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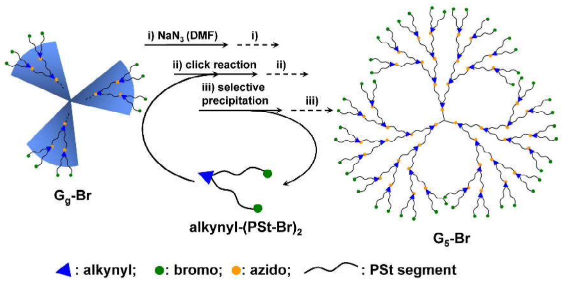

Arm-first divergent approach combining with selective precipitation has been developed to synthesize dendrimer-like polystyrenes efficiently and economically.

# Efficient and Economical Synthesis of Dendrimer-Like Polystyrene with Long Subchains through Arm-first Divergent Strategy

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**ABSTRACT**: An efficient and economical route to synthesize well-defined dendrimer-like polymers with long subchains has been developed based on the "arm-first" divergent approach. At first, a linear seesaw-type polystyrene (PSt) macromonomer with one alkynyl group at the center and one bromo group at each end was prepared as the constituent unit, and a tri-arm star PSt with three terminal bromo groups as the first generation of dendrimer-like PSt ($G_1$). Then, the second generation of dendrimer-like PSt ($G_2$) carrying six terminal bromo groups was obtained through: (1) transformation of the terminal bromo group of the former generation ($G_1$) into azido group; (2) alkynyl-azido click reaction between dendrimer-like polymer and linear seesaw-type macromonomers; (3) removal and recovery of excess macromonomers through precipitation in a selective non-solvent. Repeating those steps led to the achievement of dendrimer-like PSt up to the fifth generation ($G_5$) with polydispersity index below 1.18. Interestingly, excess PSt macromonomers were separated from the mixture of click reaction by selective precipitation instead of time-consuming fractionation and re-used in the following generation growth, promoting the efficiency and economy of the overall synthesis. The whole generation growth was monitored by nuclear magnetic resonance spectroscopy, Fourier transform infrared spectroscopy and gel permeation chromatograph with a multi-angle laser light scattering detector. Thermal and solution properties of dendrimer-like PSts were investigated in view of generation number, based on the measurements of glass transition temperature and intrinsic viscosity.

**Keywords:** demdrimer, ATRP, click chemistry, polystyrene, long subchain

## INTRODUCTION

Dendrimer-like polymers are one individual category of dendrimers with well-controlled linear subchains between the branch points.[1] They can combine the advantageous properties of regular dendrimers and linear polymers. On one hand, these polymers have precise numbers of branching points and periphery functionalities, which provide the reduced intermolecular entanglement and the multiplicity of reactive sites. On the other hand, they have linear polymer segments with well-controlled lengths, endowing them larger molecular weight and less brittleness compared with those regular dendrimers. These properties make such dendrimer-like polymers attractive candidates for many material applications including targeted drug delivery, viscosity modifiers, supports for catalysts and scaffolds for further synthesis.[2-4] These dendrimer-like PSts are well-defined with regulated branched architectures and many controllable structural variables, which make them the ideal model systems to investigate the polymer correlations between the structure and properties, such as glass transition, theology and visco-elasticity. So far, a number of dendrimer-like polymers have been prepared through either divergent and convergent approaches.[5-8]

In the convergent method, dendrimer-like polymers are usually prepared by repeating the linkage of central functionalized or living dedron precursors onto the multifunctional cores. In practice, two- and three-generation dendrimer-like polymers with well-defined structures were synthesized by Hadjichristidis,[9, 10] Hutchings,[11] and Monteiro[12]. However, the linkage efficiency is relatively low due to the stereo-hindrance of the focal group, especially for the higher generations.

In the divergent approach, the generation segments are sequentially formed by either in-situ polymerization of small monomers from the initiation sites of the previous dendrime-like polymers or the linkage of pre-existing macromonomers from separate polymerization onto the previous dendrime-like polymers (arm-first divergent approach). Divergent method involving in in-situ polymerization of small monomers has been employed in the synthesis of a series of poly(ethylene oxide),[13-15] polystyrene,[16-20] and polycaprolactone[21, 22] dendrimer-like (co)polymers. In this method, most of the synthesized polymers are limited to the $G_4$ stage and the relative molecular weight of $10^5$ g·mol$^{-1}$. Given the great difference in the solubility between dendrimer-like polymers and small monomers, it is easy to separate them by ordinary precipitation. However, incomplete initiation and heterogeneous chain growth for each terminal initiation site likely occur, especially in higher generation growth, which could lead to structural defects. Divergent method involving in arm-first strategy has been developed by Hirao and his co-workers.[23-26] In recent years, many well-defined dendrimenr-like polymers with high generation and high molecular weight have been synthesized via this arm-first divergent method.[6, 27-29] However, because the dendrimer-like polymers and the excess linear macromonomers are both polymers, how to separate them in a convenient way is a great problem. Time-consuming precipitation fraction only offers a small amount of product. For such situations, the synthesis of high-generation and high-molecular-weight dendrimer-like polymers with well-defined and characterized structures in an efficient way is still a great challenge even at the present time.

In this study, we explore an efficient and economical approach to synthesize dendrimer-like PSt through arm-first divergent strategy combining atom transfer radical polymerization (ATRP) and click chemistry. ATRP was used to synthesize seesaw-type polystyrene macromonomer with one central alkynyl group and two terminal bromo groups [alkynyl-(PSt-Br)$_2$], where bromo ends would be transformed into azido groups after the linkage onto dendrimer-like PSt. Alkynyl-azido click reaction was used to link the seesaw-type PSt macromonomer onto the dendrimer-like PSt, which can afford higher coupling efficiency. What's more, the products were obtained by convenient precipitation in a selective non-solvent instead of fractionation and the excess macromonomers left in the selective non-solvent were reused in the synthesis of the next generation. We believe that this process can serve as a platform to synthesize a new class of dendrimer-like (co)polymers.

## EXPERIMENTAL

### Materials

Styrene (St, 99%, Sinopharm Chemical Reagents), was dried and distilled under vacuum over $CaH_2$. Linear seesaw macromonomer of PSt having one alkynyl group anchored at the chain centre and two bromo groups at both chain ends [alkynyl-(PSt-Br)$_2$] with $M_n$ = 6400 was synthesized according to our previous literatures.[30] CuBr (Sinopharm Chemical Reagents Co.) was purified as follows. After crude CuBr was reduced by 0.01 M $Na_2SO_3$ aqueous solution, the solid was filtered and washed with 1wt % HBr aqueous solution. Finally, pure CuBr was obtained by washing with acetic acid and alcohol trice. THF was refluxed over $CaH_2$ for 6 h, dried with sodium/benzophenone, and distilled under reduce pressure before use. DMF was first dried with anhydrous magnesium sulfate and then distilled under reduced pressure before use. 2-Bromoisobutyryl bromide (Sigma-Aldrich), *N*, *N*, *N*′, *N*′′, *N*′′-pentamethyldiethylenetriamine (PMDETA, Sigma-Aldrich), 2, 2'-bipyridine (bpy, Sinopharm Chemical Reagents) and other chemical reagents (Aladdin) were used as received.

**Preparation of 1, 1, 1-tris(4-(2-bromoisobutyryloxy)phenyl)ethane (TBIBPE)**

1,1,1-Tris[4-(2-bromoisobutyryloxy)phenyl]ethane (TBIBPE) was synthesized according to a literature procedure.[31] A 250-mL three-necked round-bottom flask was charged with 2-bromoisobutyryl bromide (14.72 g, 64 mmol) and THF (80 mL). The flask was equipped with a pressure-equalizing addition funnel, which was filled with a solution of 1,1,1-tris(4-hydroxyphenyl)ethane (5 g, 16 mmol), triethylamine (10 g, 0.10 mol) and THF (80 mL). The reactor was cooled to 0 °C in an ice-water bath and the solution inside the addition funnel was added dropwise under nitrogen. After the reaction mixture was stirred overnight at room temperature, the salts were removed by filtration and discarded. The solvent of filtration was removed by rotary evaporation. Then, the obtained solid was re-dissolved in ethyl acetate (200 mL) and extracted with 5% NaOH (*aq.*) and distillated water. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed. Pure TBIBPE (yield: 4.3 g, 35%) was obtained as a white solid by re-crystallization from ethyl acetate/hexane.

### Preparation of azido-terminated tri-arm star polystyrene $\mu$-(PSt-N$_3$)$_3$

The bromo-terminated 3-arm star polystyrene [$\mu$-(PS-Br)$_3$] was prepared by ATRP of St using TBIBPE as the initiator, CuBr/bpy as the catalyst, and THF as solvent under $[St]_0/[TBIBPE]_0/[CuBr]_0/[bpy]_0 = 600 : 1 : 3 : 9$. Into a 25-mL dry glass vial with a magnetic stirring bar, St (12.5 g, 120 mmol), TBIBPE (150 mg, 0.20 mmol), bpy (280 mg, 1.8 mmol) and THF (10 mL) were added successively. After mixing thoroughly, the polymerization vial was degassed by three freeze-vacuum-thaw cycles, then added with CuBr (86 mg, 0.60 mmol) and sealed under vacuum. The sealed tube was immersed into an oil bath at 110 ºC. After the polymerization was carried out for 1 h, the tube was rapidly cooled to room temperature. The polymer solution was diluted with THF, and the mixture was passed through a short column of neutral alumina to remove metal salt, and precipitated in methanol. The polymer was dried for 24 h under vacuum at 25 ºC (*Conv.* = 8 %; $M_{n,GPC} = 3000$; $M_w/M_n = 1.05$).

Thus, the obtained $\mu$-(PS-Br)$_3$ (750 mg, 0.25 mmol) was dissolved in DMF (15 mL) and sodium azide (489 mg, 7.52 mmol) was added. The reaction mixture was stirred at 35 ºC for 48 h. After the filtration and evaporation to remove most DMF, $\mu$-(PSt-N$_3$)$_3$ (yield: 0.72 g, 96%) was obtained by the precipitation in methanol and dryness under vacuum at room temperature overnight.

### Preparation of seesaw macromonomer alkynyl-(PSt-Br)$_2$

A 50-mL dry glass vial with a magnetic stirring bar was charged with 1,3-dibromomethyl-5-propargyloxy-benzene (DBMPB, 240 mg, 0.75 mmol), bpy (702 mg, 4.50 mmol), St (23.4 g, 225 mmol) and THF (18 mL) were added successively. After mixing thoroughly, the polymerization vial was degassed by three freeze-vacuum-thaw cycles, then charged with CuBr (216 mg, 1.50 mmol) and sealed under vacuum. The sealed vial was immersed into an oil bath at 110 ºC. After the polymerization was carried out for 2.5 h, the vial was rapidly cooled to room temperature. The polymer solution was diluted with THF, and the mixture was passed through a short column of neutral alumina to remove metal salt. After twice precipitation in methanol, alkynyl-(PSt-Br)$_2$ (*Conv.*= 21%, $M_{\mathrm{n,GPC}}$ = 6400, $M_{\mathrm{w}}/M_{\mathrm{n}}$ = 1.12) was obtained after being dried under vacuum at room temperature overnight.

### Determination of volume ratio of the selective non-solvent to separate alkynyl-(PSt-Br)$_2$ from dendrimer-like PSt

Under 30 °C, alkynyl-(PSt-Br)$_2$ ($M_{\mathrm{n}}$ = 6400 g·mol$^{-1}$, 100 mg) and ether (20.0 mL) were added into a 100-mL round-bottom flask with a magnetic stirring bar, resulting in a clear solution. Then, the *n*-hexane was added slowly (0.5 mL/min) into the flask through a micro-injector. On the moment when *n*-hexane (25.2 mL) had been added, the solution became a little cloudy. Thus, the mixed solvent of *n*-hexane and ether ($V_{n\text{-hexane}}$ : $V_{\text{ether}}$ = 1.25) was chosen to remove excess alkynyl-(PSt-Br)$_2$ in the crude product at 30 °C.

### Preparation of G$_2$-G$_5$ dendrimer-like PSt

Each generation growth of dendrime-like PSt was carried out by clicking the central alkynyl group of excess alkynyl-(PSt-Br)$_2$ onto the end azido groups of pre-existing dendrime-like PSt. Take the two-generation dendrime-like PSt (G$_2$) as an example. G$_1$-N$_3$ ($M_{\mathrm{n}}$ = 3000 g·mol$^{-1}$, 0.30 g, 0.1 mmol), alkynyl-(PSt-Br)$_2$ ($M_{\mathrm{n}}$ = 6400 g·mol$^{-1}$, 2.88 g, 0.45 mmol), PMDETA (51.9 mg, 0.3 mmol) and THF (10 mL) were added into a 20-mL polymerization vial with a magnetic stirring bar. After mixing thoroughly, the vial was degassed by three freeze-vacuum-thaw cycles and sealed under vacuum, then added with CuBr (43.2 mg, 0.3 mmol) and sealed under vacuum. After the click reaction stood at 40 ºC for 48 h, the mixture was diluted with THF and passed through a neutral alumina column. The crude product was obtained by precipitation from methanol and dried overnight at room temperature. Then the two-generation dendrime-like PSt with bromo terminal groups ($G_2$-Br) was obtained after removing excess alkynyl-(PSt-Br)$_2$ by precipitation from the selective non-solvent of *n*-hexane and ether ($V_{\text{n-hexane}} : V_{\text{ether}} = 1.25$) twice at 30 °C.

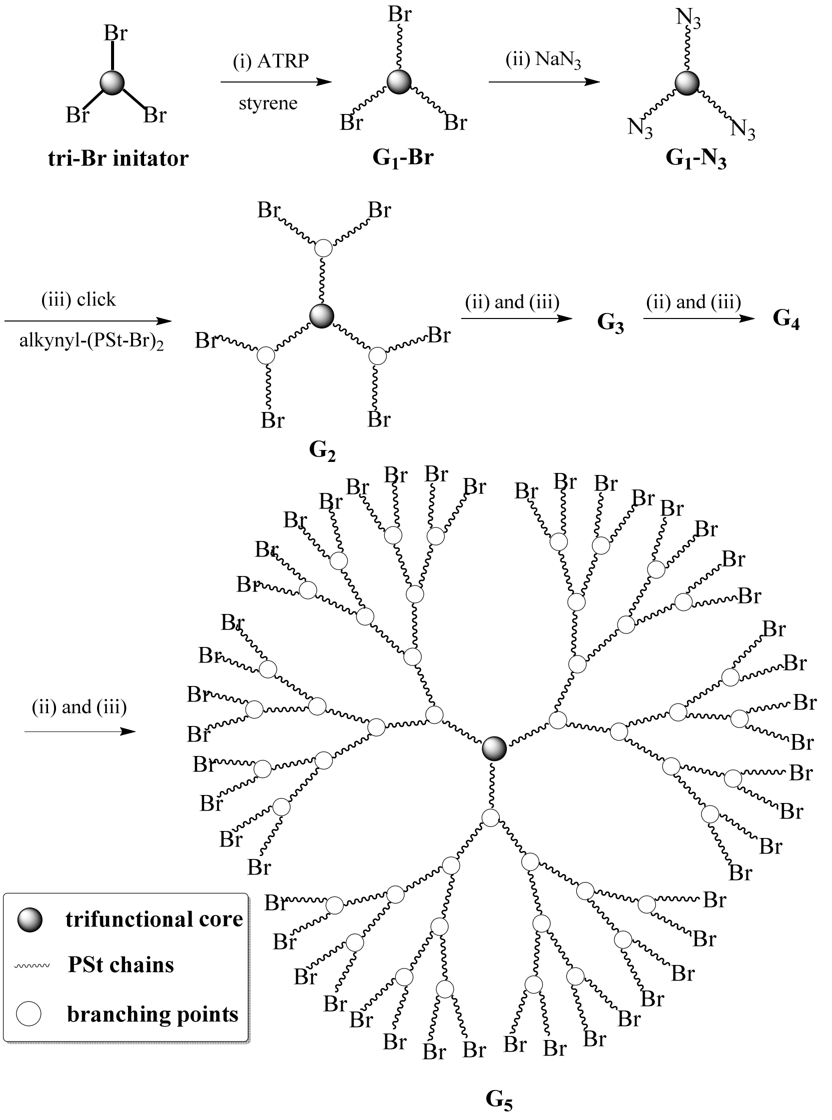
**Characterization**

Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a Bruker DRX-300 NMR (300 MHz) instrument in $CDCl_3$ at room temperature with tetramethylsilane as internal standard. The apparent number- and weight-averaged molecular weight ($M_n$ and $M_w$) were determined at 25 °C on gel permeation chromatography (GPC) instrument (Waters 1515) equipped with three Waters Styragel columns (HR2, HR4, and HR6) and a Wyatt WREX-02 refractive index (RI) detector using a conventional universal calibration with linear PSt standards. The absolute weight-average molar mass ($M_{\text{w, MALLS}}$) was determined simultaneously from a multiangle laser light scattering (MALLS) detector (Wyatt DAWNEOS). THF was used as eluent at a flow rate of 1.0 mL/min (THF is a good solvent for the dendrimer-like PSt used in our experiments). The MALLS detector uses a GaAs laser

(685 nm and 30 mW) and has 18 diodes placed at different angles, ranging from 22.5° to 147.0°. The data was analyzed using ASTRA for Windows software (Ver.4.90.07, Wyatt). Differential scanning calorimetry (DSC) diagrams were recorded on TA Q2000 DSC (TA Instruments) under a nitrogen atmosphere. Approximately 5 mg of each sample was used in the measurement. First, the sample was heated from room temperature to 200 °C, held at this temperature for 5 min to diminish thermal history, and then cooled to −10 °C at a rate of 10 °C/min. Afterwards, the sample was heated from −10 to 200 °C at a heating rate of 10 °C/min. To determine the glass transition temperatures ($T_g$), the DSC data were analyzed using the Universal Analysis 2000 Software (TA Instruments). Intrinsic viscosity was measured by Ubbelohde viscometer (inner diameter = 0.55mm) at 30.00 °C with toluene as the solvent.

## RESULT AND DISCUSSION

Dendrimer-like PSt with long subchains and well-defined structure were prepared by arm-first divergent method combing with ATRP and click chemistry. As shown in Scheme 1, the overall procedure includes mainly two iterative reaction steps: (1) transformation of the terminal bromo group of dendrime-like PSt into azido group; (2) clicking alkynyl-$(PSt\text{-}Br)_2$ onto azido-capped dendrimer-like PSt ($G_g$-$N_3$).



**Scheme 1** Arm-first divergent synthesis of dendrimer-like PSt from tri-functional core

**Preparation of tri-functional initiator and $G_1$-$N_3$.**

$^1$H NMR spectrum of the tri-functional initiator TBIBPE is shown in Figure 1A, where the characteristic signals of C(Ar)-C$H_3$ (3H, 2.18 ppm), C(Br)-C$H_3$ (18H, 2.06 ppm) and Ar-*H* (12H, 7.02~7.36 ppm) indicate the successful synthesis of the initiator. Three-arm PSt having three bromo terminal groups [$\mu$-(PSt-Br)$_3$, $G_1$-Br] was synthesized by ATRP of St with TBIBPE as the initiator. High [monomer]/[initiator] ratio and lower monomer conversion were chosen to minimize the extent of irreversible termination between PSt arms and ensure high functionality of bromo end-group. Figure 1B shows GPC diagrams of $\mu$-(PSt-Br)$_3$ obtained with bpy and PMDETA as the ligand, which suggests that bpy had the better ability to control the molecular weight distribution.

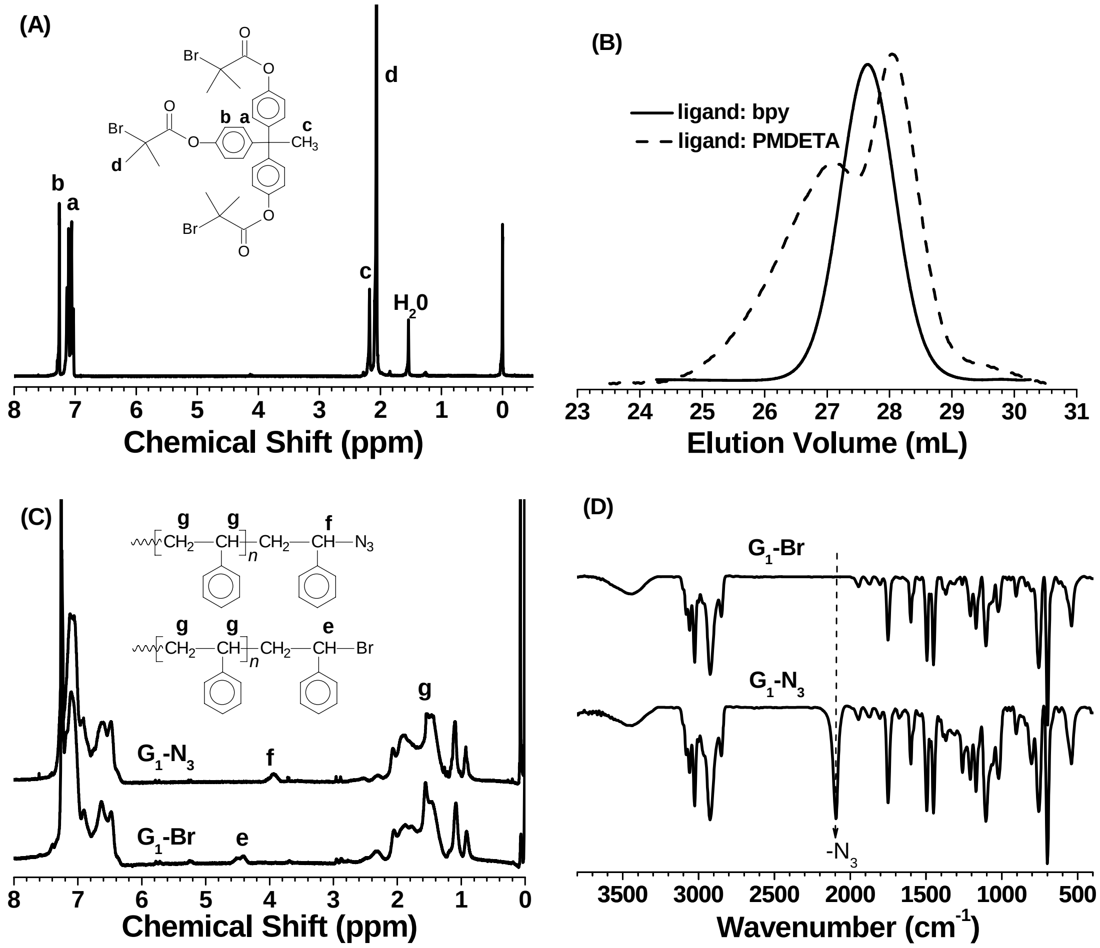


**Figure 1.** (A) $^1$H NMR spectrum of TBIBPE; (B) GPC diagrams of $\mu$-(PSt-Br)$_3$ from bpy and PMDETA; (C) $^1$H NMR spectra of $\mu$-PSt$_3$ before and after end-group conversion; (D) FTIR spectra of $\mu$-PSt$_3$ before and after end-group conversion.

After that, the bromo end groups were transformed into azido groups by nucleophilic substitution with excess sodium azide, resulting in triazido-terminated $\mu$-(PSt-N$_3$)$_3$ (G$_1$-N$_3$). As shown in $^1$H NMR spectrum of G$_1$-N$_3$ (Figure 1C), the disappearance of signal of C*H*-Br proton at 4.46 ppm and the appearance of signal of C*H*-N$_3$ proton at 3.97 ppm confirms the transformation of end group, while all the characteristic signals of PSt are distinguished. FTIR spectra (Figure 1D) of three-arm PSt offer the same results, such as the existence of azido stretching absorbance at 2096 $cm^{-1}$ and phenyl out-of-plane vibration absorbance at 696 $cm^{-1}$. The apparent number-averaged molecular weight from GPC measurement ($M_{n,GPC}$) is 3000 for $G_1$-Br with low polydispersity index of 1.08. The absolute number-averaged molecular weight from NMR measurement is calculated to be 3400 based on the integral ratio of C*H*-Br proton at 4.46 ppm ($H_e$) and the protons in the range of 0.8-2.5 ppm, including the methylene and methine protons from PSt backbone ($H_g$) and the methyl protons from TBIBPE ($H_c$ and $H_d$). This value is fairly close to $M_{w,MALLS}$ (seen in Table 1), suggesting $\mu$-(PSt-Br)$_3$ ($G_1$-$N_3$) does have three arms (chain ends).

## Generation growth of dendrimer-like PSt from $G_2$ to $G_5$

The synthetic outline for generation growth of dendrimer-like PSt from $G_2$ to $G_5$ is illustrated in Scheme 1. To keep the structural homogeneity, only one seesaw macromonomers of alkynyl-(PSt-Br)$_2$ with $M_n$ = 6400 was used for the whole generation growth. Different analytical techniques were used to confirm each growth and the variation of end group. Precipitation in selective non-solvent was used to separate dendrimer-like PSt from excess alkynyl-(PSt-Br)$_2$ and the recovered alkynyl-(PSt-Br)$_2$ was re-cycled in the next generation growth. Take the synthesis of $G_3$-Br from $G_2$-Br as an example.

Firstly, the bromo end groups of $G_2$-Br were transformed into azido groups by nucleophilic substitution with excess sodium azide to obtain $G_2$-$N_3$. Figure 2A shows their $^1$H NMR spectra, focused on the methine protons next to the bromo groups at

4.46 ppm and the azido groups at 3.97 ppm. The disappearance of signals at 4.46 ppm and the appearance of signals at 3.97 ppm indicates that the transformation reaction should be completed.

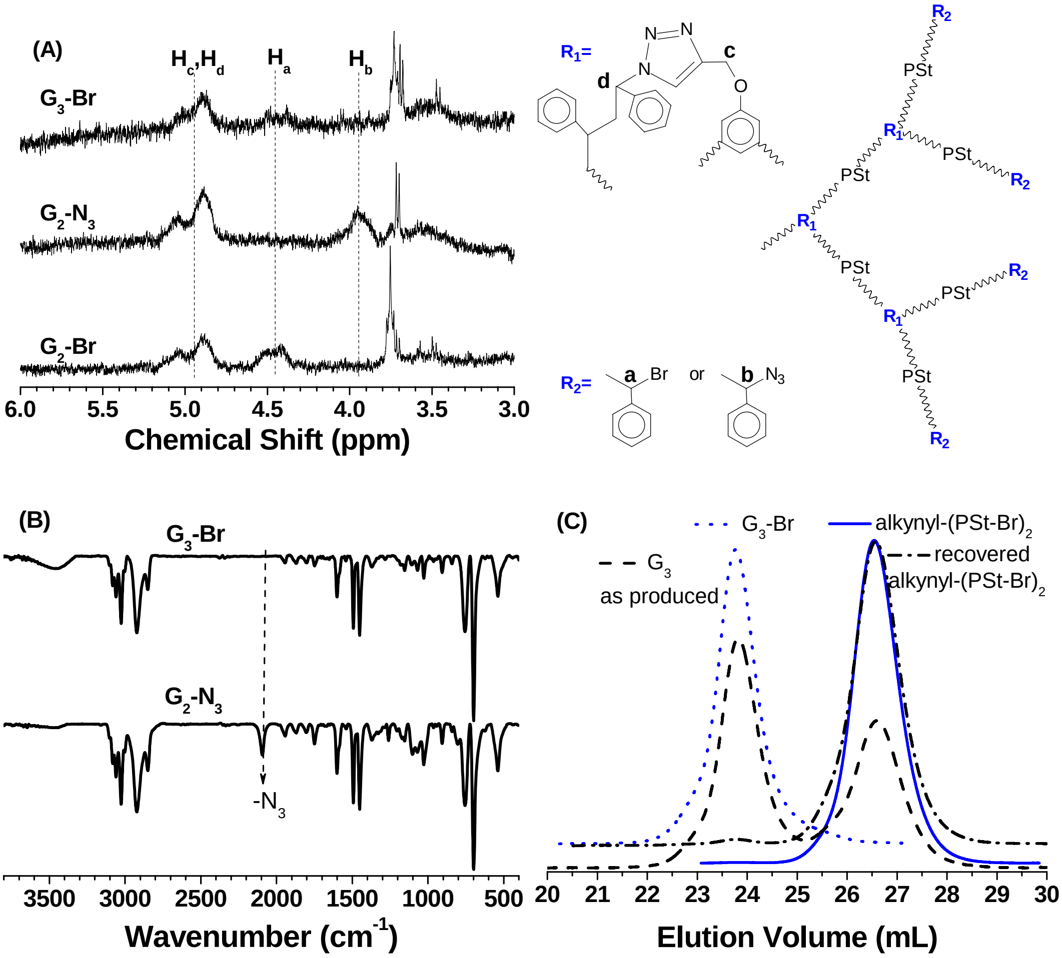


**Figure 2.** (A) $^1$H NMR spectra for $G_2$-Br, $G_2$-$N_3$ and $G_3$-Br; (B) FTIR spectra of $G_2$-$N_3$ and $G_3$-Br; (C) GPC profiles to monitoring the generation growth and purification of reaction mixture.

Secondly, seesaw macromonomer of alkynyl-$(PSt\text{-}Br)_2$ was linked onto $G_2$-$N_3$ through efficient alkynyl-azido click chemistry. Excess macromonomers were used both to ensure the linkage of each azido group in the pre-existing generation and avoid irreversible coupling reaction between dendrimers.[32] As shown in Figure 2B, FTIR spectra of purified three-generation dendrime-like PSt with bromo end-groups ($G_3$-Br) displays a disappearance of azido stretching absorbance at 2096 $cm^{-1}$, indicating that the high efficiency of the click reaction between $G_2$-$N_3$ and seesaw-type PSt macromonomers.

$^1$H NMR analysis also offers the number of chain ends for each dendrime-like PSt molecule ($N_{\mathrm{end}}$), by comparing the integral height of the protons in the range of 4.7~5.2 ppm ($I_{4.7\sim5.2}$) and 0.8~2.5 ppm ($I_{0.8\sim2.5}$). The protons of 0.8~2.5 ppm are the methylene and methine protons from PSt repeating units and the methyl protons from TBIBPE, as indicated in Figure 1A and 1C. Since more and more PSt subchains would be introduced into dendrime-like polymers with the generation, the attribution of methyl protons from TBIBPE to $I_{0.8\sim2.5}$ could be neglected. Thus, $I_{0.8\sim2.5}$ is proportional to the total number of St repeating units in one dendrime-like macromolecule ($N_{\mathrm{St}}$). Considering the theoretical number of terminal arms for each generation ($N_{\mathrm{theor}}$) and their chain length (number of St repeating units), $N_{\mathrm{St}}$ is expressed as Eq. 1.

$$N_{\mathrm{theor}} = 3\times 2^{g-1};\quad N_{\mathrm{St}} = \frac{M_{\mathrm{w,NMR,G_1}}}{104} + \sum_{g=2}^{5} 3\times 2^{g-1} \times \frac{M_{\mathrm{w,NMR,macromonomer}}}{104\times 2} \qquad \text{Eq.1}$$

where $g$ is the generation number, and $M_{\mathrm{w,NMR,G1}}$ and $M_{\mathrm{w,NMR,macromonomer}}$ are the absolute molecular weight of $G_1$ and macromonomer, respectively. Keep in mind, the values of absolute molecular weight measured by $^1$H NMR analysis are fairly close to those from MALLS-GPC measurement for G1 and macromoner, since two polymers have relatively low molecular weight. According to Eq. 1, the quotient of $N_{\mathrm{theor}}/N_{\mathrm{St}}$ decreases sharply with the generation, suggesting that the methine proton next to bromo end-group ($H_a$) would be the improper choice for NMR analysis. Figure 2A shows the obvious deterioration of $H_a$ from $G_2$ to $G_3$.

The protons of 4.7~5.2 ppm are the methylene protons between triazole ring and oxygen atom ($H_c$), and the methine proton of St unit neighboring triazole ring ($H_d$) (seen in Figure 2). Their amount ratio of $N_c/N_d$ keeps 2 for all dendrime-like PSt since those two kinds of protons are simultaneously produced upon once alkynyl-azido click reaction. $N_c$ for the different generation of dendrime-like PSt is given as Eq. 2.

$$N_c = 2N_d = 0(g=1)\,;\quad N_c = 2N_d = \sum_{g=2}^{5} 3\times 2^{g-2} \qquad \text{Eq.2}$$

According to Eq. 2, the quotient of $N_c/N_{St}$ ($g$ = 2~5) would hardly decrease with the generation (seen in Figure 2A), offering the satisfactory reliability to NMR analysis of chain end with $H_c$ and $H_d$ protons. Assuming no occurrence of the coupling between two bromo end-groups, the chain end number per dendrime-like molecule by NMR analysis ($N_{end}$) is expressed as Eq. 3.

$$N_{end} = 2\times\frac{I_{4.97}/(N_c+N_d)}{I_{0.8\sim2.5}/(3\times N_{St})}\times\frac{3\times2^{g-2}}{\sum_{g=2}^{5}3\times2^{g-2}} \qquad \text{Eq. 3}$$

Combining Eq. 1~3, the values of $N_{end}$ could be obtained based on NMR analysis. The results and $N_{theor}$ are summarized in Table 1. The values of $N_{end}$ and $N_{theor}$ for each dendrime-like PSt sample ($G_1$~$G_5$) might be considered equal within experimental deviation. Thus, the present arm-first divergent synthesis is feasible to obtain dendrime-like PSt with the generation number up to five. However, the existence of excess alkynyl-$(PSt\text{-}Br)_2$ should be one key problem to overcome.

**Table 1.** Synthesis and characterization of dendrimer-like star Polystyrenes.

| samples | $M_{\text{theo.}}$ [a] | $M_{\text{n,GPC}}$ [b] | $M_{\text{w,GPC}}$ [b] | PDI[b] | $M_{\text{w,MALLS}}$ [c] | number of terminal arms | | | $[\eta]$ [f] | $T_g$ [g] |
|---|---|---|---|---|---|---|---|---|---|---|
| | (×10$^3$ g·mol$^{-1}$) | (×10$^3$ g·mol$^{-1}$) | (×10$^3$ g·mol$^{-1}$) | | (×10$^3$ g·mol$^{-1}$) | *Thero* | $N_{\text{end}}$ [d] | $N_{\text{arm.}}$ [e] | (mL·g$^{-1}$) | (°C) [e] |
| $G_1$ | 3.4 | 3.0 | 3.2 | 1.08 | 3.3 | 3 | 3.0 | 3.0 | 4.74 | 83.82 |
| $G_2$ | 25.6 | 22 | 24.2 | 1.10 | 25 | 6 | 6.0 | 5.9 | 9.70 | 83.97 |
| $G_3$ | 70.0 | 45 | 53.1 | 1.18 | 61 | 12 | 11.8 | 9.7 | 19.57 | 101.70 |
| $G_4$ | 158.8 | 88 | 102.1 | 1.16 | 130 | 24 | 22.7 | 18.7 | 21.38 | 104.04 |
| $G_5$ | 336.4 | 150 | 186 | 1.24 | 265 | 48 | 47.5 | 36.5 | 18.15 | 104.51 |

a: $M_{\text{theo}}$ was calculated from the total number of St repeating units

b: $M_{\text{n,GPC}}$, $M_{\text{w,GPC}}$ and PDI were obtained from GPC with refractive index detector.

c: $M_{\text{w,MALLS}}$ was determined from GPC with multiangle laser light scattering (MALLS) detector.

d: $N_{\text{end}}$ was calculated from NMR analysis based on Eq. 1~3.

e: $N_{\text{arm}} = (M_{\text{w,MALLS,i}} - M_{\text{w,MALLS,}i\text{-1}})/(M_{\text{w,MALLS,macromonomer}}/2)$, $M_{\text{w,MALLS, macromonomer,}}$ is 7400 g·mol$^{-1}$.

f: Intrinsic viscosity was measured by Ubbelohde viscometer at 30.00 °C.

g: Glass transition temperature was measured at a scanning rate of 10 °C·min$^{-1}$ in nitrogen and obtained from the second heating run.

Methanol is not the proper non-solvent to purify the obtained crude product by precipitation since both seesaw-type PSt macromonomers and dendrime-like PSt samples are not soluble in methanol. In our previous work, washing with ether was used to remove remaining seesaw-type PSt macromonomers with low molecular weight from hyberbranched PSt with high molecular weight.[30] Considering the time-consuming shortage of precipitation fraction, an alternative precipitation in the selective non-solvent was taken. The mixture of *n*-hexane and ether at volume ratio of 1.25 is the non-solvent for PSt with high molecular weight including $G_2$, but the good solvent for PSt with low molecular weight such as the present alkynyl-$(PSt\text{-}Br)_2$ ($M_n$ = 6400). Therefore, the excess seesaw macromonomers could be easily removed by the simple precipitation, which was monitored by GPC measurement as shown in Figure 2C. The GPC profile of the crude product of $G_3$-Br exhibits two distinct peaks. One has the same eluent volume as seesaw macromonomer and the other has a lower eluent volume. After the precipitation in the selective non-solvent, the obtained precipitate has similar GPC profile and the same eluent volume compared with the crude product, suggesting that it should be dendrime-like PSt with higher generation. This GPC profile is symmetrical and narrow, demonstrating the perfect generation growth. As well, the polymer lefts in the precipitation solution were recovered by evaporating the solvent and its GPC profile is almost the same as that of original alkynyl-$(PSt\text{-}Br)_2$, except that a tiny signal can be observed at the location of the new-coming dendrime-like PSt ($G_3$-Br). Therefore, the left polymers are mostly alkynyl-$(PSt\text{-}Br)_2$ macromonomers and the trace $G_3$-Br could be removed completely by twice precipitation in the selective non-solvent. $^1$H NMR spectrum of the purified recovered seesaw macromonomers also confirms that they are the same as the original ones, so that we can recycle them in the synthesis of next generation.

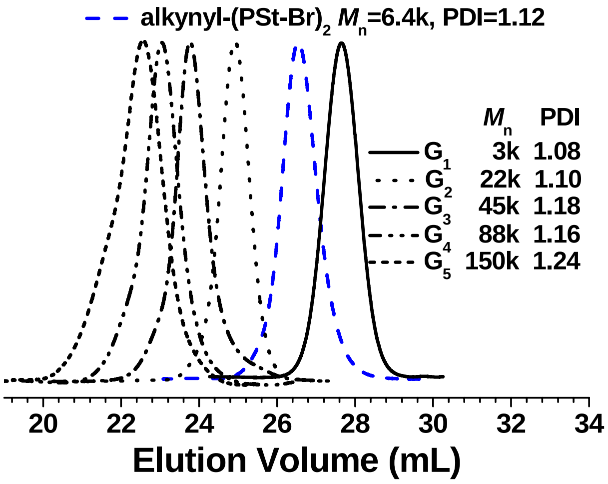


**Figure 3.** GPC profiles of dendrimer-like polystyrenes of different generations

The same synthesis procedure was repeated to produce other dendrimer-like PSts with higher generation number and monitored by different analytical techniques. Figure 3 demonstrates GPC profiles of dendrimer-like PSt from $G_1$ to $G_5$ after the excess seesaw-type macromonomers were completely removed by the precipitation in the non-solvent mixture of *n*-hexane and ether. It can be seen that monomodal distribution of apparent molecular weight could be observed for all the generation and apparent molecular weight increases with the generation growth as expected. Most GPC traces are unimodal and symmetrical but that of $G_5$ is asymmetric with a shoulder peak at the larger molecular weight side, which may be attributed to intermolecular coupling through the bromo end-groups of $G_5$ during the click reaction.[33]

To achieve the absolute molecular weight of different dendrime-like PSt ($G_1$~$G_5$), GPC measurement with MALLS detector was also performed and the obtained weight-averaged molecular weights are summarized in Table 1. $M_{\mathrm{w,MALLS}}$ of different dendrime-like PSt also increases with the generation number while the variation between the values of $M_{\mathrm{w,MALLS}}$ and $M_{\mathrm{w,GPC}}$ for each generation become larger and larger with the generation number. This observation is consistent with the fact that branched polymer has lower spatial size compared with its linear counterpart and the decrease magnitude of polymer size rises with more and more branching points introduced into higher generation.

Also, the arm number of each generation ($N_{\mathrm{arm}}$) could be estimated from the $M_{\mathrm{w,MALLS}}$ difference between the neighboring generations and the $M_{\mathrm{w,MALLS}}$ of linear alkynyl-(PSt-Br)$_2$. The equation is given as Eq. 4 and the results are also summarized in Table 1.

$$N_{\mathrm{arm}} = \frac{M_{\mathrm{w,MALLS},g} - M_{\mathrm{w,MALLS},g\text{-}1}}{M_{\mathrm{w,MALLS,macromonomer}} / 2} \quad (g = 2, 3, 4, 5) \qquad \text{Eq. 4}$$

where $M_{\mathrm{w,MALLS},g}$ is the $M_{\mathrm{w,MALLS}}$ value of dendrime-like PSt with $g$-generation and $M_{\mathrm{w,MALLS,macromonomer}}$ is that of alkynyl-(PSt-Br)$_2$. The dependence of $N_{\mathrm{arm}}$ on the generation number ($g$) should be $3 \times 2^{g\text{-}1}$, equal to $N_{\mathrm{theor}}$. The in-consistence of experimental $N_{\mathrm{arm}}$ and theoretical $N_{\mathrm{theor}}$ may be caused by the fact that the measured $M_{\mathrm{w,MALLS}}$ would not really reflect the molecular weight of dendrime-like PSt. As for GPC-MALLS measurement, $M_{\mathrm{w,MALLS}}$ is obtained based on the principle of static light scattering (SLS) and the primary requirement is of $q{\cdot}C < 1$, where $q$ and $C$ is the scattering factor and the concentration. However, the increasing size of dendrime-like PSt might result in the in-appropriation of SLS requirement.

## Thermal properties of dendrimer-like PSt with different generations

The thermal properties of dendrimer-like polymers are usually different from their linear analogues due to the branching effect.[34] In this study, the glass transition temperature ($T_g$) of the obtained dendrimer-like polystyrenes were measured by DSC at a scanning rate of 10 °C·min$^{-1}$, as stated in Figure 4A. The $T_g$ value of different dendrimer-like PSt increases with the generation growth, indicating the interplay of chain ends and overall molecular weight.

Although many literatures demonstrate that the glass transition of dendritic polymers is related to core chemistry, end-group chemistry and generation numder,[35, 36] there exists the contradiction about the dependence of $T_g$ on the reciprocal of molecular weight (1/$M$). Several studies disclosed that the conventional Flory-Fox equation (Eq. 5) does not fully represent the glass transition behavior of dendritic polymers because of the significant number of end-groups at very high generations,[37] while other groups confirmed the pertinence of Eq. 5.[38]

For linear polymers, the chain-end free volume theory indicates the dependence of glass transition temperature on molecular weight by Eq. 5, where $T_{g,\infty}$ is the value of $T_g$ extrapolated to infinite molecular weight, 2 is the number of chain ends, $\rho$ is the density, $N$ is Avogadro's number, $\theta$ is the free volume per chain end, and $\alpha$ is the expansion coefficient of free volume. Eq. 5 is often simplified to Eq. 6**,** where $K$ is a constant. This allows $T_{g,\infty}$ and $K$ to be obtained from a plot of $T_g$ *vs* 1/$M$.

$$T_g = T_{g,\infty} - \frac{2\rho N\theta}{\alpha M} \qquad \text{Eq. 5}$$

$$T_g = T_{g,\infty} - K\frac{1}{M} \qquad \text{Eq. 6}$$

However, $K$ is not constant for dendritic polymers since they have an ever-increasing number of chain ends. Thus, Wooley et al.[37] suggested a modified Flory-Fox equation (Eq. 7), where $n_{\mathrm{e}}$ is the number of end groups.

$$T_{\mathrm{g}} = T_{\mathrm{g},\infty} - \frac{\rho N\theta}{\alpha} \times \frac{n_{\mathrm{e}}}{M} \qquad \text{Eq. 7}$$

As the parameters ($\rho$, $\theta$ and $\alpha$) for one specific polymer are constant, this equation may be simplified to

$$T_{\mathrm{g}} = T_{\mathrm{g},\infty} - K'\frac{n_{\mathrm{e}}}{M} \qquad \text{Eq. 8}$$

Since the value of $n_{\mathrm{e}}/M$ for dendritic polymers does not approach zero at infinite molecular weight, Eq. 8 was further modified to Eq. 9,[34,37] from which $T_{\mathrm{g}\infty}$ could be obtained as the y-intercept from a plot of $T_{\mathrm{g}}$ vs $[n_{\mathrm{e}}/M - (n_{\mathrm{e}}/M)_{\infty}]$.

$$T_{\mathrm{g}} = T_{\mathrm{g},\infty} - K'\left[\frac{n_{\mathrm{e}}}{M} - \left(\frac{n_{\mathrm{e}}}{M}\right)_{\infty}\right] \qquad \text{Eq. 9}$$

The value for $(n_{\mathrm{e}}/M)_{\infty}$ was derived mathematically to be $1.35 \times 10^{-4}$ on based Eq. 10, where $M_{\mathrm{w,MALLS,G1}}$ is 3300 g·mol$^{-1}$ for tri-arm PSt ($G_1$,) and $M_{\mathrm{w,MALLS,\ macromonomer,}}$ is 7400 g·mol$^{-1}$ for alkynyl-(PSt-Br)$_2$ determined from GPC measurement with MALLS detector.

$$\left(\frac{n_{\mathrm{e}}}{M}\right)_{\infty} = \lim_{n\to\infty}\frac{n_{\mathrm{e,theo,G_n}}}{M_{\mathrm{theo,G_n}}} = \lim_{g\to\infty}\frac{3\times 2^{g-1}}{M_{\mathrm{w,MALLS,G_1}} + 3\times(2^{g-1}-1)M_{\mathrm{w,MALLS,macromonomer}}} \qquad \text{Eq. 10}$$

An overlay plots of $T_{\mathrm{g}}$ *vs* $[n_{\mathrm{e}}/M - (n_{\mathrm{e}}/M)_{\infty}]$ for dendrimer-like PSt from $G_2$ to $G_5$ is shown in Figure 5B. Linear regression of $T_{\mathrm{g}}$ vs $[n_{\mathrm{e}}/M - (n_{\mathrm{e}}/M)_{\infty}]$ and application of Eq. 9 give $T_{\mathrm{g},\infty}$ and $K'$ values of 105.87 °C and $2.15\times10^{5}$, respectively, with a correlation coefficient of 0.99. This result demonstrates that the glass transition behavior of dendrime-like polystyrenes with long and uniform sunchains would also follow modified Flory-Fox equation considering the generation progression. However, $T_g$ of $G_1$ in the present case does not fall in the fitting lines. The probable reason might be the difference of terminal-arm length. Although terminal-arms of $G_1$ to $G_5$ are all PS segments, every terminal-arm of $G_1$ has only about 9 styrene units, shorter than that of $G_2$ to $G_5$ having 32 styrene units. The difference in length makes the terminal-arms of $G_2$ to $G_5$ more flexible, which may result the difference in $\theta$ of Eq. 5. This is one probable reason about why $T_g$ of $G_1$ does not fall in the fitting lines.

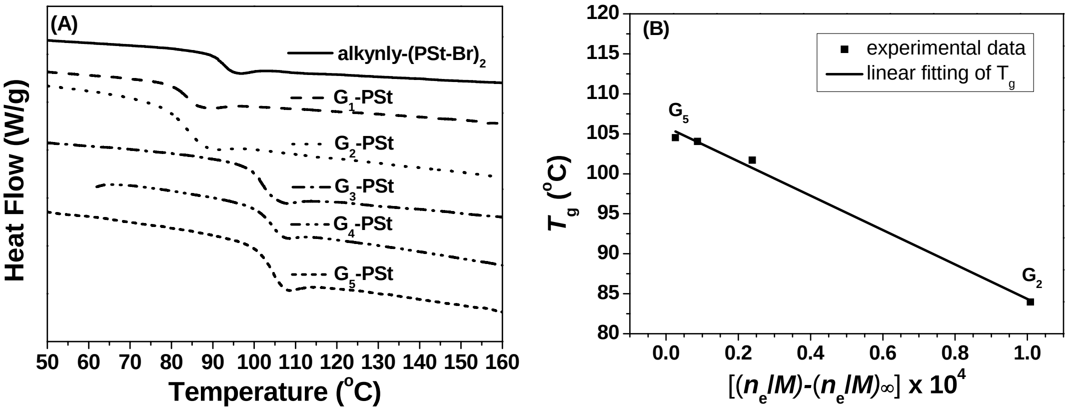


**Figure 4.** (A) DSC heat flow curves for linear alkynyl-(PSt-Br)$_2$ macromonomer and dendrimer-like polystyrenes in the second heating run under the heating rate of 10 °C/min. (B) Modified Flory-Fox analysis of $T_g$ vs $[(n_e/M)-(n_e/M)_\infty]$ for dendrimer-like PSt.

## Viscosity properties of different dendrimer-like PSt

A unique property of dendrimers and dendrimer-like polymers is that their intrinsic viscosities do not monotonically depend on overall molecular weight. For polyether dendrimes based on 3,5-dihydroxybenzyl alcohol, Mourey et. al. have observed that intrinsic viscosity $[\eta]$ passed through a characteristic maximum with generation number while hydrodynamic radius ($R_h$) increased approximately linearly with dendrimer generation.[3] For dendrime-like polymers with long subchains, the reports from different groups also have disclosed that the dependence of intrinsic viscosity on molecular weight does not follow Mark-Houwink-Sakurada equation ($[\eta] = KM^{\alpha}$).[6, 16, 17, 39]

Figure 5 shows the variation of $[\eta]$, measured by Ubbelohde viscometer, along with the generation and $\log M_{\mathrm{w,MALLS}}$. Different from the linear polymers, with the increase of the generation number ($g$) and molecular weight ($M_{\mathrm{w,MALLS}}$), $[\eta]$ increases to a maximum corresponding to $G_4$, then decrease. This trend can be explained well by Einstein's equation (Eq. 11) for hard spheres, where dendrime-like polymers are considered as hard spheres. In this equation, $V_{\mathrm{h}}$ is hydrodynamic volume, $N_{\mathrm{A}}$ is Avogadro's constant, $M_{\mathrm{w}}$ is the molecular weight and $M_{\mathrm{w,MALLS}}$ was used for the calculation.

$$[\eta] = \frac{2.5 N_{\mathrm{A}} V_{\mathrm{h}}}{M_{\mathrm{w}}} = \frac{10\pi N_{\mathrm{A}} R_{\mathrm{h}}^{3}}{3M_{\mathrm{w}}} \qquad \text{Eq. 11}$$

Unlike linear polymer, this bell-shaped curves of $[\eta]$-$g$ and $[\eta]$-$\log M_{\mathrm{w,MALLS}}$ for the present dendrimer-like PSts reflects the different dependence of hydrodynamic volumes and molar masses with the number of generations ($g$). Molar masses in dendrimer-like PSts increase exponentially with $g$ according to $2^{g\text{-}1}$ and their hydrodynamic volume grows with $g^3$; $[\eta]$ varying proportionally to $g^3/2^{g\text{-}1}$, it passes therefore through a maximum with increasing $g$. By the derivative of $[\eta]\sim g^3/2^{g\text{-}1}$, the value of $g$ ($g_{\max}$) at which $[\eta]$ reaches its maximum is 4.33, just between the generation number of $G_4$ and $G_5$.

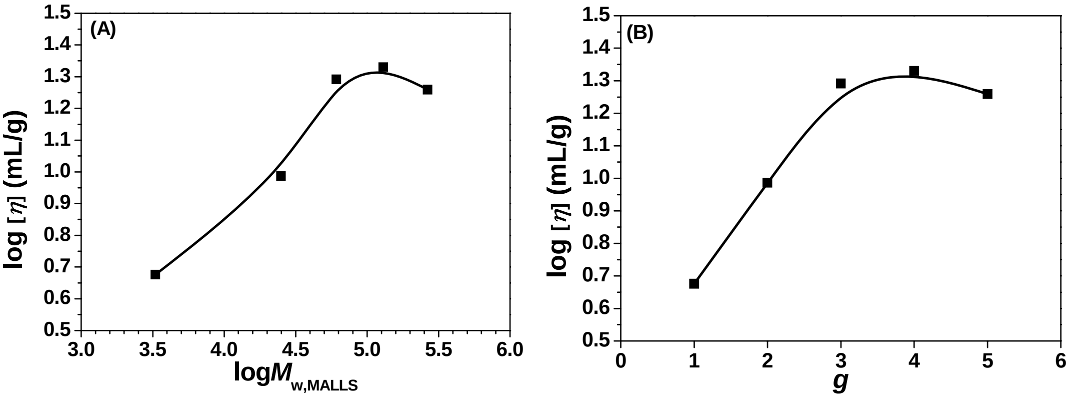


**Figure 5.** Evolution of log[$\eta$] against log$M_{\mathrm{w,MALLS}}$ (A) and generation number (B) for dendrimer-like polystyrenes.

The branching factor ($g'$), defined as the ratio of [$\eta$] of dendrime-like PSt to that of linear PSt with the same molecular weight ([$\eta$]$_{\mathrm{linear}}$) is an important factor to estimate the macromolecule extend in solution. $G_1$, the tri-arm polystyrene with only 9 styrene units for each arm, has the value of $g'$ larger than 1, suggesting that $G_1$ have larger molecular size than linear PSt having 27 styrene units. It is reasonable that longer linear polymeric segment exhibits better flexible. The $g'$ values of other dendrime-like PSts are lower than 1 and decrease with the generation number to 0.21 at $G_5$. With the generation growth of dendrime-like PSt, more and more terminal arms are introduced. The crowded outer segments might restrict the adjustment of inner segments and force them to adopt contracted conformation. The densely packed chain segments reduce their size and chain interaction, resulting in the decrease in intrinsic viscosity.

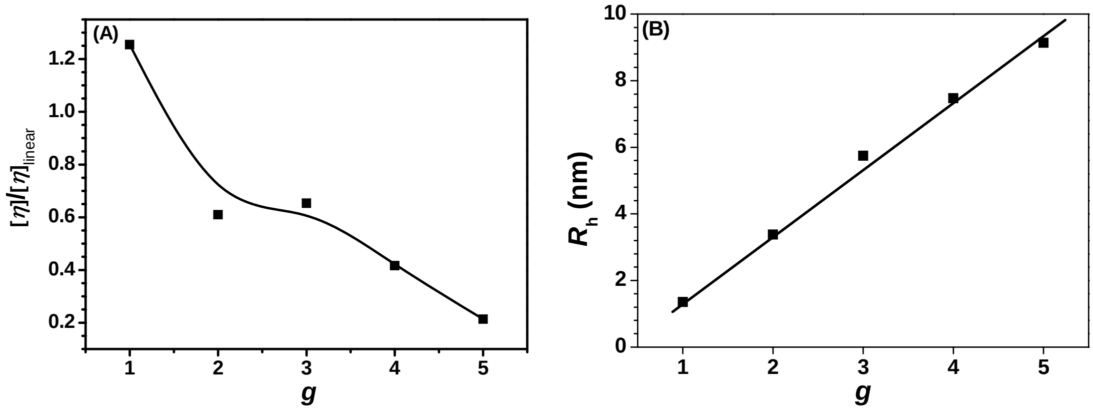


**Figure 6.** (A) Dependence of the branching factor on generation number of for dendrimer-like PSt with long subchains, (B) Dependence of the hydrodynamic radius ($R_\mathrm{h}$) on generation number of for dendrimer-like PSt with long subchains.

The molecular size of dendrime-like polymers can also be evaluated from another form of Einstein's equation (Eq. 12), using $[\eta]$ and $M_w$ determined experimentally.

$$R_h = (\frac{3M_w[\eta]}{10\pi N_a})^{1/3} \qquad \text{Eq. 12}$$

As shown in Figure 6, $R_\mathrm{h}$ increases nearly linearly with the generation number for dendrimer-like PSt, with a correlation coefficient of 0.993, indicating that $V_\mathrm{h}$ grows in $g^3$ as the regular dendrimers from small molecule monomers.

## CONCLUSION

An efficient and economical approach has been developed to synthesize well-defined high-generation dendrimer-like polystyrenes in an "arm first" divergent way. ATRP was used to obtain macromonomer of alkynyl-(PSt-Br)$_2$ with narrow molecular weight distribution and high functionality of reactive groups, and alkynyl-azido click chemistry was used to anchor alkynyl-(PSt-Br)$_2$ onto the pre-exsting dendrime-like PSt with azido end-groups. The excess alkynyl-(PSt-Br)$_2$

left in the mixtures of click reaction was removed by a convenient precipitation in the selective non-solvent and recycled in the following generation growth. All of the polymers obtained possessed the observed molecular weights in good agreement with those calculated ones and extremely narrow molecular weight distribution. Glass transition temperatures of dendrime-like PSt ($G_2$~$G_5$) obeyed the modified Flory-Fox equation. The investigation of viscosity property indicated that the long subchains of dendrime-like PSt should adopt more and more compact conformation with the increase of generation number. We believe that this efficient and economical process can be extended to the synthesis of other dendrimer-like polymers and copolymers.

## ACKNOWLEDGMENTS

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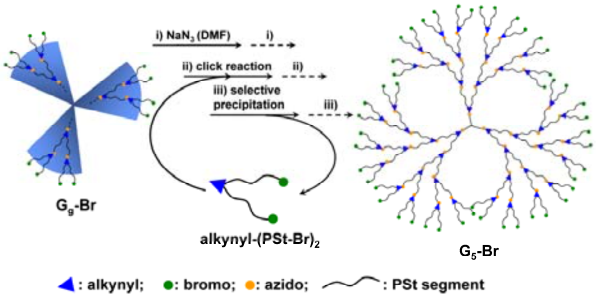
# Graphic Abstarct

## Efficient and Economical Synthesis of Dendrimer-Like Polystyrene with Long Subchains through Arm-first Divergent Strategy

Xue-Song Ge, Chen He, Wei-Dong He,* Sheng-Qi Chen



Arm-first divergent approach combining with selective precipitation has been developed to synthesize dendrime-like polystyrene efficiently and economically.