4H), 2.90–3.21 (m, 4H).

Synthesis of 4,4′-Azobis(*N*-triphenylmethyl-4-cyanovaleramide) (3)

Tritylamine (1.64 g, 6.3 mmol) and pyridine (549 mg, 6.9 mmol) were dissolved in 20 mL of dry CH_2Cl_2. The system was flushed with N_2 and then cooled to 0 °C. Then **2** (1.00 g, 3.15 mmol) was dissolved in 10 mL of dry CH_2Cl_2 and flushed with N_2. The acid chloride solution was transferred via forced siphon to the amine solution and the reaction mixture was allowed to stir at 25 °C under a positive pressure of N_2 for 24 h. The resulting precipitate was filtered, and the clear, orange supernatant was washed with deionized water (5 × 20 mL) and brine (1 × 20 mL) and was then dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was dried *in vacuo*. The resulting solid was then triturated with 50 mL of diethyl ether, filtered, and then dried under vacuum, to yield 1.36 g (57%) of the pure product **3**.

^{1}H-NMR ($CDCl_3$) δ 1.61 (s, 3H), 1.62 (s, 3H), 2.50–2.55 (m, 8H), 6.60 (s, 1H), 6.61 (s, 1H), 7.10–7.40 (m, 30H); ^{13}C-NMR ($CDCl_3$) δ 23.60, 23.84, 31.68, 33.42, 70.73, 71.79, 117.93, 127.10, 128.01, 128.61, 144.37, 168.99; IR (KBr) 1692, 1489, 1450, 1384, 697 cm^{-1}.

Synthesis of PNIPAM-CONH-Tr(4)

A solution of *N*-isopropylacrylamide (15.01 g, 133 mmol) and **3** (127 mg, 0.166 mmol) in 200 mL of MeOH was degassed and heated to 70 °C under positive pressure of N_2. After 17 h, the MeOH was removed under reduced pressure and the polymer was dried under vacuum. The crude product was then reprecipitated from 100 mL of THF into 750 mL of hexanes three times, to yield 14.00 g (93%) of the pure product **4**.

^{1}H-NMR ($CDCl_3$) d 1.18 (bs, 6H), 2.25–1.40 (bm, 3H), 4.00 (bs, 1H), 6.40 (bs, 1H).

Fractional Precipitation of PNIPAM-CONH-Tr

The trityl-terminated PNIPAM derivative was fractionated using the literature procedure used previously to fractionate PNIPAM.[21] The lowest molecular weight sample (M_w = 4.58 × 10^4 g/mol) had an extra peak (corresponding to the triphenylmethyl end groups) at δ 7.20 ppm in the ^{1}H-NMR spectrum ($CDCl_3$).

Synthesis of PNIPAM-CONH$_2$ (5)

The cleavage of the lowest M_w sample (M_w = 4.58 × 10^4 g/mol) is representative of the procedure used to cleave each sample. PNIPAM-CONH-Tr (500 mg) was dissolved in 10 mL of neat trifluroacetic acid (the solution immediately turned bright yellow) and was allowed to stir at 25 °C for 4 h. The yellow solution was then added to 100 mL of anhydrous ethanol and the solvent was then removed under reduced pressure. Fresh ethanol (100 mL) was then added and this process was repeated three more times to remove all of the trifluroacetic acid. The oil was then dried under vacuum. The product was dissolved in 10 mL of THF and precipitated into 75 mL of hexane. The white powder was filtered and dried and then dissolved in 10 mL THF and precipitated into 75 mL of anhydrous diethyl ether. The fine white precipitate was separated via centrifugation at 25 °C and the white solid was dried under vacuum, yielding 370 mg (73%) of the pure product. ^{1}H-NMR spectroscopy (D_2O) was used to confirm the removal of the triphenylmethyl group from the lowest molecular weight sample only. PNIPAM-CONH-Tr and PNIPAM-CONH$_2$ had identical ^{1}H-NMR spectra in D_2O except for one peak at δ 7.38 ppm (corresponding to the triphenylmethyl end groups) that only appeared in the PNIPAM-CONH-Tr spectra. In the case of fraction 5, the product of detritylation had a slightly lower polydispersity index of 1.13 which is lower than the PDI of 1.22 for the precursor trityl-containing polymer. We attribute the change in the PDI to the numerous precipitation steps performed on this sample after detritylation.

Synthesis of 80% Isotactic PNIPAM

This synthesis used a literature procedure[30] using benzyl dithiobenzoate[6] as the chain transfer agent.

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