

Facile synthesis of dendrimer-like star-branched poly(isopropylacrylamide) via combination of click chemistry and atom transfer radical polymerization

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We report a facile synthesis method of dendrimer-like star-branched poly(*N*-isopropylacrylamide) (PNIPAM) via the combination of click chemistry and atom transfer radical polymerization (ATRP) by employing the arm-first approach. First, the α -azido- ω -chloro-heterodifunctionalized building block, N_3 -PNIPAM-Cl (G0-Cl), was synthesized via ATRP by 3-azidopropyl 2-chloropropionate as the initiator. Taking advantage of click chemistry, the first generation (G1) of dendrimer-like star-branched PNIPAM, G1-(Cl)₃, was readily prepared via the click coupling reaction between G0-Cl and tripropargylamine. For the construction of second generation (G2) dendrimer-like star-branched PNIPAM, G2-(Cl)₆, terminal chloride moieties of G1-(Cl)₃ were first converted to azide, and then reacted with excess tripropargylamine to give G1-(alkynyl)₆; G2-(Cl)₆ was subsequently prepared via click reaction between G1-(alkynyl)₆ and G0-Cl. Gel permeation chromatography (GPC) and matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry were employed to confirm the successful construction of dendrimer-like star-branched polymers. The unique thermal phase transition behavior of this dendrimer-like star-branched polymer in aqueous solutions was further investigated by turbidimetry and micro-differential scanning calorimetry (Micro-DSC).

dendrimer-like, branched, ATRP, click chemistry

1 Introduction

Dendrimer-like star-branched polymers are a special type of hyperbranched polymer consisting of dendritically branched polymer arms radiating from a common junction point [1–5]. Unlike conventional dendrimers which is restricted with their size (5–15 nm), the dimensions of dendrimer-like star branched polymers constructed from polymeric building blocks can be readily regulated by changing their generations [6]. Furthermore, possessing combined advantages such as dendritic topology, adjustable dimension, and their unique microenvironment, this novel type

of branched polymer is expected to have intriguing solution properties as compared to conventional linear polymers [7–11].

Synthetic strategies employed for dendrimer-like star branched polymers can be categorized into two main types: “core-first” [12–18] and “arm-first” [19–24] methodologies. In the “core-first” methodology, multifunctional initiator is typically utilized for the polymerization of a certain monomer to afford the “core”, and their end groups were then converted into two or more initiation sites which were employed for the construction of next generations via living ring-opening polymerization (ROP) or atom transfer radical polymerization (ATRP). Hedrick *et al.* [1, 12] synthesized a series of dendrimer-like star-branched polymers by utilizing repeated ROP of ϵ -caprolactone (CL) via the “core-first”

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approach. However, the uniformity of each polymer segment remained a big challenge for this strategy. Most importantly, it is difficult to retain the initiation efficiency from each initiation site during the preparation, especially at higher generations.

As for the “arm-first” methodology, the dendrimer-like star branched polymers are built up stepwise from polymer precursors and multifunctional core molecule, which is able to solve the above-mentioned issue. Hadjichristidis *et al.* [20] prepared a series of second (G2) and third generation (G3) dendritic polybutadienes (PBd) through the coupling of three-arm PBd living anions with methyltrichlorosilane by using high vacuum anionic polymerization techniques. Although the dendrimer-like star branched structure can be precisely controlled in this approach, the construction of higher generation dendrimer-like star branched polymers still remains a problem. As the molecular weight increases, the coupling process gets more difficult.

Click chemistry has drawn much attention in the past few years which emerged to be a highly efficient technique possessing advantages such as mild reaction conditions, high specificity, facile purification, and quantitative yield [25, 26]. The great potential of this coupling procedure has been quickly recognized since its discovery and then widely used for the construction of well-defined polymers with varying chain architectures [27–32]. Monteiro *et al.* [6, 33, 34] further extended this methodology to the preparation of dendrimer-like star branched polymers. They prepared a variety of the first-generation dendrimer-like star branched polymers based on polystyrene (PS) or poly(acrylic acid) (PAA) via the combination of ATRP and click chemistry. Chen *et al.* [35] reported the synthesis of third-generation dendrimer-like star-branched polymers based on PS or PS/poly(*tert*-butyl acrylate) (PtBA) building blocks via the combination of ATRP and click chemistry utilizing the “core-first” methodology, the success of which critically relies on the initiation efficiency. We speculate that if the dendrimer-like star branched polymer was built via the “arm-first” strategy in combination with high efficiency click coupling reactions, increased controllability over the molecular structure of dendrimer-like star branched polymers might be achieved.

Herein, we describe the facile preparation of dendrimer-like star-branched poly(*N*-isopropylacrylamide) (PNIPAM) via the combination of click chemistry and ATRP utilizing the arm-first strategy. The α -azido- ω -chloro-heterodifunctional precursor, N_3 -PNIPAM-Cl (G0-Cl), and a trifunctional molecule, tripropargylamine, were used as starting building blocks for the fabrication of dendrimer-like star-branched PNIPAM. Taking advantage of click chemistry, the first (G1) and second generations (G2) of dendrimer-like star-branched PNIPAM, G1-(Cl)₃ and G2-(Cl)₆, can be facily synthesized with high selectivity and efficiency.

2 Experimental

2.1 Materials

N-Isopropylacrylamide (NIPAM, 97%, Tokyo Kasei Kagyo Co.) was purified by recrystallization from a mixture of benzene and *n*-hexane (1/3, *v/v*) prior to use. Copper (I) chloride (CuCl, 99%), copper (I) bromide (CuBr, 99%), sodium azide (NaN₃, 99%), 3-chloropropanol (98%), tripropargylamine (98%), *N,N,N,N,N*-pentamethyldiethylenetriamine (PMDETA), and 2-chloropropionyl chloride (97%) were purchased from Aldrich and used as received. Tris(2-aminoethyl)amine (TREN) (96%) was purchased from Acros and used as received. 3-Azidopropyl 2-chloropropionate [36], 3-azidopropyl 2-chloropropionate [36], and tris(2-(dimethylamino) ethyl)amine (Me₆TREN) [37] were synthesized according to literature procedures. All other reagents were purchased from Shanghai Chemical Reagent Co. and used as received.

2.2 Sample preparation

General approaches employed for the preparation of dendrimer-like star-branched PNIPAM via the combination of ATRP and click chemistry are shown in Scheme 1.

Synthesis of α -azido- ω -chloro-terminated PNIPAM (G0-Cl)

The mixture of NIPAM (11.31 g, 0.1 mol), Me₆TREN (0.92 g, 4 mmol), and *tert*-butyl alcohol (22.6 g) were deoxygenated by bubbling with nitrogen for at least 30 min. CuCl (0.40 g, 4 mmol) was added and the solution mixture was stirred for 10 min to allow the formation of CuCl/Me₆TREN complex. 3-Azidopropyl 2-chloropropionate (0.77 g, 4 mmol) was then added to the reaction mixture via a syringe to start the polymerization. The reaction was allowed to stir under the protection of nitrogen at 25 °C for 6 h. The polymerization was terminated by addition of a few drops of saturated CuCl₂ solution in *tert*-butyl alcohol, and the reaction mixture was precipitated into a mixture of ethyl ether/hexane (1:1, *v/v*). The sediments were then dissolved with CH₂Cl₂ and passed through a neutral alumina column to remove copper catalyst. The eluent was concentrated and precipitated into a mixture of ethyl ether/hexane (1:1, *v/v*). The obtained product was dried overnight at room temperature in a vacuum oven for 24 h ($M_{n,GPC} = 3900$, $M_w/M_n = 1.08$; $M_{n,MALDI-TOF} = 2100$, PDI = 1.03).

Synthesis of G1-(Cl)₃ via click coupling reactions

A mixture of G0-Cl (4.41 g, 2.1 mmol), tripropargylamine (92 mg, 0.7 mmol), and PMDETA (0.36 g, 2.1 mmol) in 30 mL DMF were deoxygenated by bubbling with nitrogen for at least 30 min. CuBr (300 mg, 2.1 mmol) was then added, and the reaction mixture was allowed to stir at room temperature overnight under the protection of N₂. The solution mixture was concentrated and precipitated into an excess of

ethyl ether. The sediments was collected, dissolved in CH_2Cl_2 , and then passed through a neutral alumina column to remove copper catalyst. The eluent was concentrated and precipitated into an excess of ethyl ether. The sediments was collected via filtration and dried in a vacuum oven overnight at room temperature to afford the second generation dendrimer-like star-branched PNIPAM, G1-(Cl)_3 ($M_{n,\text{GPC}} = 13900$, $M_w/M_n = 1.07$, $M_{n,\text{MALDI-TOF}} = 6500$, $\text{PDI} = 1.05$).

Synthesis of azide-functionalized G1 dendrimer-like star-branched PNIPAM ($\text{G1-(N}_3)_3$)

G1-(Cl)_3 (0.65 g, 0.1 mmol Cl moieties) was dissolved in 20 mL DMF, and then NaN_3 (65 mg, 1 mmol) was added. The reaction mixture was allowed to stir at 45 °C for 48 h. After all the solvents were removed under reduced pressure, the crude product was dissolved with CH_2Cl_2 , and passed through a neutral alumina column. The eluent was concentrated and precipitated into ethyl ether. The sediments were collected and dried overnight at room temperature in a vacuum oven ($M_{n,\text{GPC}} = 14300$, $M_w/M_n = 1.07$).

Synthesis of G1-(alkynyl)_6

$\text{G1-(N}_3)_3$ (0.52 g, 0.08 mmol azide functionalities), PMDETA (0.17 g, 1 mmol), and tripropargylamine (0.13 g, 1 mmol) were added into a glass ampoule containing 10 mL DMF. After the reaction mixture was degassed by three successive freeze-pump-thaw cycles, CuBr (0.14 g, 1 mmol) was added. The ampoule was then sealed under vacuum and subjected to an oil bath preheated to 80 °C. After 2 h, the reaction mixture was concentrated under reduced pressure, dissolved with CH_2Cl_2 , and then passed through a neutral alumina column to remove the catalyst. The eluent was then concentrated and precipitated into excess of ethyl ether. The above dissolution-precipitation cycle was repeated for three times. The sediments were collected and dried overnight at room temperature in a vacuum oven ($M_{n,\text{GPC}} = 14200$, $\text{PDI} = 1.07$).

Synthesis of G2 dendrimer-like star-branched PNIPAM (G2-(Cl)_6)

G0-Cl (0.65 g, 0.31 mmol), G1-(alkynyl)_6 (0.35 g, 0.15 mmol alkynyl moieties), and 20 mL DMF were charged into a glass ampoule. After the reaction mixture was degassed by three successive freeze-pump-thaw cycles, CuBr (0.14 g, 1 mmol) was added to start the click reaction. The reaction mixture was allowed to stir at room temperature overnight. All the solvents were removed under reduced pressure; the crude product was dissolved with CH_2Cl_2 , and then passed through a neutral alumina column to remove the catalyst. The eluent was concentrated and precipitated into excess of ethyl ether. The dissolution-precipitation cycle was repeated for three times to remove excess G0-Cl . The sediments was collected and dried overnight at room temperature in a vacuum oven ($M_{n,\text{GPC}} = 32800$, $M_w/M_n = 1.09$; $M_{n,\text{MALDI-TOF}} = 19200$, $\text{PDI} = 1.07$).

2.3 Characterization

^1H NMR spectra were recorded on a Bruker 300 MHz spectrometer using CDCl_3 as solvent. Fourier transform-infrared (FT-IR) spectra were recorded on a Bruker VECTOR-22 IR spectrometer. The spectra were collected at 64 scans with a spectral resolution of 4 cm^{-1} . Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC) equipped with a Waters 1515 pump and a Waters 2414 differential refractive index detector (set at 30 °C). It used a series of three linear Styragel columns at an oven temperature of 45 °C. The eluent was DMF at a flow rate of 1.0 mL/min. A series of low-polydispersity polystyrene standards were employed for calibration. Matrix-assisted laser desorption/ionization time-of-flight mass spectrum (MALDI-TOF MS) was recorded in the linear mode on a Bruker BIFLEXe III using a nitrogen laser (337 nm) and an accelerating potential of 20 kV. 2,5-Dihydroxybenzoic acid (DHB) (Aldrich) was used as the matrix and NaBF_4 was added to improve ionization. The samples were prepared by mixing THF solutions of the polymer and matrix (50 mg/mL) with saturated methanolic NaBF_4 at a weight ratio of 1:50:2 (polymer/matrix/ NaBF_4). Micro-differential scanning calorimetry (Micro-DSC) measurements were conducted on a VP-DSC microcalorimeter (MicroCal Inc) at an external pressure of 180 kPa. The cell volume was 0.157 mL. The heating rate was 1.0 °C/min, and the instrument response time was set at 5.6 s. All the micro-DSC data were corrected for instrument response time and analyzed using the software in the calorimeter. UV-vis spectra and transmittance measurements were acquired on a Unico UV-vis 2802PCS spectrophotometer. The transmittance of the solution was measured at a wavelength of 500 nm using a thermostatically controlled cuvette. Values for the cloud point of polymer solutions were determined as the temperature corresponding to 1.0 % decrease in optical transmittance.

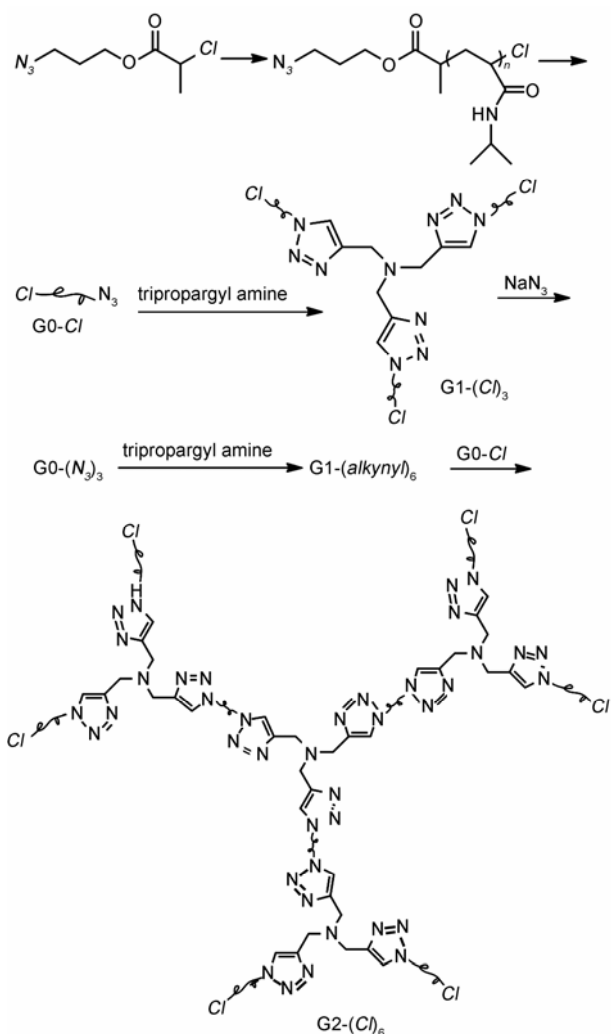
3 Results and discussion

3.1 Synthesis of G1 and G2 dendrimer-like star-branched PNIPAM.

Synthetic schemes employed for the preparation of G1 and G2 dendrimer-like star-branched PNIPAM are shown in Scheme 1.

The α -azido- ω -chloro-heterodifunctional precursor, N_3 -PNIPAM-Cl (G0-Cl), was synthesized at first by using the azido-functionalized ATRP initiator. Taking advantage of the high efficiency and quantitative yield of click chemistry, the G1 dendrimer-like star-branched PNIPAM, G1-(Cl)_3 , was synthesized via the click coupling reaction of G0-Cl with tripropargylamine. The second generation dendrimer-like star-branched PNIPAM, G2-(Cl)_6 , was prepared via the click coupling reaction of G1-(alkynyl)_6 with G0-Cl .

The α -azido- ω -chloro-heterodifunctional precursor, N_3 -



Scheme 1 Schematic illustration of the synthesis of G_0-Cl , $G_1-(Cl)_3$, and $G_2-(Cl)_6$ dendrimer-like star poly(*N*-isopropylacrylamide) (PNIPAM) polymers.

PNIPAM- Cl (G_0-Cl), was synthesized via the ATRP of NIPAM monomer by using 3-azidopropyl 2-chloropropionate as the initiator and $CuCl/Me_6TREN$ as the catalyst. This polymerization system was proved to be successful and efficient for NIPAM monomer, and the degree of polymerization (DP) can be facilely adjusted via the feed ratio and monomer conversion [38]. 1H NMR spectrum of N_3 -PNIPAM- Cl (G_0-Cl) is shown in Figure 1(a). On the basis of the integral ratio between resonance signal ascribed to the methylene protons adjacent to the azide group at ~ 3.5 ppm (peak

(a)) and methenyl protons adjacent to amide groups of PNIPAM at ~ 4.0 ppm (peak (e)), DP of PNIPAM was estimated to be 17, thus the polymer was denoted as N_3 -PNIPAM $_{17-Cl}$. It should be noted that DP of PNIPAM was relatively low, which guarantees its further efficient click reactions; the low DP also ensures its easy purification due to that N_3 -PNIPAM $_{17-Cl}$ is actually soluble in ethyl ether whereas PNIPAM with higher DPs is not soluble; besides, the monomer conversion was kept to be relatively low ($< 70\%$), ensuring the integrity of end chloride functionality. FT-IR spectrum of G_0-Cl is shown in Figure 2(a), and an absorption band characteristic of azide group at 2105 cm^{-1} can be clearly observed. GPC trace of G_0-Cl is mono-modal and quite symmetric, revealing an M_n of 3,900 and an M_w/M_n of 1.08 (Figure 3). MALDI-TOF MS of G_0-Cl reveals repeating set of peaks extended from 1,000 to 3,200 m/z with the highest intensity located at $\sim 2100\text{ m/z}$ and PDI of 1.03 (Figure 4), which is in good agreement with the molecular weights determined by 1H NMR. The structural parameters of G_0-Cl are summarized in Table 1.

The subsequent click reaction between G_0-Cl and tripropargylamine in DMF afforded G1 dendrimer-like star-branched PNIPAM, $G_1-(Cl)_3$. After the click reaction, quantitative chain end transformation was confirmed. From the 1H NMR spectrum of $G_1-(Cl)_3$ (Figure 1(b)), we can clearly observe the resonance signal of methylene protons adjacent to the azide group (peak (c)) shifted from ~ 3.5 ppm to ~ 4.5 ppm, which should be ascribed to the formation of 1,2,3-triazole rings. Furthermore, the appearance of resonance signals of methylene protons in tripropargylamine moieties at 3.7 ppm (peak (a)), accompanied with the resonance signals of the proton in 1,2,3-triazole ring at ~ 7.9 ppm (peak (b)) further indicated that the click coupling reaction was successful. FT-IR spectrum of $G_1-(Cl)_3$ is shown in Figure 2(b). As compared to G_0-Cl , absorption bands at 2100 cm^{-1} characteristic of azide group completely disappear, indicating the complete consumption of azide groups.

GPC analysis of $G_1-(Cl)_3$ revealed an M_n of 13900 and an M_w/M_n of 1.07 (Figure 3, Table 1). As compared to the G_0-Cl precursor, we can observe a clear shift to the higher molecular weight side for $G_1-(Cl)_3$. Most importantly, the GPC trace is monomodal and symmetric and we can not discern any peaks or shoulders at the lower molecular weight side, strongly suggesting the click coupling reaction was highly efficient.

MALDI-TOF mass spectrum of $G_1-(Cl)_3$ is shown in

Table 1 Characterization of dendrimer-like star poly(*N*-isopropylacrylamide)s

Samples	$M_{n,GPC}^a$	M_w/M_n^a	$M_{n,MALDI}^b$	M_w/M_n^b	ΔH^c (kJ/mol)	LCST ($^{\circ}C$) ^d
G_0-Cl	3900	1.08	2100	1.03	4.1	38
$G_1-(Cl)_3$	13900	1.07	6500	1.05	3.7	32
$G_2-(Cl)_6$	32800	1.09	19200	1.07	2.4	26

a) Number-average molecular weight, M_n , and polydispersity, M_w/M_n , determined by GPC using DMF as the eluent. b) Determined by MALDI-TOF mass spectrometry. c) Enthalpy changes per mole of NIPAM repeating units associated with the thermal phase transition determined by micro-DSC from 1.0 g/L aqueous solutions. d) Lower critical solution temperature (LCST) was defined as the temperature corresponding to a 1% decrease of transmittance.

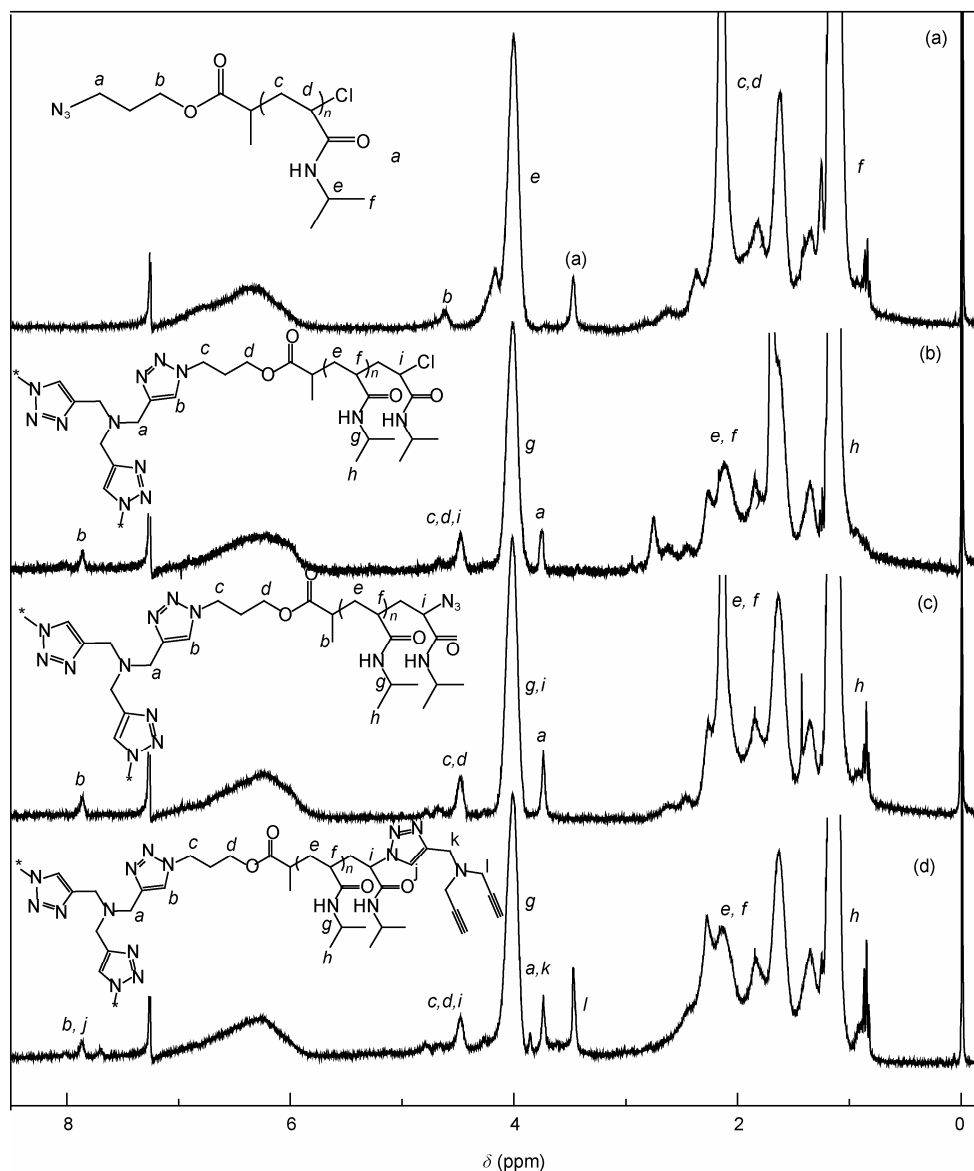


Figure 1 ^1H NMR spectra recorded for (a) G0-Cl , (b) G1-(Cl)_3 , (c) $\text{G1-(N}_3)_3$ and (d) G1-(alkynyl)_6 in CDCl_3 .

Figure 4(b). It revealed repeating set of peaks centered at $\sim 6500\text{ m/z}$ with an M_w/M_n of 1.05. It should be noted that there exist no shoulders in the lower molecular weight side in the range of 2000–4000 Da, strongly supporting that the G0-Cl precursor has been completely consumed, and dendrimer-like star-branched G1-(Cl)_3 was successfully constructed.

For the preparation of G2-(Cl)_6 , the terminal Cl moieties in G1-(Cl)_3 were at first converted to azide moieties to afford $\text{G1-(N}_3)_3$. After azidation, resonance signals of the terminal methine protons in G1-(Cl)_3 at $\sim 4.5\text{ ppm}$ shifted to 4.0 ppm (peak (i)). A comparison of the FT-IR spectra of G1-(Cl)_3 and $\text{G1-(N}_3)_3$ revealed the reappearance of absorbance peak at 2100 cm^{-1} , which is characteristic of the terminal azide moiety. The subsequent click reaction between $\text{G1-(N}_3)_3$ and tripropargylamine in DMF at room

temperature give G1-(alkynyl)_6 . In the current case, an excess of tripropargylamine was used to ensure that only one propargyl group in tripropargylamine participates in the click coupling reaction, thus each azido moiety can be converted to two alkynyl groups. Monteiro *et al.* [34] reported the click reaction of PS-N_3 with an excess of tripropargylamine to obtain dialkynyl-functionalized PS, which was subsequently employed for the preparation of AB_2 miktoarm star polymers. The click reaction between $\text{G1-(N}_3)_3$ and tripropargylamine was conducted in DMF at room temperature, and excess of tripropargylamine was removed via repeated precipitation. We can clearly observe the appearance of new resonance signals at $\sim 3.5\text{ ppm}$ (peak (l)) in its ^1H NMR spectrum (Figure 1(d)), which should be ascribed to methylene protons neighboring to alkynyl moieties. Simultaneously, absorption bands in the FT-IR spec-

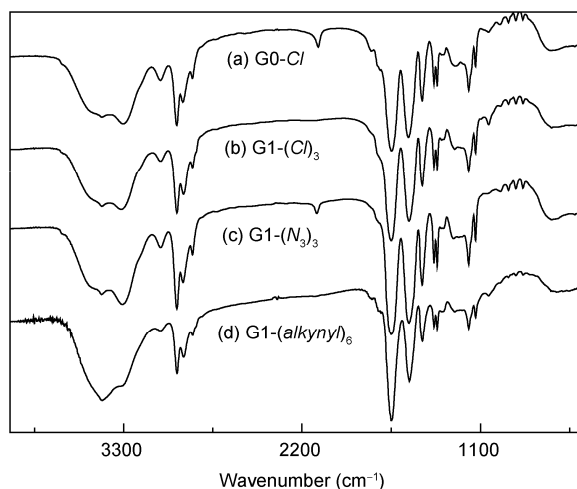


Figure 2 FT-IR spectra recorded for (a) $G0-Cl$, (b) $G1-(Cl)_3$, (c) $G1-(N_3)_3$, and (d) $G1-(alkynyl)_6$.

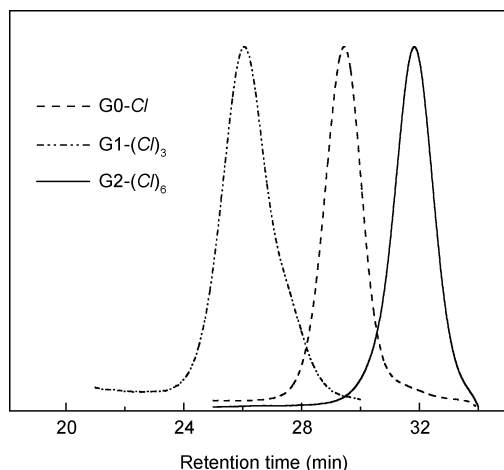


Figure 3 DMF GPC traces recorded for $G0-Cl$, $G1-(Cl)_3$, and $G2-(Cl)_6$.

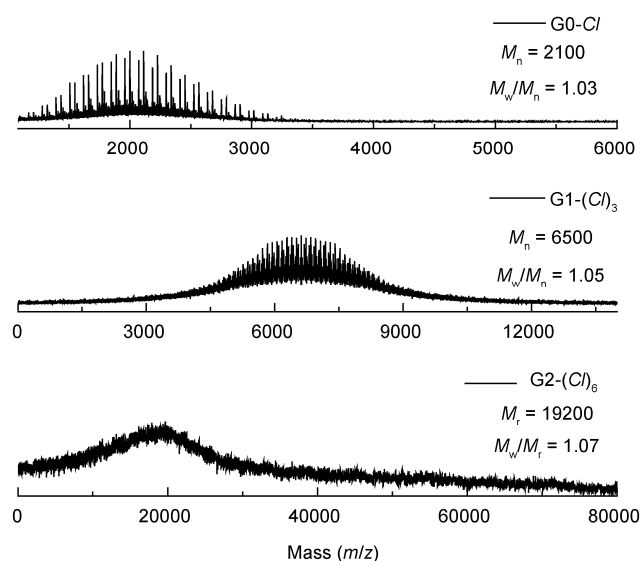


Figure 4 MALDI-TOF mass spectra of (a) $G0-Cl$, (b) $G1-(Cl)_3$, and (c) $G2-(Cl)_6$.

trum at 2100 cm^{-1} characteristic of azide group completely disappeared (Figure 2(d)), indicating the complete consumption of azide groups. It should be noted that terminal alkynyl functionalities also exhibit weak absorbance peak at $\sim 2100\text{ cm}^{-1}$ in Figure 2(d), which it can be hardly discerned.

$G1-(alkynyl)_6$ was then employed for the subsequent click reaction with $G0-Cl$ to afford $G2-(Cl)_6$. GPC elution peak of $G2-(Cl)_6$ revealed a considerably shift to the higher molecular weight side compared to that of $G1-(alkynyl)_6$, accompanied with the increase of M_n from 14200 to 32800 (Figure 3 and Table 1). The elution peak of $G2-(Cl)_6$ was also monomodal and quite symmetric, indicating that the click coupling reaction was highly selective and efficient. MALDI-TOF mass spectrum was utilized to further confirm the structure of $G2-(Cl)_6$. Figure 4(c) shows repeating set of peaks centered at $\sim 19200\text{ m/z}$ with polydispersity of 1.07. As the molecular weight of $G0-Cl$ was determined to be $\sim 2100\text{ m/z}$ by MALDI-TOF MS, the MALDI-TOF MS data strongly suggests that all alkynyl moieties have been consumed and $G2$ dendrimer-like star-branched PNIPAM, $G2-(Cl)_6$, was successfully synthesized.

3.2 Thermal phase transition behavior of $G0-Cl$, $G1-(Cl)_3$, and $G2-(Cl)_6$

It is well-known that PNIPAM is a thermoresponsive polymer which exhibits reversible thermal phase transitions in aqueous medium above $\sim 32\text{ }^\circ\text{C}$ (lower critical solution temperature, LCST) [39]. Whittaker *et al.* [40] synthesized 4-arm PNIPAM star polymers via RAFT polymerization and investigated their thermal phase transitions in aqueous solution. They found that star polymer exhibits significantly lower LCST compared to the linear ones. Thus, it should be of great interest to investigate the thermal phase transition behavior of dendrimer-like star-branched PNIPAM.

$G0-Cl$, $G1-(Cl)_3$, and $G2-(Cl)_6$ in aqueous solutions temperature dependence of optical transmittance at 500 nm was recorded and shown in Figure 5. For linear $G0-Cl$, the optical transmittance exhibits abrupt changes at temperatures above $38\text{ }^\circ\text{C}$, for $G1-(Cl)_3$, the LCST decreases to $32\text{ }^\circ\text{C}$. $G2-(Cl)_6$ was determined to be $26\text{ }^\circ\text{C}$. This phenomenon can be explained in terms of the n -cluster effects [41]. Due to the high chain density inside the dendrimer-like star-branched topology, PNIPAM segments were densely packed and the interactions between the polymer chains and water molecules was highly weakened, which may led to the sharp decrease of LCST.

It has been well-documented that the disruption of hydrogen bonds between amide groups and water molecule during the collapse and aggregation of PNIPAM chains can be easily detected via microcalorimetry [38, 42]. For linear PNIPAM with high molecular weight, the enthalpy changes associated with the thermal phase transition has been determined to be in the range of $5.5\text{--}7.5\text{ kJ/mol}$ of NIPAM re-

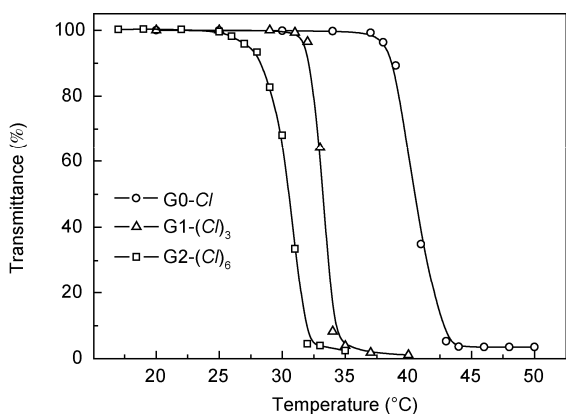


Figure 5 Temperature dependence of optical transmittance at 500 nm obtained for aqueous solutions of $G0-Cl$, $G1-(Cl)_3$, and $G2-(Cl)_6$. The lower critical solution temperature (LCST) was defined as the temperature corresponding to a 1% decrease of transmittance.

peating units; whereas for PNIPAM with other chain topologies such as star-shaped and cyclic-shaped, the enthalpy changes were relatively lower. The micro-DSC measurement was taken for the temperature dependence of partial heat capacity (C_p) of linear $G0-Cl$, dendrimer-like star-branched $G1-(Cl)_3$ and $G2-(Cl)_6$ in aqueous solutions, and the results are shown in Figure 6 and Table 1. For linear $G0-Cl$, the micro-DSC curve revealed one broad endothermic peak with $\Delta H = 4.1$ kJ/mol, which is typical of low MW PNIPAM chains, and the results are quite comparable to those reported by Stover *et al.* [38, 42]. Micro-DSC analysis of $G1-(Cl)_3$, and $G2-(Cl)_6$ showed relatively sharp

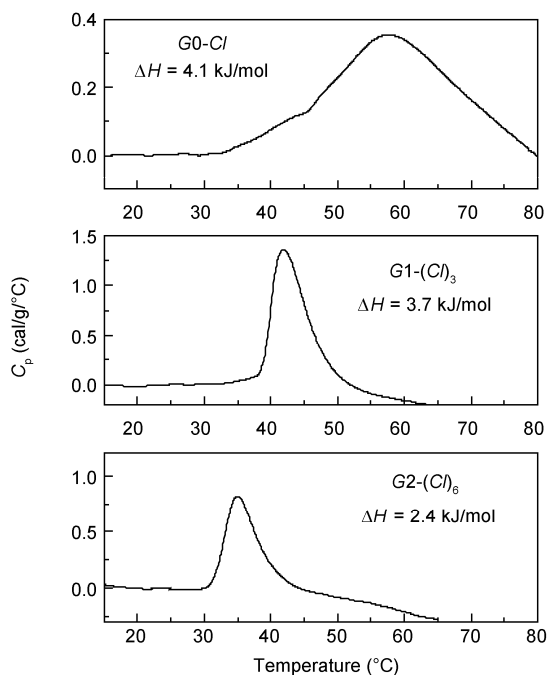


Figure 6 Temperature dependence of the specific heat capacity (C_p) obtained for 1.0 g/L aqueous solutions of $G0-Cl$, $G1-(Cl)_3$, and $G2-(Cl)_6$ during the heating process. The heating rate was 1.0 °C/min.

endothermic peaks with ΔH being 3.7 and 2.4 kJ/mol of NIPAM repeating units, respectively. We deduced that the high local chain density in dendrimer-like star-branched polymers, especially for $G2-(Cl)_6$, restricts the mobility of water molecules as compared to those in linear chains, which will hinder the formation of hydrated structures.

4 Conclusions

We report the facile preparation of the first and second generations of dendrimer-like star-branched PNIPAM via a combination of ATRP and click chemistry methods by utilizing the arm-first strategy. The α -azido- ω -chloro-heterodifunctional precursor, N_3 -PNIPAM- Cl ($G0-Cl$), was first synthesized via ATRP by using 3-azidopropyl 2-chloropropionate as the initiator. The first generation of dendrimer-like star-branched PNIPAM, $G1-(Cl)_3$, was prepared via the click coupling reaction between azide-functionalized $G0-Cl$ and tripropargylamine. For the construction of the $G2-(Cl)_6$, each chloride terminal functionality of $G1-(Cl)_3$ was converted to two alkynyl groups at first and then "click" reacted with linear $G0-Cl$ to afford $G2-(Cl)_6$. The thermal phase separation behavior of dendrimer-like star-branched PNIPAM, $G1-(Cl)_3$, and $G2-(Cl)_6$, in aqueous medium was quite different from the $G0-Cl$ precursor. The LCST of $G2-(Cl)_6$ was determined to be 26 °C, which is much smaller than that of $G0-Cl$ (38 °C). Simultaneously, micro-DSC analysis of dendrimer-like star-branched PNIPAMs: $G1-(Cl)_3$, and $G2-(Cl)_6$ exhibited relatively lower enthalpy change of 3.7 and 2.4 kJ/mol of NIPAM repeating units, respectively.

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