

Study on Micellization of Poly(*N*-isopropylacrylamide-butyl acrylate) Macromonomers in Aqueous Solution

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Received 2 February 2010; accepted 14 March 2010

DOI 10.1002/app.32441

Published online 24 May 2010 in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: A kind of thermo-sensitive macromonomer, styrene-terminated poly(*N*-isopropylacrylamide-butyl acrylate) [P(NIPAm-BA)] has been synthesized in this work. With the help of ultraviolet spectrum (UV), proton nuclear magnetic resonance (¹H-NMR), potentiometric titration and dynamic light scattering (DLS), the molecular structure, thermo-sensitive characteristics, and micellization behaviors of this kind of macromonomer have been investigated. The obtained results demonstrate that, the molecu-

lar structure of thermo-sensitive macromonomer, including the content of comonomer unit on the backbones and the variety of terminal groups, has great influence on its low critical solution temperature (LCST) and critical micelle concentration (CMC). © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 118: 671–677, 2010

Key words: thermo-sensitive macromonomer; micellization; *N*-isopropylacrylamide; butyl acrylate

INTRODUCTION

Thermo-sensitive polymers have attracted much attention in recent decades because of potential biomedical applications including protein separation,^{1–3} gene transfer,^{4–8} enzymes immobilization,⁹ and drug delivery.¹⁰ Some water-soluble polymers with hydrophobic moieties, such as PNIPAm¹¹ and poly(*N*-vinylisobutyramide),¹² have obvious thermo-sensitive characteristics and exhibit phase transition behavior at lower critical solution temperature (LCST) due to the hydrophilic/hydrophobic balance of molecular chains which changes with temperature. This thermoreversible phase transition phenomenon was first reported by Heskins and Guillet in 1968.¹³ Hereafter, the physical properties¹⁴ and the potential applications^{15–17} of thermo-sensitive polymers have been widely investigated.

As an important thermo-sensitive polymer, PNIPAm has a good application prospect in protein sep-

aration especially for its thermo-reversibility. Ding et al.,¹⁸ Fong et al.,¹⁹ and Flaudy and Freitag²⁰ produced temperature-sensitive membranes for protein separation according to the thermo-sensitivity of PNIPAm. Hiroo et al.²¹ developed PVDF-based membranes by grafting PNIPAM and its copolymers on PVDF substrate. Grafted PVDF membrane responses timely to temperature changes and adjusts the pore's "open" and "off" accordingly. Chen et al.²² prepared thermo-sensitive polystyrene microspheres with PNIPAm branches on their surfaces by macromonomer polymerization technique in both alcoholic and aqueous alcoholic media.²³

The wide scientific and technological interest in water-soluble polymers (PNIPAm) arises from its well-known and largely studied LCST behavior in aqueous solution. This phenomenon takes place within a narrow temperature range and it appears as a polymer phase separation from water when temperature increases above 33°C.^{17,24} It is well-known that the aggregation property of PNIPAm strongly depends on polymer concentration and the amount of organic fragments attached to the polymer chain.^{25–28} The hydrophilicity of comonomers significantly affect the LCST of NIPAm-based copolymers and when combined with hydrophobic monomers, the LCST of NIPAm copolymers decreases with the increasing of comonomer content.²⁹

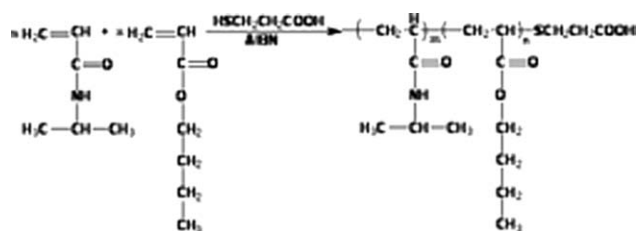
A number of vinyl-type macromonomers have so far been synthesized and polymerized.^{30–35} The terminal groups of these macromonomers contain

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Contract grant sponsor: National Science Foundation of China; contract grant number: 20874004.

Contract grant sponsor: Beijing New-Star Program of Science and Technology; contract grant number: 2009B10.

Contract grant sponsor: Program for Changjiang Scholars and Innovative Research Team in University; contract grant number: PCSIRT-IRT0807.



Scheme 1 Synthesis of carboxyl-terminated P(NIPAm-BA) oligomer.

double bond which can carry on further addition polymerization, and most of them exhibit a hydrophobic characteristic. The LCST and the micellization behavior of macromonomer will affect the polymerization process as well as the morphology and chain structure of the copolymer products once the macromonomer participates in the polymerization. To find out the micellization behavior and thermo-sensitive characteristics of macromonomer in aqueous solution, we synthesized a new type of macromonomer [styrene-terminated P(NIPAm-BA)] which comprise of NIPAm and varied amounts of comonomer (BA). The molecular structure, thermo-sensitive characteristics and micellization behaviors of this kind of macromonomer has been characterized by potentiometric titration, UV, $^1\text{H-NMR}$, and DLS. In addition, the influence of the content of comonomer and the variety of terminated groups on LCST and critical micelle concentration (CMC) has also been discussed in this work.

EXPERIMENTAL

Materials

N-isopropylacrylamide (NIPAm) (99%) was purchased from Belgium Acros Company and recrystallized from toluene solution by adding hexane and cooling. *N,N*-dimethylformamide (DMF) (99%), from Shi Ying Factories, Changping, Beijing. β -mercapto-propionic acid (MPA) (99%), Alfa Aesar Company, used as received. Azobisisobutyronitrile (AIBN), Beijing Chemical Reagents Company, purified by recrystallization before use. Chloromethyl styrene (CMS) (90%), Belgium Acros Company, used with-

out further purification. Butyl acrylate (BA), polymer grade, Beijing Eastern Chemical Works.

Preparation of carboxyl-terminated P (NIPAm-BA)

Carboxyl-terminated NIPAm-BA copolymeric oligomer (Scheme 1) employed as the precursor of macromonomer was prepared based on the method described in the literatures.^{23,36}

NIPAm, BA, MPA, and AIBN were first dissolved in 18 mL of ethanol in a round-bottomed flask. Then the resultant solution was bubbled by nitrogen for 15 min to remove oxygen. Polymerization was carried out at 60°C for 6 h with magnetic stirring. The oligomer was precipitated by adding hot water to the reaction mixture, then redissolved in cool water and finally subjected to dialysis using a membrane tube (molecular weight cut off, MWCO = 3500) for 3 days. After freeze-drying, the pure carboxyl-terminated NIPAm-BA oligomer was obtained.

The compound formulation and the yield of carboxyl-terminated P(NIPAm-BA) are showed in Table I.

Esterification of carboxyl-terminated P (NIPAm-BA)

In this work, carboxyl-terminated P(NIPAm-BA) was finally transformed into the aimed macromonomer by esterification, as is showed in Scheme 2.

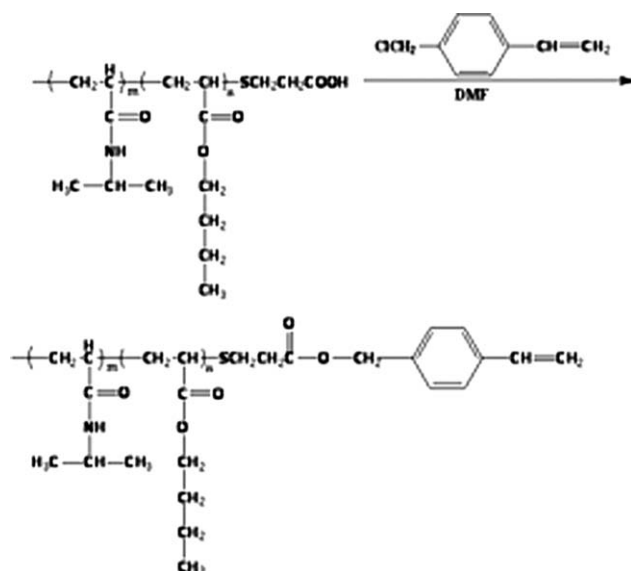
Typically, carboxyl-terminated P(NIPAm-BA) oligomer, CMS and sodium hydroxide solution (0.5 mol/L) were first dissolved in 40 mL of DMF in a round-bottomed flask. The reaction was carried out at 30°C with magnetic stirring for 48 h. The resultant polymer was precipitated by addition of hot water to the reaction mixture. The precipitate was dissolved in cool water and subjected to dialysis using a membrane tube (MWCO = 3500) for 3 days. Dialysis product was freeze-dried to obtain pure product [styrene-terminated P(NIPAm-BA)].

The compound formulation and the yield of styrene-terminated P(NIPAm-BA) are showed in Table II

TABLE I
The Compound Formulation and the Yield of Carboxyl-Terminated P(NIPAm-BA) Oligomer

Sample	BA amount based on total monomers (%)	BA (g)	NIPAm (g)	Yield(%)	LCST(°C)
P1	11.1	0.7545	6.0415	77.9	16.5
P2	9.0	1.1220	11.3407	78.6	18.5
P3	6.9	0.5100	6.8062	78.9	24.0
P4	4.0	0.5166	12.3905	78.2	27.5
P5	2.0	0.1828	8.9531	77.4	32.0

Reaction condition: 60°C \times 6 h.



Scheme 2 Esterification of carboxyl-terminated P(NIPAm-BA) with CMS.

UV spectrum

UV spectra of P(NIPAm-BA) samples were recorded at room temperature using UV-visible spectrophotometer (Hitachi U-3010). All P(NIPAm-BA) samples were dissolved in distilled water and the concentration was about 0.1%.

¹H-NMR

All NMR spectra were recorded on a Bruker-AM 300 NMR spectrometer at room temperature, operated at 300 MHz for ¹H-NMR. All P(NIPAm-BA) samples were dissolved in D₂O and the concentration of about 1%.

Potentiometric titration

Potentiometric titration was employed to determine the molecular weight of carboxyl-terminated P(NIPAm-BA) oligomer and esterification degree of styrene-terminated P(NIPAm-BA). The number average molecular weight of carboxyl-terminated P(NIPAm-BA) is available through pH/conductivity

determination considering the presence of terminal COOH groups on the oligomers. Carboxyl-terminated P(NIPAm-BA) solution and styrene-terminated P(NIPAm-BA) solution were titrated with NaOH solution, respectively. The esterification degree of styrene-terminated P(NIPAm-BA) could be obtained according to the comparison of titration curves. DELTA326 conductivity meter and DELTA 320 pH meter (Mettler-Toledo Instruments, Shanghai) were used in this study. All potentiometric titrations were carried out at room temperature under N₂ atmosphere. In a typical experiment, 50 mL of 0.5% polymer sample in 0.001 M KCl was added to the titration vessel. The initial pH was adjusted to 3 and 0.1 M NaOH was added about every 30 sec.

DLS

The LCST value of P(NIPAm-BA) is determined by DLS. DLS measurement was performed on dynamic light scattering (DLS) detector (BI-90Plus, Brookhaven Instruments, Holtsville, NY) which employs the technique of photon correlation spectroscopy of quasi-elastically scattered light. The scattered light was collected at a scattering angle of 90°. The wavelength of the laser light source was 658 nm and the power was 35 mw.

All the measurements were carried out at 25°C and the particle size was evaluated by light intensity. The results were obtained from multimodal size distribution (MSD) option and non-negatively constrained least squares (NNLS) algorithm was taken to fit the data.

RESULTS AND DISCUSSION

Characterization of P(NIPAm-BA) macromonomer

In this work, the molecular structure of P(NIPAm-BA) macromonomer has been characterized by UV, NMR, and potentiometric titration. The UV spectra of P(NIPAm-BA) before and after esterification are showed in Figure 1. There is an absorption peak related to benzene at about 250 nm, indicating the presence of styrenic monomer structure after the

TABLE II
The Compound Formulation and the Yield of Styrene-Terminated P(NIPAm-BA)

Sample	Carboxyl-terminated P(NIPAm-BA) (g)	0.5 mol/L NaOH (mL)	CMS (g)	DMF (mL)	Yield (%)
Pz1	3.5958	1.15	0.2398	40	74.8
Pz2	7.5435	2.20	0.4659	90	75.6
Pz3	3.5090	0.98	0.2199	40	75.9
Pz4	6.6104	1.86	0.4218	70	81.1
Pz5	3.3760	2.05	0.2347	40	74.2

Reaction condition: 30°C × 48 h.

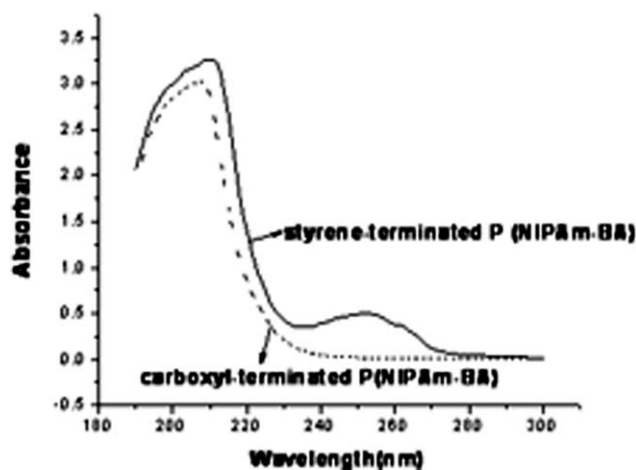


Figure 1 UV spectra of P(NIPAm-BA) (Sample: P3 in Table I and Pz3 in Table II).

esterification of carboxyl-terminated P(NIPAm-BA) with CMS.³⁷

Figure 2 is the ¹H-NMR spectrum of a typical P(NIPAm-BA) macromonomer obtained. As is shown in Figure 2, the peak *a* (at 0.870–1.093 ppm) can be assigned to the methyl hydrogen of NIPAm and BA units. Peak *b* (at 1.093–1.669 ppm) is the peak of methylene hydrogen. Peak *c* (at 1.962–2.072 ppm) is the peak of methine hydrogen. Peak *d* (at 3.847 ppm) is the peak of methine hydrogen of isopropyl group from NIPAm units. Peak *e* (at 7.710 ppm) indicates the structure of benzene ring.

The content of acrylate units in the macromonomer was calculated based on ¹H-NMR. For sample Pz3 in Table II, the BA unit content was 6.0% (mol), which was close to the BA content, 6.2% (mol), in monomer feed during NIPAm-BA copolymerization. This result indicates that BA and NIPAm exhibited a comparable reactivity under the polymerization conditions employed in this work. It can be seen from Figure 3 that the LCST of carboxyl-terminated P(NIPAm-BA) decreases linearly with the increase in BA content in the monomer feed during copolymerization. The facts from NMR and linear relation between the LCST and BA content suggest that BA

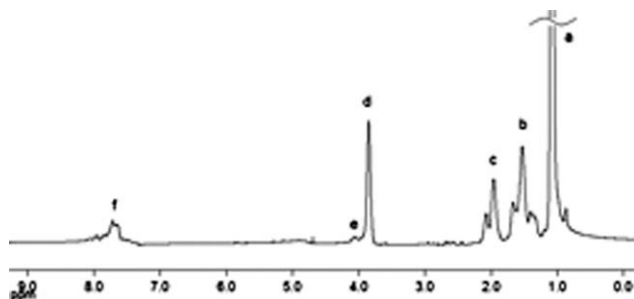


Figure 2 ¹H-NMR spectrum of P(NIPAm-BA) macromonomer (Sample: Pz3 in Table II).

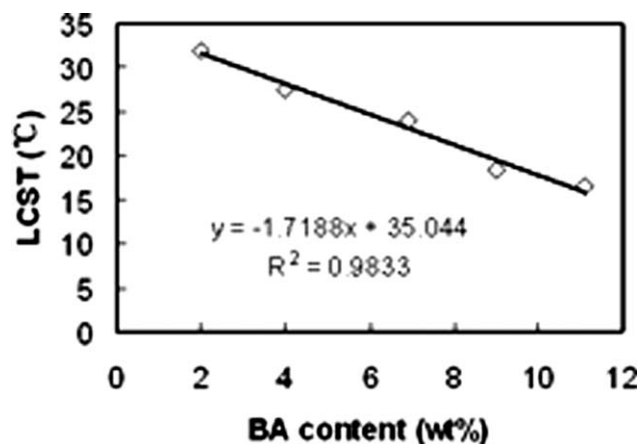


Figure 3 The relation between the LCST of carboxyl-terminated P(NIPAm-BA) and the BA content in the monomer feed during copolymerization.

units are randomly linked with NIPAm on the copolymer chains.

The molecular weight and the esterification degree of P(NIPAm-BA) macromonomers were determined by potentiometric titration. Figure 4 shows the titration curves of carboxyl-terminated P(NIPAm-BA) and styrene-terminated P(NIPAm-BA), respectively. It can be observed that at the beginning of the titration, with the addition of sodium hydroxide, hydrochloric acid was gradually neutralized and the conductivity decreased linearly, but at the end of the titration, the addition of excessive amount of sodium hydroxide leads to a linear increase in conductivity. A flat plateau appears in the curve of carboxyl-terminated P(NIPAm-BA), indicating the presence of weak acidic groups, which are carboxylic acid ends on the polymer chains. The amount of sodium hydroxide consumed by carboxylic acid groups can be calculated from the volume difference between the two break points (T1 and T2). Therefore, the total carboxylic acid amount and the equivalent molecular mass per carboxylic acid can be further calculated (Table III). The molecular weights of styrene-terminated P(NIPAm-BA) macromonomer can also be calculated by transforming the carboxylic acid ends to styrenic terminals and are listed in Table III.

It can be seen from Figure 3 that the titration curve of styrene-terminated P(NIPAm-BA) shows no flat form, confirming that there was no detectable carboxyl end groups left in this macromonomer product and the carboxyl groups in carboxyl-terminated P(NIPAm-BA) are transformed into styrene groups completely after esterification.

Temperature-sensitive behavior of P(NIPAm-BA)

The temperature-sensitive behavior of P(NIPAm-BA) oligomer or macromonomer in aqueous solution was examined with the aid of DLS. Figure 5 shows a

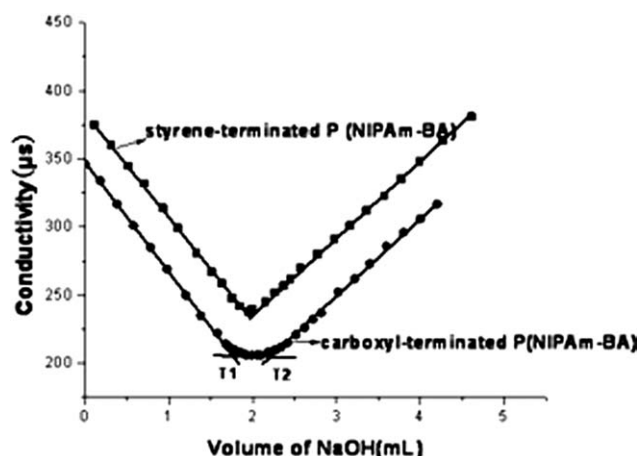


Figure 4 Titration curves of P(NIPAm-BA) before and after esterification (Sample: P3 in Table I and Pz3 in Table II).

typical example of DLS results (sample P3). It can be observed from the curve of the light scattering intensity versus temperature [Fig. 5(a)] that, when the temperature is below 22°C, the light scattering intensity stays the same as the temperature increases. When the temperature is above 30°C, with temperature increasing, the upward trend of the light scattering intensity decreases. Obviously, the scattering intensity significantly increased between 22 and 30°C. The critical point is 22°C, at which the changing rate of the scattering intensity reaches the maximum. Figure 5(b) shows the relationship between particle size and temperature. A sharp increase of particle size happens at 20°C, which roughly equals to the temperature at which the light scattering intensity begins to increase apparently. This indicates that polymer chains aggregated to phase transition in this temperature range to form colloidal particles. Below 20°C, the apparent particle size is equal to the equivalent diameter of polymer coils, only presenting a slight change with the temperature. When temperature is higher than 25°C, the dehydration effect

TABLE III
Number Average Molecular Weight of P(NIPAm-BA) Macromonomers

Sample	Carboxyl-terminated P(NIPAm-BA)		Styrene-terminated P(NIPAm-BA)
	M_w^a (theoretical value)	M_w^b (measured by titration)	M_w^3
Pz1	7706	8637	8763
Pz2	7490	7400	7526
Pz3	7396	5043	5169
Pz4	7437	6742	6868
Pz5	6578	7675	7801

^a M_w^1 was calculated based on the molar ratio of MPA to the total amount of NIPAm and BA monomers.

^b M_w^3 was calculated by transforming the carboxylic acid ends to styrenic terminals.

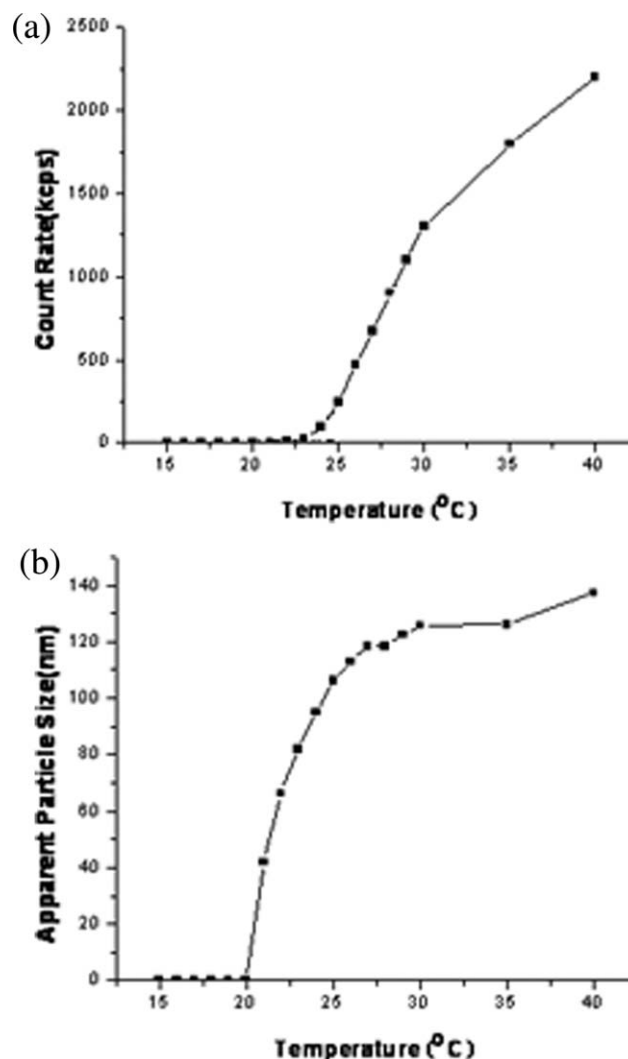


Figure 5 Light scattering intensity (a) and particle size (b) of P(NIPAm-BA) oligomer at different temperatures (Sample: P3, concentration: 0.01 wt %).

leads to an increase of the refractive index of colloidal particles, and finally results in continuous increasing of light scattering intensity with temperature.

It is known that the content of comonomer will affect the micellization behaviors of copolymer. To better understand the micellization characteristics of P(NIPAm-BA) oligomer and macromonomer, the influence of the content of BA on the turbidity (Fig. 6) and CMC (Fig. 7) of the oligomer has been investigated in this work. The turbidity-concentration curves of P(NIPAm-BA) oligomer has been measured by particle sizer at 20°C. Figure 6 shows the turbidities of carboxyl-terminated P(NIPAm-BA) oligomers with various BA content at difference concentrations. As is shown in Figure 6, a higher BA content leads to a more remarkable changes in turbidity with the increase of polymer concentration.

CMC in the oligomer aqueous solution was figured out based on the concentration at the break point in the curves shown in Figure 6. CMC values thus

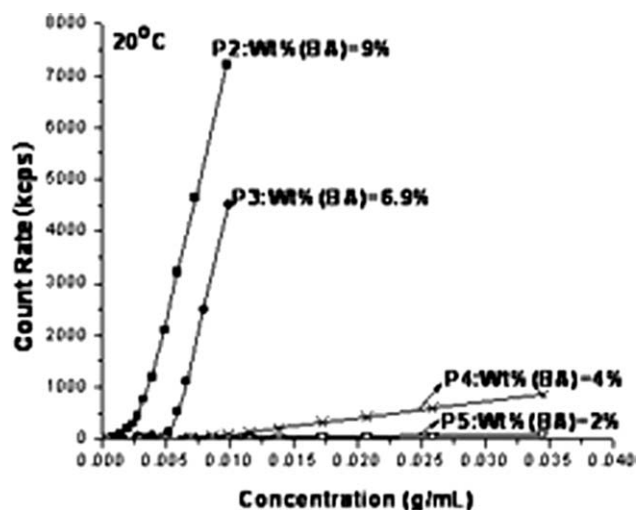


Figure 6 Turbidity-concentration curves of P(NIPAm-BA) oligomers with different BA contents.

obtained was plotted against the BA content in the oligomer (Fig. 7). It can be observed that a higher BA content results in a lower CMC of the carboxyl-terminated P(NIPAm-BA) in aqueous solution. Interestingly, the CMC decreases linearly as the increase of BA content in the P(NIPAm-BA) oligomer.

The influence of temperature on the turbidity of carboxyl-terminated P(NIPAm-BA) has also been investigated. As can be seen in Figure 8, the higher the temperature (below LCST), the more sharply the turbidity changes as the increase of the concentration of the oligomer. The break point in the count rate-concentration curve appears at a lower concentration when the turbidity was measured at a higher temperature. This allows one to expect a lower CMC at high temperatures for the same oligomer.

Figure 9 presents direct comparison of turbidities at various concentrations of P(NIPAm-BA) before

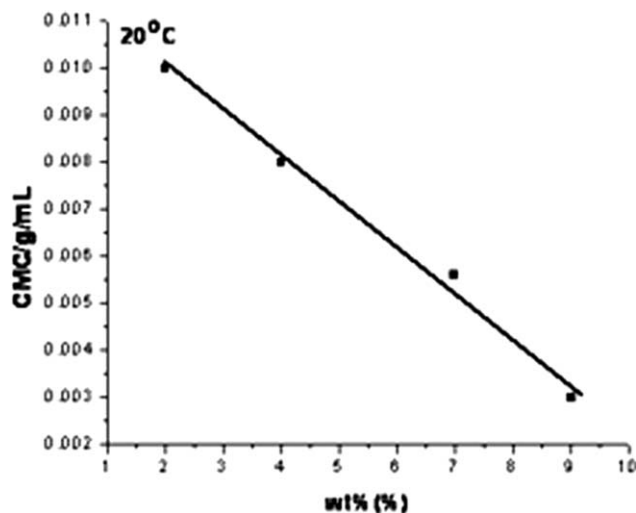


Figure 7 The effect of BA weight content on the CMC of P(NIPAm-BA) oligomer in aqueous solution at 20°C.

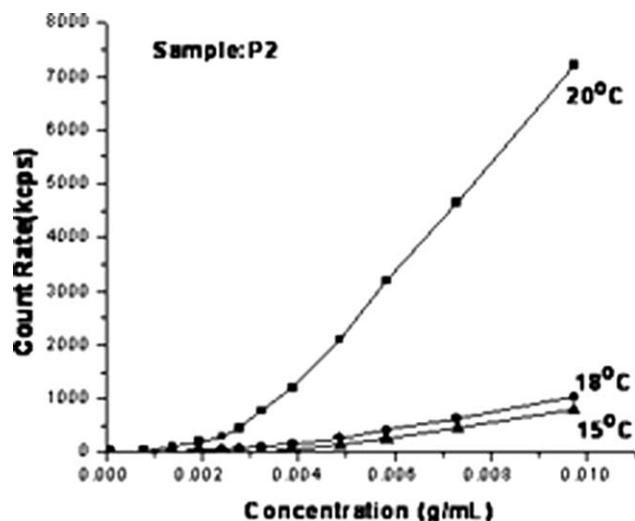


Figure 8 The relationship between turbidity and the concentration of P(NIPAm-BA) oligomer at different temperatures. (Sample: P2).

and after esterification. At the temperatures [20°C and 15°C as shown in Figure 9(a,b), respectively] investigated, esterified P(NIPAm-BA) shows

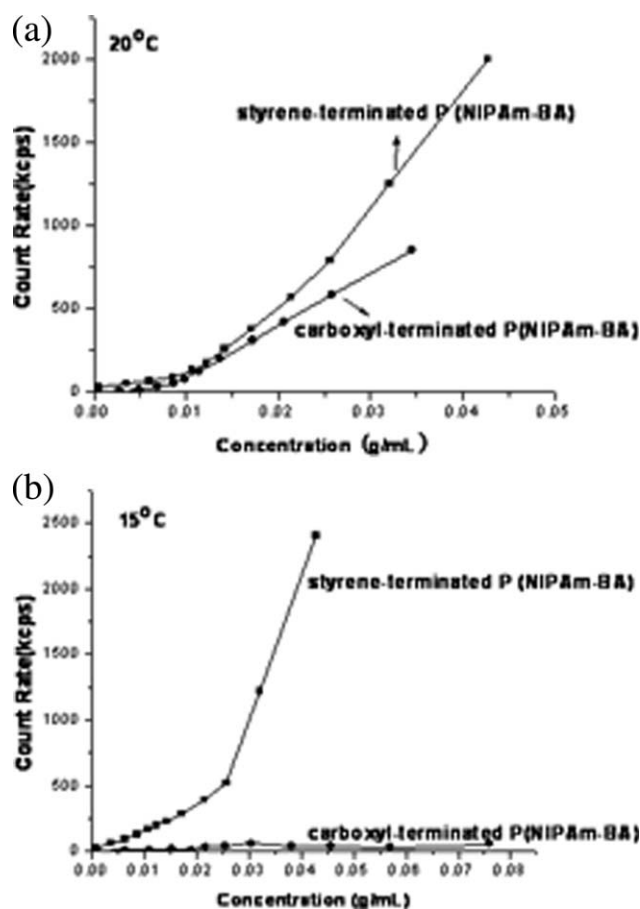


Figure 9 The relationship between turbidity and the concentration of P(NIPAm-BA) with different terminal groups. (Sample: P4 and Pz4).

significant larger count rate than its precursor. Compared to hydrophilic carboxylic acid end, the styrenic terminal positively influences the micellization of P(NIPAM-BA) macromonomer due to high hydrophobicity of styrene structure. Indeed, the turbidity measurement provides additional proof to confirm that the carboxyl ends of P(NIPAm-BA) oligomer have been successfully converted into styrenic ends through esterification reaction.

To control the thermo-sensitivity of NIPAM-based macromonomer, one may introduce comonomer units randomly into polymer chains through copolymerizing approach. Meanwhile, the effect of the structure of the end group of NIPAM-based oligomer on its solution and colloidal behaviors allows one to adjust the property of thermo-sensitive macromonomer by modifying its terminals. In other words, the real solution and colloidal properties of NIPAM-based thermo-sensitive macromonomer depends not only on its backbone composition but also on its terminal structure. The information on the thermally induced behaviors of the so-called macromonomer is also helpful in understanding its kinetics during polymerization and the thermo-responsive behavior of the branches thus generated.

CONCLUSIONS

A kind of new macromonomer (styrene-terminated P(NIPAm-BA)) has been synthesized in this work and its micellization in aqueous solution has been investigated. The results obtained indicate that the LCST value and the CMC in aqueous solution of P(NIPAm-BA) oligomer decreases with the increase of BA content on the backbones. Furthermore, styrenic P(NIPAm-BA) macromonomer exhibits a stronger micellization tendency than its precursor, carboxyl-terminated oligomer.

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