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Effect of Topology on the Properties of Poly(*N*-isopropylacrylamide) in Water and in Bulk

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Summary: Three macrocyclic poly(*N*-isopropylacrylamide)s (PNIPAM) with molecular weight (MW) ranging from 6 to 19 kg/mol were synthesized by 'click' ring closure of the corresponding α-azido ω-propargyl telechelic linear PNIPAMs, themselves prepared by reversible addition fragmentation chain transfer (RAFT) polymerization of *N*-isopropylacrylamide. Differential scanning calorimetry (DSC) studies revealed that both the thermal phase separation in water and the glass transition in bulk of PNIPAM were affected by polymer topology. In aqueous solution, the cyclic polymers exhibit a higher phase separation temperature and broader phase transition range than the corresponding linear counterparts. In bulk, the cyclic polymers display a higher glass transition temperature of lesser molecular weight dependence, as compared to their linear precursors.

Keywords: poly(*N*-isopropylacrylamide); cyclic polymer; reversible addition fragmentation chain transfer (RAFT); thermal phase transition

Introduction

Poly(*N*-isopropylacrylamide) (PNIPAM) is well-known for its thermo-responsive behavior in water.[1] Aqueous solutions of PNIPAM exhibit a thermo-induced phase separation at around 32 °C, known as the lower critical solution temperature (LCST). Since the phase separation is sharp and reversible, PNIPAM has been widely exploited for applications in sensing technology,[2] bio-engineering,[3] and drug delivery.[4] The PNIPAMs synthesized by conventional free radical polymerizations suffer from the disadvantages of high polydispersity and lack of control over molecular weight and over end group functionality. The advent of the living/controlled free radical polymerizations, especially atom transfer radical polymerization (ATRP) and reversible addition fragmentation chain transfer (RAFT) polymerization, provided feasible approaches to prepare PNIPAMs with well defined molecular weight and structure, thus making it possible to study the effect of topological factors, such as chain length and shape on the LCST behavior of PNIPAM. In the studies of chain length effect on LCST, it was revealed that the LCST was concomitantly affected by the structure of the end groups of the polymer chains and by the chain length.[5] Generally, hydrophobic end groups tend to decrease the LCST while hydrophilic end groups tend to increase it. The end group effect is more pronounced for low molecular weight polymers and it diminishes as the molecular weight increases.[6] Interestingly, when the hydrophobic interactions among polymer end groups are strong enough to form distinct micellar structures, the hydrophobic effect is suppressed owing to the isolation of hydrophobic groups and water.[7,8] Unlike their linear counterparts, cyclic polymers have no chain ends. It is expected that studies of cyclic PNIPAMs will provide further insight into the topological effect on the LCST behavior of PNIPAM in water. This very reason has motivated us to synthesize macrocyclic

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poly(*N*-isopropylacrylamide) with the aim to explore the effect of topological constraints on the solution and bulk properties of PNIPAM.

Synthesis of Cyclic Poly(*N*-isopropylacrylamide)

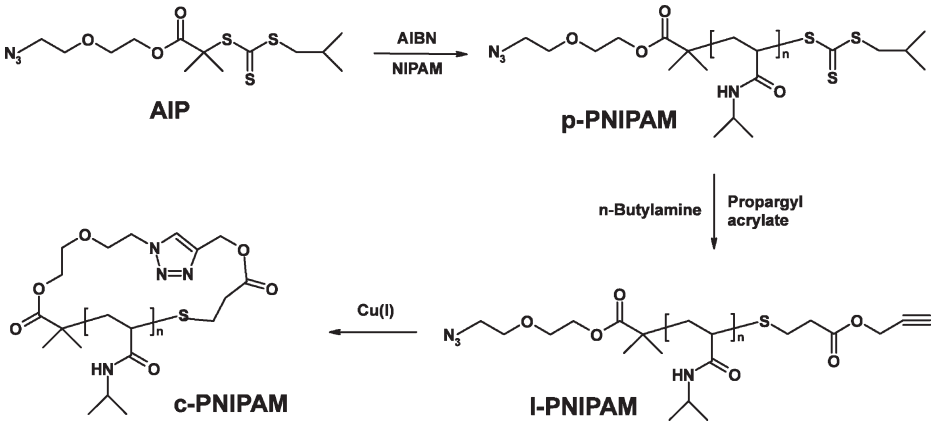
The synthesis of cyclic PNIPAMs was accomplished in three steps (Scheme 1). First, the precursor telechelic PNIPAMs (*p*-PNIPAM) were synthesized by RAFT polymerization of *N*-isopropylacrylamide (NIPAM) in 2,6-dioxane using an azido-functionalized trithiocarbonate, 2-(2-azidoethoxy)ethyl 2-(1-isobutyl)sulfanylthiocarbonylsulfanyl-2-methyl propionate (AIP) as chain transfer agent. The precursor polymer (*p*-PNIPAM), which carries an azidoethoxyethyl group at one end and an isobutylsulfanylthiocarbonyl (IBS) group at the other were further modified by transforming the IBS groups into propargyl groups via a one-pot aminolysis/Michael addition sequence in THF using n-butylamine as aminolysis agent and propargyl acrylate as Michael addition agent, generating the desired α-azido ω-propargyl telechelic linear polymers (*l*-PNIPAM).[9] Finally, the ring closure reaction was achieved by 'click' chemistry in water at 30 °C catalyzed by a $CuSO_4$/sodium ascorbate mixture under very dilute conditions.[10] Overall, three cyclic PNIPAMs (*c*-PNIPAM) were synthesized with number average molecular weight (M_n) of 6.9, 12.7, 19.4 kDa and polydispersity (PDI) less than 1.2 as determined by gel permeation chromatography with multi-angle laser light scattering detector (GPC-MALLS) system (Table 1).

Table 1.
Data of molecular weight, polydispersity, phase transition temperatures, enthalpies, and glass transition temperatures for linear and cyclic PNIPAMs.

Polymer	M_n (kDa)	PDI	T_M (°C)	ΔH (kJ/mol)	Tg (°C)
l-PNIPAM-6k	6.8	1.10	40.3	6.06	122.0
c-PNIPAM-6k	6.9	1.11	45.8	3.86	134.5
l-PNIPAM-12k	12.7	1.08	36.6	6.40	134.0
c-PNIPAM-12k	12.7	1.11	41.6	4.47	138.1
l-PNIPAM-19k	19.2	1.09	35.6	6.40	138.2
c-PNIPAM-19k	19.4	1.16	39.6	5.38	141.5

Comparison of Linear and Cyclic PNIPAMs in Solution and in Bulk

The phase separation of the cyclic PNIPAMs and their linear counterparts in aqueous solution were monitored by high sensitivity differential scanning microcalorimetry (HS-DSC). Figure 1 represents the microcalorimetric endotherms for *l*-PNIPAM-6k and *c*-PNIPAM-6k in water at the concentration of 1.0 g/L. The *l*-



Scheme 1.
Synthesis procedure for cyclic poly(*N*-isopropylacrylamide).

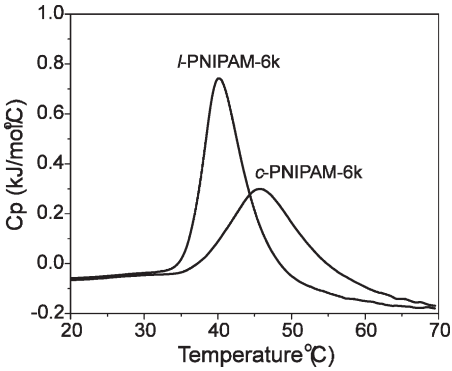


Figure 1.
Temperature dependence of the specific heat capacity (Cp) of *l*-PNIPAM-6K and *c*-PNIPAM-6K in water at the concentration of 1.0 g/L and heating rate of 1.0 °C/min.

PNIPAM-6k exhibits a sharp endotherm with temperature of transition maximum (T_M) of 40.3 °C while the endotherm of *c*-PNIPAM-6k displays a broader transition with T_M shifted to a higher temperature of 45.8 °C.

Such broadening effect and upward shift of phase transition temperature were also observed for the other two cyclic PNIPAMs of higher MW (Table 1). As depicted in Figure 2, the T_M values of *c*-PNIPAMs are systematically higher than those of the corresponding *l*-PNIPAM precursors. As the MW of PNIPAM increases, the gap in T_M between linear and cyclic PNIPAMs narrows. This implies that as the ring size becomes larger, the effect of topological constraint on the LCST of cyclic polymers becomes smaller. For both the linear and cyclic polymers, the T_M decreases as the MW increases. The inverse MW dependence of LCST for the linear PNIPAMs can be attributed to the hydrophilic end group effect while for cyclic PNIPAMs, it may be due to the formation of the hydrophilic triazole segment in the ring.[11] It should be mentioned that the ring size of the cyclic polymers exerts a marked effect on the enthalpy change in the phase transition. As listed in Table 1, the enthalpy of the phase transition (ΔH) for *l*-PNIPAMs in the MW range of 6 to 19 kDa remains rather constant between 6.06 and 6.40 kJ/mol per NIPAM unit, which is in consistent with the reported ΔH values of 5.5 – 7.5 kJ/mol per repeating unit upon phase transition for linear PNIPAM.[12,13] In contrast, the phase transition enthalpies of cyclic PNIPAMs are significantly lower than those of ordinary linear PNIPAM with ΔH values of 3.86, 4.47, and 5.38 kJ/mol for *c*-PNIPAM-6k, *c*-PNIPAM-12k, and *c*-PNIPAM-19k, respectively. As the MW of cyclic PNIPAMs increases, the ΔH of the phase transition for cyclic PNIPAMs approaches the values of linear PNIPAM.

The glass transition temperature (Tg) of linear and cyclic PNIPAMs in bulk was evaluated by differential scanning microcalorimetry (DSC). In Figure 3, we plot the Tg values of linear and cyclic PNIPAMs. The

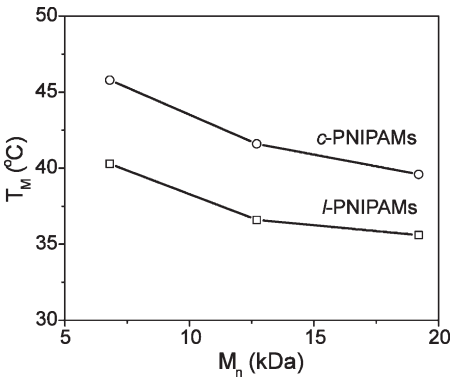


Figure 2.
Plot of T_M *vs.* M_n for linear and cyclic PNIPAMs in aqueous solution (1.0 g/L) in the molecular weight range of 6 to 19 kDa.

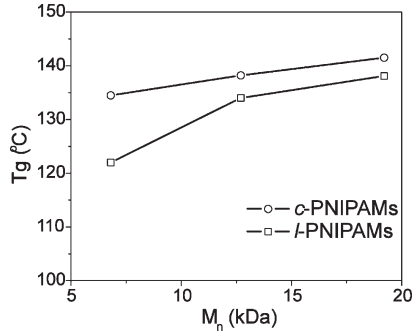


Figure 3.
Plot of Tg *vs.* M_n for linear and cyclic PNIPAMs.

cyclic PNIPAMs possess higher Tg than their linear precursors with the tendency that the difference in Tg narrows as the MW increases. Note that the Tg of a linear PNIPAM with MW of ~9 kDa was measured to be 132 °C as reported by Garay et al.,[14] which is in line with our Tg values of linear PNIPAMs. The higher Tg of cyclic PNIPAMs supports viewpoint of the free chain end effect on Tg. This is in agreement with previous observations on other polymers such as polystyrene[15] and poly(2-vinylpyridine)[16] for which the Tg of cyclic polymers is systematically higher than that of the countpart linear polymers of the same molecular weight. Also similar to the aformentioned polymers, the Tg of cyclic PNIPAMs shows a much weaker MW dependence than the Tg of linear PNIPAMs.[16]

Conclusion

Our results demonstrate that the topological effect of ring constraints can affect the properties of cyclic PNIPAMs in both solution and bulk. In aqueous solution, the existence of repulsive forces between rings due to the topological prohibition of intermolecular linking triggers an upward shift of the LCST. The steric constraints, which favor the formation of intrachain hydrogen bonds between NIPAM units at the expense of water/NIPAM hydrogen bonds, lead to smaller enthalpies of phase transition for cyclic PNIPAMs. In bulk, the cyclic PNIPAMs possess higher Tg than their linear precursors due to the absence of free chain ends. All these effects minimize with increasing molecular weight of the cyclic polymers.

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