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Amphiphilic Dendrimer-like Copolymers with High Chain Density by Living Anionic Polymerization

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Abstract We report here a method for the preparation of amphiphilic dendrimer-like copolymers with dendritic polystyrene (PS) core and protonated poly(2-vinyl pyridine) (P2VP) or poly(methacrylic acid) (PMAA) shell. The method employed the efficient coupling reaction of anionic living polymer chains and chlorosilane. The synthesis started from a functionalized 3rd generation dendritic polystyrene, G3PS-g-SiCl, used as the precursor. The dendrimer-like copolymer of styrene and 2-vinyl pyridine, G3PS-g-P2VP, was synthesized by direct coupling of living P2VPLi to the precursor. The dendrimer-like copolymer of styrene and *tert*-butyl methacrylate, G3PS-g-PtBMA, was synthesized by an indirect procedure in which a living polymer containing mainly PtBMA segment was attached to the precursor. Both methods resulted in the formation of dendrimer-like copolymers with the high molecular weights (up to 8.5×10^6 Da), large molecular sizes (diameter up to 73 nm), and dense shells (number of arms up to 1300). These products, G3PS-g-P2VP and G3PS-g-PtBMA, were protonated with trifluoroacetic acid and acidic hydrolyzed, respectively. After transformation, amphiphilic dendrimer-like copolymers, G3PS-g-P2VPH⁺ and G3PS-g-PMAA, were obtained. Preliminary results on the solution properties of the amphiphilic products were presented.

Keywords Dendrimer-like polymer; Living anionic polymerization; Amphiphilic copolymer

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INTRODUCTION

Dendrimer-like polymers are a unique class of dendrimers where the branching points in neighboring generations are connected by polymer chains.^[1–8] These polymers not only exhibit globular molecular conformation and multiplicity of the peripheral groups as regular dendrimers, but also possess higher tunability on the molecular level such as the density of branching, molecular weight, molecular size, *etc.*^[9,10]

The synthesis of the dendrimer-like polymers involves either “core-first” divergent or “arm-first” convergent method.^[1,11] In the divergent method, the polymerization of monomer is typically initiated by a multifunctional precursor, and then each of the polymer chain-ends is arborized by a branching agent to form at least two new initiation sites.^[12–21] Usually, controlled/“living” radical polymerizations such as atom transfer radical polymerization (ATRP) and ring opening polymerization (ROP) are used for chain growth. Molecular weight growth along with generation is achieved by repeating the polymerization process and chain-end modification.^[11–16,22–25] In the convergent method, the coupling of living chains or dendrons is fulfilled by efficient reactions such as carbanion-chlorosilane reaction,^[26,27]

Williamson etherification reaction,^[28] and azide-alkyne cycloaddition.^[29–31]

Hirao and coworkers developed an iterative divergent “grafting-to” methodology in which living anionic polymer chains were prepared separately before being attached to the termini of the preceding generations.^[32–35] This methodology rests on the quantitative deprotection to construct new branching points followed by living anionic polymerization to synthesize precisely controlled branching polymer chains. Employing this methodology, a large number of well-defined and high-generation dendrimer-like polymers with molecular weight even higher than 1.0×10^7 Da have been synthesized.^[36]

In 2012, we explored a continuous approach by using the reaction of a living anionic chain with monoadduct of 1,3-bis(1-phenylvinyl)benzene (MDDPE) and *sec*-BuLi to construct branch unit.^[37] This process did not require protection and deprotection, thus the synthetic efficiency was greatly improved. However, the presence of multiple carbanion in each molecule led to the formation of pseudo-gel, although the situation was alleviated by addition of chelating agents. In a subsequent contribution, we developed another facile divergent end-grafting approach following Hirao’s divergent “grafting-to” methodology. This approach utilized a living block copolymer, polyisoprene-*b*-polystyrenyl lithium (PI-*b*-PSLi), as the building block for target dendrimer-like polymers.^[38,39] The block copolymer contained very short PI seg-

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ment, e.g., 8–10 repeating units of isoprene, for epoxidation and subsequent ring-opening addition with the incoming PI-*b*-PSLi. Since the PI segment provided multiple sites (usually 4–7) for branching, this approach allowed the rapid increase of molecular weight along with generation. Nevertheless, the approach suffered from the limitation of epoxy reactivity. For instance, anionic living polymers with electron withdrawing groups, such as poly(2-vinyl pyridine) and polymethacrylates living chains, showed very low reactivity with epoxy group.^[40]

We hereby report the synthesis of dendrimer-like copolymers containing polystyrene/poly(*tert*-butyl methacrylate) and polystyrene/poly(2-vinyl pyridine) *via* new routes based on anionic polymerization and chlorosilane coupling. The advantage of the present route is to prepare dendrimer-like polymers with high molecular weights as well as high density of the peripheral segments and functionalities. Thus, for each dendrimer-like molecule, approximately 1300 segments of poly(*tert*-butyl methacrylate) and poly(2-vinyl pyridine) were respectively introduced as out-sphere to dendritic polystyrene precursors. The obtained dendrimer-like copolymers were easily transformed into amphiphilic dendrimer-like copolymers with ionic shell by protonation of P2VP to poly(2-vinylpyridinium trifluoroacetate) and hydrolysis of *Pt*BMA segments to poly(methacrylic acid), respectively.

EXPERIMENTAL

Materials

n-Butyllithium (*n*-BuLi, 2.5 mol/L solution in hexane, Aldrich), *sec*-butyllithium (*sec*-BuLi, 1.3 mol/L solution in cyclohexane, Aldrich), di-*n*-butylmagnesium (MgBu₂, 1.0 mol/L in heptane, Aldrich), tri-*n*-octylaluminum (25 wt% in hexane, Aldrich), and trifluoroacetic acid (TFA, 99%, Adamas) were used as received. Calcium hydride (CaH₂, 99%), toluene (99%), and anhydrous methanol (99%) were purchased from National Pharmaceutical and used as received. Tetrahydrofuran (THF, National Pharmaceutical) was refluxed over CaH₂ and distilled from *n*-BuLi on the vacuum line before use. Styrene (St, 99%, Adamas), α -methylstyrene (α -MeSt, 99%, Adamas), 2-vinylpyridine (2VP, 97%, TCI), and *tert*-butyl methacrylate (*t*BMA, 98%, TCI) were distilled over CaH₂ and stored at –20 °C. St and α -MeSt were further distilled over MgBu₂ on the vacuum line before use. 2VP and *t*BMA were further distilled over tri-*n*-octylaluminum on the vacuum line before use. 1,1-Diphenylethylene (DPE, 98%, Alfa Aesar) was purified by silica gel column using petroleum ether as the eluent. Lithium chloride (LiCl, 99%) was purchased from Aldrich, and was dried by vacuum oven (40 °C, 24 h) before use. 1,3-Bis(1-phenylvinyl)benzene (MDDPE) was synthesized according to a previous method.^[37] The 3rd generation dendritic polystyrene with multiple peripheral chlorosilane groups, G3PS-*g*-SiCl, was prepared through iterative anionic polymerization, hydrosilation, and coupling reaction, as reported elsewhere.^[41] The molecular weight was measured after the chlorosilane groups were deactivated by *n*-BuLi (G3PS-*g*-*n*Bu: $M_{n, \text{GPC}} = 4.6 \times 10^5$ Da, $\bar{D} = 1.39$, $M_{w, \text{MALLS}} = 2.0 \times 10^6$ Da).

Measurements

¹H-NMR measurement was performed on a Bruker (400 MHz) NMR instrument using CDCl₃ as the solvent and tetramethylsilane as an interior reference. The number-average molecular weight ($M_{n, \text{GPC}}$) was estimated by gel permeation chromatography (GPC) composed of two columns (Agilent PolarGel-M Serial No. 0006305291-17 and Agilent PolarGel-L Serial No. 0006180094-7). DMF was used as eluent (flow rate: 1.0 mL/min, 50 °C), and the calibration curves for GPC analyses were obtained using PMMA as standards. When THF was used as the eluent (flow rate: 1.0 mL/min, 35 °C), GPC analysis was performed through three TSK gel columns (pore size 1.5, 3.0, and 20.0 nm), calibrated by narrow polystyrene standards. The absolute molecular weight ($M_{w, \text{MALLS}}$) and gyration radius (R_g) were obtained by DAWN HELEOS in the online mode (GPC-MALLS), and dn/dc value was determined by Optilab rEX in the off-line mode. Fourier transform infrared spectroscopy (FTIR) was performed on a Thermofisher Nicolet 6700 Fourier transformation infrared spectrometer (potassium bromide pellet). Hydrodynamic radius (R_H) was obtained by dynamic light scattering (DLS). The experiments were carried out on an ALV/CGS-3 Goniometer system equipped with a multi- τ digital correlator (ALV-7004) and a He-Ne laser light source ($\lambda = 632.8$ nm) at a fixed scattering angle of 90°. Three preparative TSK gel columns (G4000H, G2500H, and G1000H) and an Optilab rEX (Wyatt) detector were used for the purification of dendrimer-like copolymer. THF was used as the eluent at a flow rate of 4.0 mL/min at 35 °C.

Synthesis of Dendrimer-like Polymer (G4-PS)

A flask was dried by six cycles of evacuating/heating with hot air/Ar-purging. Dry THF (200 mL) and St (14 mL, 0.122 mol) were added with dry syringes. The flask was cooled to approximately –80 °C, followed by adding 1 mL of *sec*-BuLi (1.3 mmol). St was polymerized for 20 min, yielding PSLi (PS: $M_{n, \text{GPC}} = 10.5 \times 10^3$ Da, $\bar{D} = 1.08$). Then, G3PS-*g*-SiCl (1 g) in toluene was added to the solution of PSLi, and the reaction stood 30 min before termination by degassed methanol. G4-PS was obtained by fractionation using toluene/methanol and precipitation in methanol ($M_{n, \text{GPC}} = 8.0 \times 10^5$ Da, $\bar{D} = 1.32$, $M_{w, \text{MALLS}} = 1.5 \times 10^7$ Da).

Synthesis of Dendrimer-like Copolymer Containing Polystyrene and Poly(2-vinyl pyridine)

G3PS-*g*-P2VP was synthesized by the coupling reaction of G3PS-*g*-SiCl with P2VPLi. First, the apparatus was dried by six cycles of evacuating/heating with hot air/Ar-purging, then 100 mL of THF and 0.25 mL of DPE (1.4 mmol) were added to a flask with dry syringes. After the flask was placed in a bath kept at approximately –80 °C, 1 mL of *sec*-BuLi (1.3 mmol) was added, and the mixture was allowed to react for 20 min, yielding DPHLi. Further, 4.2 mL of 2VP (40 mmol) was added to the flask, and the polymerization was continued for 30 min to afford P2VPLi (P2VP: $M_{n, \text{GPC}} = 3.9 \times 10^3$ Da, $\bar{D} = 1.09$). Subsequently, P2VPLi was used as living arms to react with G3PS-*g*-SiCl (1 g), and the reaction stood for 30 min. Finally, G3PS-*g*-P2VP was purified by fractionation using toluene/*n*-hexane ($M_{n, \text{GPC}} = 9.8 \times 10^5$ Da, $\bar{D} = 1.39$, $M_{w, \text{MALLS}} = 6.0 \times 10^6$ Da).

Preparation of Amphiphilic Dendrimer-like Copolymer by Protonation of P2VP Segments

Two strategies were used for transforming G3PS-*g*-P2VP into amphiphilic dendrimer-like copolymer, G3PS-*g*-P2VPH⁺. In the first method, the copolymer was directly dissolved in 0.1 mol/L trifluoroacetic acid (TFA) aqueous solution. In the second method, G3PS-*g*-P2VP was dissolved in THF followed by addition of TFA. The mixture was stirred at ambient temperature for 24 h and then diluted with 0.1 mol/L TFA aqueous solution of 10-fold volume. Finally, THF was removed by dialysis.

Synthesis of Dendrimer-like Copolymer Containing Polystyrene and Poly(*tert*-butyl methacrylate)

G3PS-*g*-PtBMA was synthesized by the coupling of G3PS-*g*-SiCl with living polymer containing mainly PtBMA segment, PtBMA-*b*-P2VPLi. First, 4.6 mL of *sec*-BuLi (6.0 mmol) was slowly dropped into 200 mL THF solution of MDDPE (1.88 g, 6.6 mmol) with vigorous stirring at approximately −80 °C for 30 min to afford the monoadduct of MDDPE. Then, 0.6 g of LiCl and 30 mL of *t*BMA were added to the flask. The mixture was stirred for 60 min and the reaction was quenched with degassed methanol.

The product, PtBMA-*b*-*sec*-BuDDPE, was obtained by slowly dropping the above solution to 10-fold volume of methanol/water ($V_{\text{methanol}}:V_{\text{water}} = 7:3$) mixture at −20 °C (PtBMA-*b*-*sec*-BuDDPE: $M_{n,\text{GPC}} = 3.8 \times 10^3$ Da, $\bar{D} = 1.12$). Subsequently, 5 g of vacuum-dried PtBMA-*b*-*sec*-BuDDPE (1.1 mmol DPE type double bond) was dissolved in THF and the solution was mixed with the polymerization solution of α -MeSt (0.5 mL) and *sec*-BuLi (0.8 mL) in THF (P α MeStLi). The solution became dark red and the reaction of P α MeStLi with DPE type double bond proceeded at approximately −80 °C for 1 h before the addition of 0.5 mL of 2VP. The polymerization stood for 10 min, giving PtBMA-*b*-P2VPLi (PtBMA-*b*-P2VP: $M_{n,\text{GPC}} = 4.5 \times 10^3$ Da, $\bar{D} = 1.12$). Finally, G3PS-*g*-SiCl was added to the solution. The coupling reaction was allowed to proceed for 30 min and quenched with degassed methanol. The product, G3PS-*g*-PtBMA, was purified by preparative GPC ($M_{n,\text{GPC}} = 7.4 \times 10^5$ Da, $\bar{D} = 1.38$, $M_{w,\text{MALLS}} = 8.5 \times 10^6$ Da).

Preparation of Amphiphilic Dendrimer-like Copolymer by Hydrolysis of PtBMA Segments

G3PS-*g*-PtBMA (0.5 g) was dissolved in 50 mL of 1,4-dioxane, and then 5 mL of concentrated HCl was dropped into the flask under stirring. The solution was refluxed at 85 °C for 6 h. Finally, dioxane and HCl were removed by dialysis using 0.1 mol/L NaOH aqueous solution or 0.1 mol/L NaOH aqueous solution containing 0.1 mol/L NaCl.

RESULTS AND DISCUSSION

The synthetic route to amphiphilic dendrimer-like copolymers was based on the coupling reaction between carbanion with chlorosilane, as shown in Scheme 1. This chemistry was used for the preparation of dendrimer-like polystyrene core (G3PS-*g*-SiCl).^[41] The coupling reaction of living poly(2-vinyl pyridine)Li with peripheral Si-Cl went smoothly, whereas the reaction of living poly(*tert*-butyl methacrylate)-

Li and Si-Cl formed labile linkage Si-C(CH₃)(COOtBu) which was unstable in protic solvents. Therefore, the attachment of PtBMA segment was performed through a specially designed procedure (*vide infra*).

Synthesis of Dendrimer-like Copolymer G3PS-*g*-P2VP

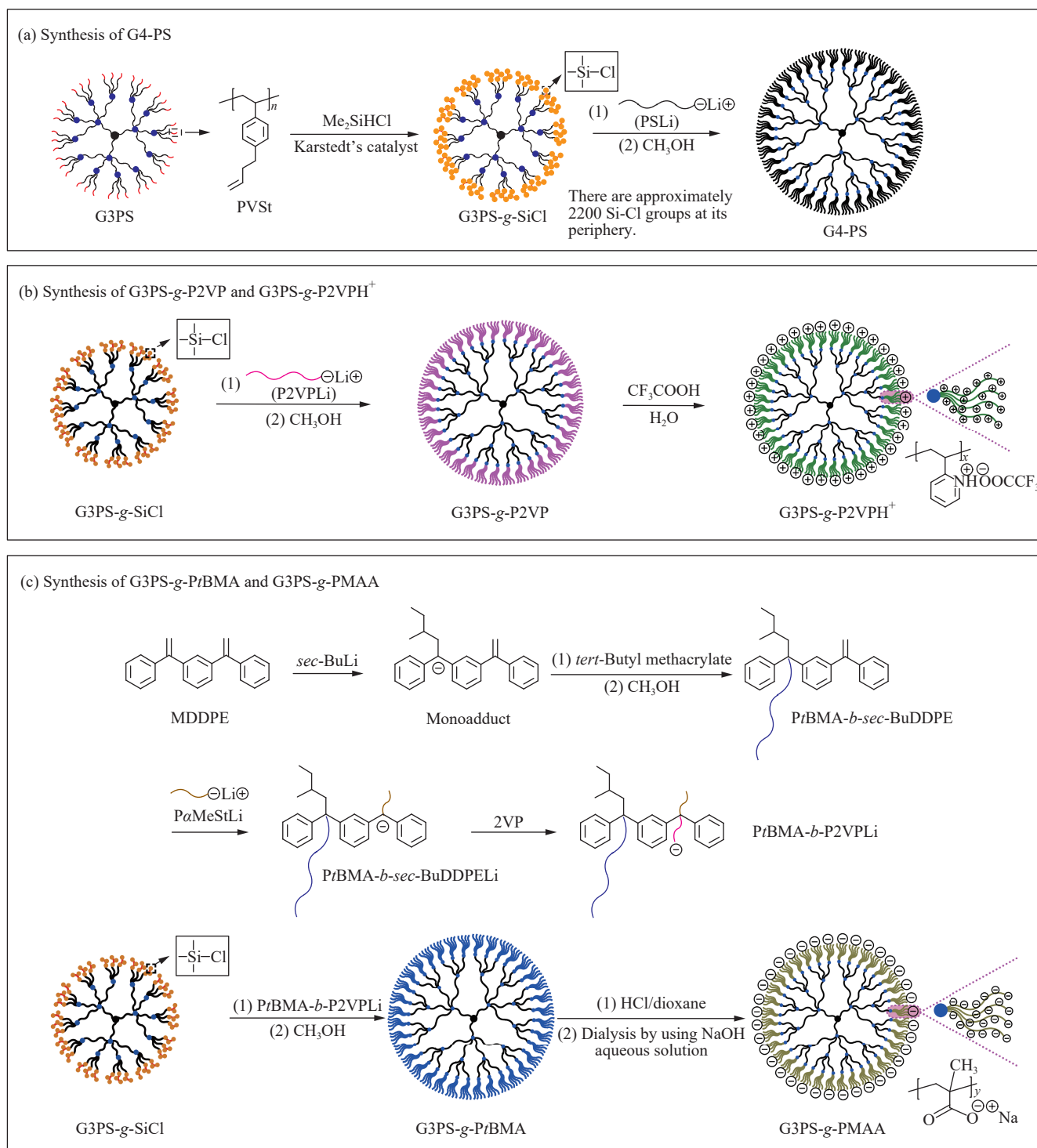
Dendrimer-like copolymer with P2VP as the out sphere was simply prepared by coupling living anionic P2VP chains to G3PS-*g*-SiCl. P2VPLi was prepared by living anionic polymerization of 2VP initiated by the adduct of *sec*-BuLi and DPE (DPHLi). The designed molecular weight of P2VP was 3.2×10^3 Da, while the measured values by GPC and MALLS on samples taken from the polymerization system were $M_{n,\text{GPC}} = 3.9 \times 10^3$ Da and $M_{w,\text{MALLS}} = 3.1 \times 10^3$ Da, respectively. The coupling reaction was performed by charging a toluene solution of G3PS-*g*-SiCl into living P2VPLi solution in THF at approximately −80 °C. The deep red color of the solution remarkably faded within 5 min. The reaction was kept for 30 min to ensure a high grafting efficiency, and the final reaction mixture was quenched with methanol.

Fig. 1 shows the GPC results of dendrimer-like polymers before and after grafting with P2VPLi. The excessive P2VP chains were removed through fractionation by non-solvent (*n*-hexane) titration. The purified product exhibits a sharp and monomodal peak shifting to high molecular weight compared with G3PS. The molecular weight of G3PS-*g*-P2VP measured by GPC and MALLS was 9.8×10^5 and 6.0×10^6 Da, respectively, remarkably larger than that of G3PS. Furthermore, the striking difference between the results of GPC and MALLS indicates a much smaller hydrodynamic volume relative to linear standards due to the dense branching in the dendrimer-like product. Note that the molecular weight ($M_{n,\text{GPC}}$) of G3PS in Fig. 1 is different from $M_{n,\text{GPC}}$ in Table 1, because these results were obtained from GPC with different eluents.

From the MALLS-measured molecular weights of G3PS-*g*-P2VP and G3PS, and the molecular weight of P2VP, one can estimate the number of P2VP arms attached to the dendritic molecule, $N_{\text{arm,obs.}} = ((6033 - 2032) \times 10^3)/(3.1 \times 10^3) \approx 1300$. Considering the number of Si-Cl groups in the precursor being 2200,^[41] the efficiency of the grafting reaction was 59%. This rather low value of grafting efficiency is due to the steric hindrance caused by overcrowding of peripheral segments in the precursor.^[38] Despite imperfection, the molecular weight distribution of the final product was narrow due to the homogenous distribution of defects in the dendritic molecules.

The dendrimer-like copolymers were also characterized by ¹H-NMR spectroscopy. As shown in Fig. 2, the signal at 8.00–8.50 ppm is assigned to aromatic proton adjacent to the nitrogen atom. From integration, the molar ratio of 2VP to St units in G3PS-*g*-P2VP was calculated to be 1.78:1, in close agreement with the value calculated from molecular weight (MALLS, $((6033 - 2032) \times 10^3)/(2032 \times 10^3) = 1.97:1$).

Therefore, these results demonstrate that the present coupling chemistry has afforded dendrimer-like copolymer of styrene and 2VP, with the latter as the main component constituting the peripheral part of the globular molecule.



Scheme 1 Synthetic routes to dendrimer-like polymers: (a) G4-PS, (b) amphiphilic dendrimer-like G3PS-g-P2VPH⁺, and (c) amphiphilic dendrimer-like G3PS-g-PMAA

Synthesis of Dendrimer-like Copolymer G3PS-g-PrBMA

G3PS-g-SiCl was also used as precursor to prepare dendrimer-like copolymer of styrene and *t*BMA *via* chlorosilane coupling reaction. Unfortunately, although G3PS-g-PrBMA was able to be synthesized by the coupling reaction between living anionic PrBMA chain and G3PS-g-SiCl, it appeared to be unstable in protic solvents, such as water and methanol. The reason was that the formed Si—C(CH₃)(COO*t*Bu)

moiety would be subject to hydrolysis or alcoholysis, which thus made Si—C cleave.^[42]

To overcome this problem, we designed a special 4-step process to introduce PrBMA segments. As shown in Scheme 1(c), the first step was to synthesize a monoadduct of MDDPE and *sec*-BuLi. The reaction was quantitative in THF, using slightly excessive feed amount of MDDPE.^[37] The second step was the polymerization of *t*BMA initiated

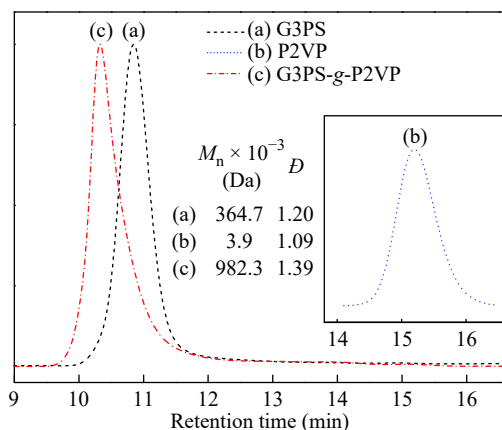


Fig. 1 GPC curves of dendrimer-like polymers (DMF was used as the eluent). G3PS-g-P2VP was purified by removing the excess P2VP, as shown in the inset.

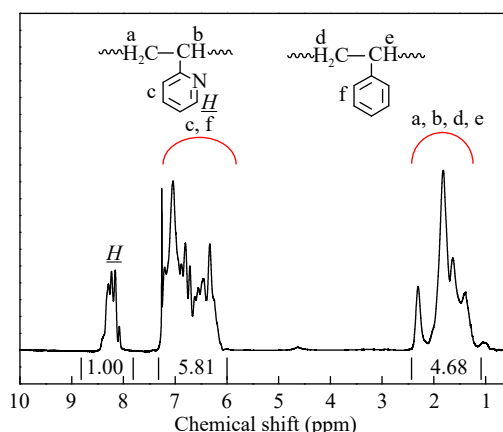


Fig. 2 ^1H -NMR spectrum of G3PS-g-P2VP (in CDCl_3)

Table 1 Characterization results of polymers involved in the present work ^a

Sample	$M_{n,\text{GPC}}^b$ $\times 10^{-3}$ (Da)	$M_{w,\text{MALLS}}^c$ $\times 10^{-3}$ (Da)	D^d	dn/dc (mL/g)	$N_{\text{arm,theo.}}^e$	$N_{\text{arm,obs.}}^f$	R_H (nm)	R_g (nm)	R_g/R_H
G3PS	455.4	2032	1.31	0.1885	260	220	21.6	—	—
G3PS-g- <i>n</i> Bu	456.4	2034	1.39	0.1839	—	—	—	—	—
G4-PS	804.1	14550	1.32	0.2034	2200	1300	47.8	40.5	0.847
P2VP	3.9	3.1	1.09	0.1362	—	—	—	—	—
G3PS-g-P2VP	982.3	6033	1.39	0.1401	2200	1300	32.9	31.6	0.960
PtBMA- <i>b</i> - <i>sec</i> -BuDDPE	3.8	4.6	1.12	0.0546	—	—	—	—	—
PtBMA- <i>b</i> -P2VP	4.5	5.1	1.12	0.0586	—	—	—	—	—
G3PS-g-PtBMA	741.0	8524	1.38	0.0603	2200	1300	36.5	33.8	0.926

^a For G3PS, G3PS-g-*n*Bu, and G4-PS, THF was used as the eluent of GPC, their dn/dc , R_H , and R_g values were measured in THF; For P2VP, G3PS-g-P2VP, PtBMA-*b*-*sec*-BuDDPE, PtBMA-*b*-P2VP, and G3PS-g-PtBMA, DMF was used as the eluent of GPC, their dn/dc , R_H , and R_g values were measured in DMF; ^b $M_{n,\text{GPC}}$ was determined by GPC; ^c $M_{w,\text{MALLS}}$ was determined by MALLS; ^d D was calculated by GPC curve; ^e $N_{\text{arm,theo.}}$ is the total number of Si—Cl groups in its precursor; ^f $N_{\text{arm,obs.}} = (M_{w,\text{MALLS}}(Gn) - M_{w,\text{MALLS}}(Gn - 1))/M_{w,\text{MALLS}}(\text{Arm}(n))$, where n is the generation number (the value should not be so accurate; a number of 1300 represents the average value of the arm number.)

by the monoadduct, giving the polymer containing a DPE type double bond at the chain end, PtBMA-*b*-*sec*-BuDDPE. The residual MDDPE was dormant during *t*BMA polymerization and was removed by precipitation in methanol/water after the polymerization. The third step involved the addition reaction of *P*αMeStLi to the DPE type double bond to form a DPE anion. *P*αMeStLi was chosen because it would not attack the ester group of PtBMA during the reaction process.^[43] DP of *P*αMeStLi was very low, *i.e.* 3–5, so that it would not cause much change to the property dominated by the PtBMA segments. The fourth step was a seeding process involving the polymerization of 2VP initiated by the DPE anion. This step was necessary because we found that the coupling efficiency between G3PS-g-SiCl and DPE anion was very low, possibly due to steric hindrance of the two phenyl rings. After seeding a short segment of 2VP (DP *ca.* 5), the anionic species bearing the PtBMA chain, simply denoted as PtBMA-*b*-P2VPLi, was easily attached to G3PS-g-SiCl to form stable dendrimer-like copolymer. All the reactions in the above steps were fast and can be completed within short periods ranging from several minutes to one hour.

Fig. 3 shows the GPC results of dendrimer-like polymers before and after the coupling reaction with living anionic polymer chain containing PtBMA segment. The excessive grafting chain was removed by preparative GPC. It is clear

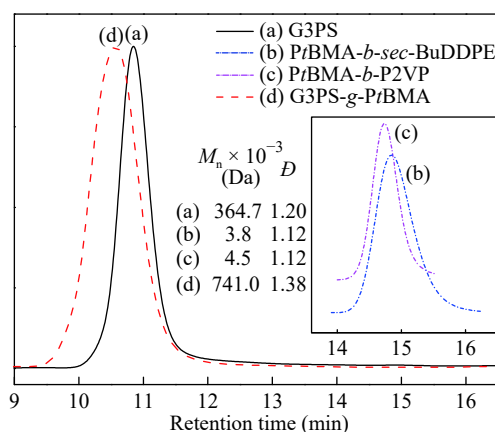


Fig. 3 GPC curves of dendrimer-like polymers (DMF was used as the eluent). G3PS-g-PtBMA was purified by removing the excess PtBMA-*b*-P2VP, as shown in the inset.

that the molecular weight of PtBMA-*b*-P2VP was similar to that of PtBMA-*b*-*sec*-BuDDPE, because the molecular weights of *P*αMeSt segment and P2VP segment are very low. Moreover, the molecular weights of polymers from G3PS to G3PS-g-PtBMA shift to higher molecular weight side while keeping narrow molecular weight distribution.

The molecular weights of G3PS-g-PtBMA measured by GPC and MALLS were 7.4×10^5 and 8.5×10^6 Da, respect-

ively. From the MALLS-measured molecular weights of G3PS-*g*-PtBMA and G3PS, and the molecular weight of PtBMA-*b*-P2VP, $N_{\text{arm,obs}}$ was calculated to be $((8524 - 2032) \times 10^3) / (5.1 \times 10^3) \approx 1300$. The efficiency of the grafting reaction was around 60% due to the steric hindrance caused by overcrowded peripheral segments in the precursor. Furthermore, the molecular weight of PtBMA measured by MALLS was 4.6×10^3 Da, so the content of PtBMA in G3PS-*g*-PtBMA was 69%.

The successful synthesis of G3PS-*g*-PtBMA was also confirmed by FTIR.^[43] As shown in Fig. 4, the stretching vibration bands of C=O and C–O bonds emerge at 1724 and 1142 cm^{-1} , respectively. Moreover, the absorption peaks at 1392 and 1368 cm^{-1} are the characteristics of *tert*-butyl group.

Solution Properties of the Dendrimer-like Copolymers after Respective Protonation and Hydrolysis

Protonation of P2VP segments at the periphery of G3PS-*g*-P2VP was performed by treatment with TFA to prepare amphiphilic dendrimer-like copolymer with multiple positive charges, G3PS-*g*-P2VPH⁺.^[44,45] G3PS-*g*-P2VP was either directly dissolved in 0.1 mol/L TFA aqueous solution, or first dissolved in THF and titrated with TFA, and finally diluted

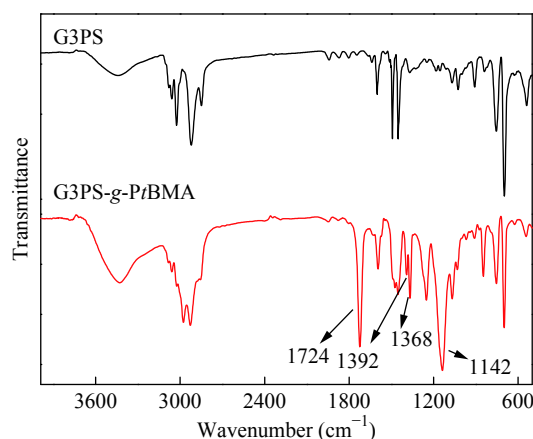


Fig. 4 FTIR spectra of G3PS and G3PS-*g*-PtBMA

with 10-fold volume of 0.1 mol/L TFA aqueous solution. THF was removed by dialysis. As shown in Figs. 5(a) and 5(b), G3PS-*g*-P2VPH⁺ exhibits the monodispersed size distribution in TFA aqueous solution irrespective of the dissolution strategy applied. Nevertheless, both systems resulted in R_{HS} much larger than that of the copolymer before protonation, indicating that aggregation happened in the

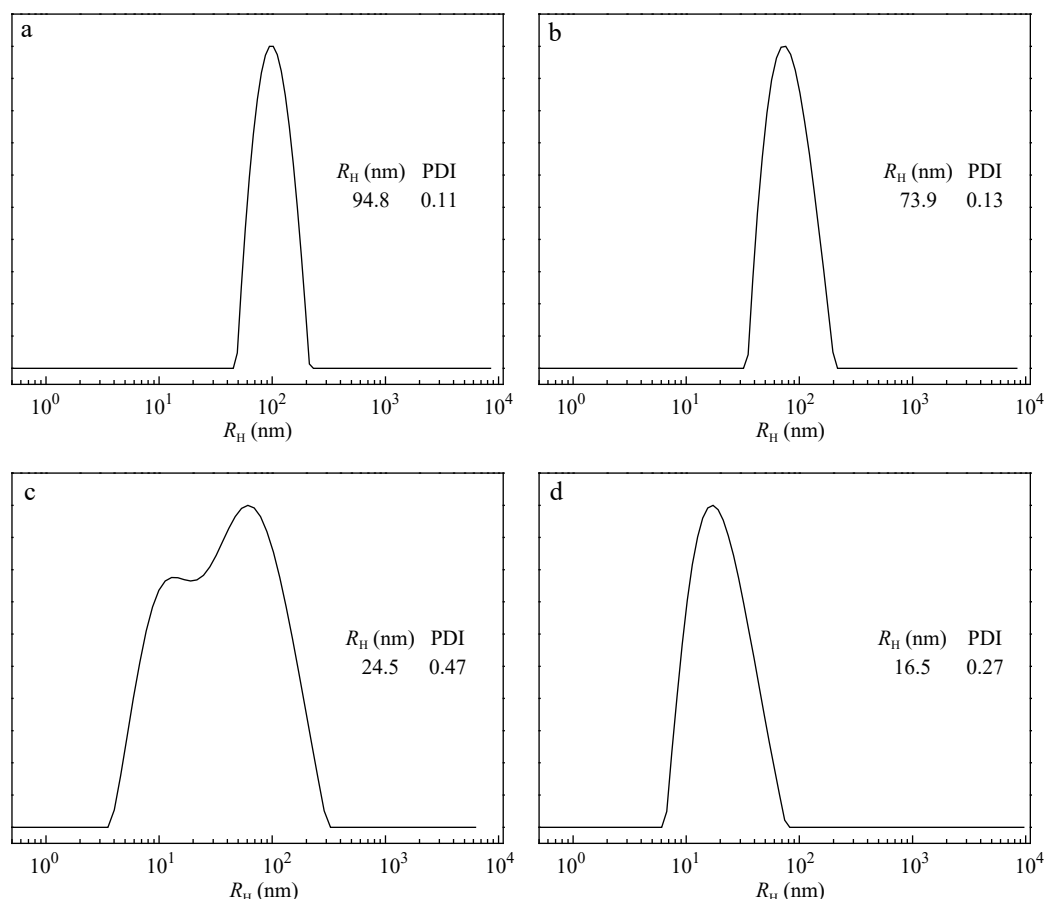


Fig. 5 Hydrodynamic radius (R_{H}) and particle size polydispersity index (PDI) of amphiphilic dendrimer-like copolymers measured by DLS: (a) G3PS-*g*-P2VP directly dissolved in 0.1 mol/L TFA aqueous solution; (b) G3PS-*g*-P2VP dissolved in THF, titrated with TFA, and finally diluted with 0.1 mol/L TFA aqueous solution (THF was removed by dialysis.); (c) G3PS-*g*-PMAA in 0.1 mol/L NaOH aqueous solution; (d) G3PS-*g*-PMAA in 0.1 mol/L NaOH aqueous solution containing 0.1 mol/L NaCl

solution. It seems that aggregation in the former direct dissolving system was more serious, thus giving even larger R_H (94.8 nm versus 73.9 nm).

Hydrolysis of G3PS-*g*-*Pr*BMA in boiling dioxane in the presence of HCl yielded an amphiphilic dendrimer-like copolymer with multiple negative charges in periphery, G3PS-*g*-PMAA. The hydrolyzed product was readily soluble in 0.1 mol/L NaOH aqueous solution. DLS result in Fig. 5(c) shows two peaks, which are attributed to the aggregation of G3PS-*g*-PMAA molecules. After adding NaCl into the solution to screen the negative charge, monodisperse size distribution was observed with smaller R_H .^[46] Notably, R_H is much smaller than that of the precursor copolymer before hydrolysis in the organic solvent. The reason is the remarkable difference between the solubility of G3PS core in both solvents. In THF, G3PS was solvated while in NaOH aqueous solution, it heavily shrank.

It is interesting to compare the ratios of R_g/R_H of G4-PS, G3PS-*g*-P2VP, and G3PS-*g*-*Pr*BMA, which roughly reflect the conformation of a polymer molecule in solution.^[38,47–49] G4-PS is a 4th generation of dendrimer-like homopolymers made from the same G3PS precursor as did for the copolymer, yet with longer segment of PS in the periphery. The res-

ults in THF or DMF are listed in Table 1. It was found that the R_g/R_H value of G4-PS in THF is 0.847, indicating a molecular conformation close to a hard sphere, whereas those of G3PS-*g*-P2VP and G3PS-*g*-*Pr*BMA in DMF are 0.960 and 0.926, respectively, which were more close to hollow sphere.^[47,48] Therefore, it seems that the dendrimer-like copolymers indeed adopted core-shell structure in the solution. Unfortunately, R_g/R_H values of G3PS-*g*-P2VPH⁺ and G3PS-*g*-PMAA are not obtained currently due to difficulties in measuring dn/dc values.

DLS was employed to confirm the shape of dendrimer-like polymer.^[13,16] As shown in Fig. 6, the beginning values of intensity correlation function curves at different scattering angles are very close to each other and R_H calculated by the intensity correlation function is completely irrelevant to the scattering angle. These results strongly indicate that G3PS-*g*-P2VP and G3PS-*g*-*Pr*BMA adopted spherical shape in DMF with the R_H values of around 32.9 and 36.5 nm, respectively.

CONCLUSIONS

Dendrimer-like copolymers of styrene/2VP and styrene/*t*BMA were synthesized, starting from a 3rd generation dendritic polystyrene precursor, G3PS-*g*-SiCl, through a chlorosilane coupling reaction with the living anionic polymer species. For the copolymer of styrene and 2VP, direct coupling between chlorosilane and P2VPLi worked well to form the target dendrimer-like copolymer, G3PS-*g*-P2VP. For the copolymer of styrene and *t*BMA, direct coupling led to the formation of unstable product. Therefore, a specific 4-step process was developed to attach *Pr*BMA segments to G3PS-*g*-SiCl for preparation of G3PS-*g*-*Pr*BMA. Although this process introduced oligo(α MeSt) and oligo(2VP) at the same time with *Pr*BMA, the content of the latter was dominant. In general, these anionic coupling reactions led to the preparation of dendrimer-like copolymers possessing a dendritic polystyrene core, G3PS, and a dense periphery of P2VP or *Pr*BMA with up to 1300 number of arms. The molecular weight was as high as 8.5×10^6 Da and molecular diameter was as large as 73 nm. The molecular weight distribution was narrow despite the presence of imperfection due to steric hindrance or space limit around the branching points. Furthermore, these products were converted into the amphiphilic dendrimer-like copolymers by protonation with TFA and acidic hydrolysis, respectively. The protonated and hydrolyzed products, G3PS-*g*-P2VPH⁺ and G3PS-*g*-PMAA, were completely soluble in the 0.1 mol/L TFA aqueous solution and 0.1 mol/L NaOH aqueous solution, respectively. Thus, the present methodology provides a feasible way to prepare amphiphilic dendrimer-like copolymers with the dense shell. Although the detailed study on conformation of the products is still under way, it is predictable that the amphiphilic dendrimer-like copolymers can be applied as cationic and anionic unimolecular micelles, nanocarriers and nanoreactors for controlled release of organic substances, and promoting organic reaction or polymerizations.

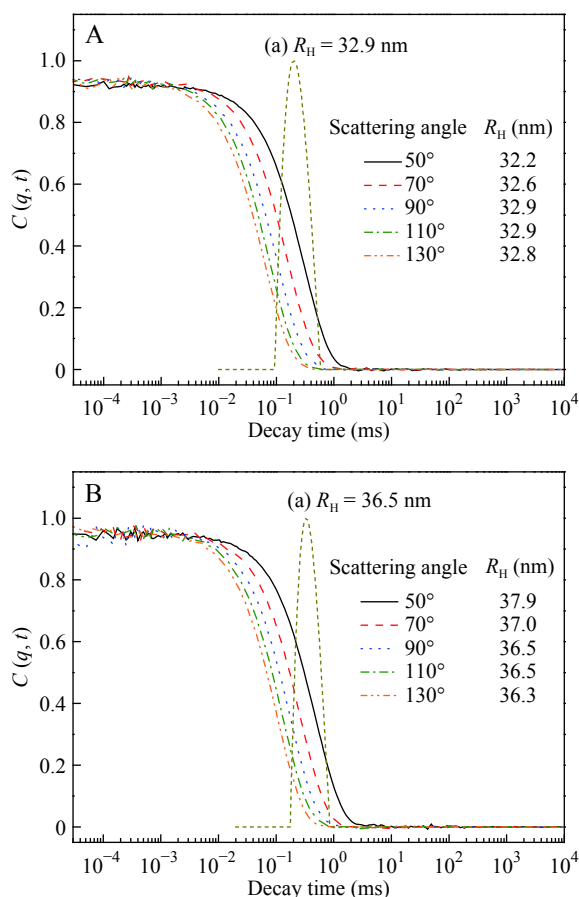


Fig. 6 Intensity correlation function curves of (A) dendrimer-like G3PS-*g*-P2VP and (B) dendrimer-like G3PS-*g*-*Pr*BMA in DMF at different scattering angles. In (A), (a) is the distribution function curve of G3PS-*g*-P2VP at the scattering angle of 90°; in (B), (a) is the distribution function curve of G3PS-*g*-*Pr*BMA at the scattering angle of 90° ($c = 5$ mg/mL).

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REFERENCES

- Taton, D.; Feng, X.; Gnanou, Y. Dendrimer-like polymers: A new class of structurally precise dendrimers with macromolecular generations. *New J. Chem.* **2007**, *31*, 1097–1110.
- Taton, D.; Gnanou, Y.; Matmour, R.; Angot, S.; Hou, S.; Francis, R.; Lepoittevin, B.; Moinard, D.; Babin, J. Controlled polymerizations as tools for the design of star-like and dendrimer-like polymers. *Polym. Int.* **2006**, *55*, 1138–1145.
- Polymeropoulos, G.; Zapsas, G.; Ntetsikas, K.; Bilalis, P.; Gnanou, Y.; Hadjichristidis, N. 50th Anniversary perspective: Polymers with complex architectures. *Macromolecules* **2017**, *50*, 1253–1290.
- Hirao, A.; Goseki, R.; Ishizone, T. Advances in living anionic polymerization: From functional monomers, polymerization systems, to macromolecular architectures. *Macromolecules* **2014**, *47*, 1883–1905.
- Hirao, A.; Yoo, H. S. Dendrimer-like star-branched polymers: Novel structurally well-defined hyperbranched polymers. *Polym. J.* **2011**, *43*, 2–17.
- Hirao, A.; Sugiyama, K.; Matsuo, A.; Tsunoda, Y.; Watanabe, T. Synthesis of well-defined dendritic hyperbranched polymers by iterative methodologies using living/controlled polymerizations. *Polym. Int.* **2008**, *57*, 554–570.
- Hirao, A.; Sugiyama, K.; Tsunoda, Y.; Matsuo, A.; Watanabe, T. Precise synthesis of well-defined dendrimer-like star-branched polymers by iterative methodology based on living anionic polymerization. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6659–6687.
- Konkolewicz, D.; Monteiro, M. J.; Perrier, S. Dendritic and hyperbranched polymers from macromolecular units: Elegant approaches to the synthesis of functional polymers. *Macromolecules* **2011**, *44*, 7067–7087.
- Grayson, S. M.; Fréchet, J. M. J. Convergent dendrons and dendrimers: From synthesis to applications. *Chem. Rev.* **2001**, *101*, 3819–3867.
- Bosman, A. W.; Janssen, H. M.; Meijer, E. W. About dendrimers: Structure, physical properties, and applications. *Chem. Rev.* **1999**, *99*, 1665–1688.
- Six, J. L.; Gnanou, Y. From star-shaped to dendritic poly(ethylene oxide)s: Toward increasingly branched architectures by anionic polymerization. *Macromol. Symp.* **1995**, *95*, 137–150.
- Francis, R.; Taton, D.; Logan, J. L.; Masse, P.; Gnanou, Y.; Duran, R. S. Synthesis and surface properties of amphiphilic star-shaped and dendrimer-like copolymers based on polystyrene core and poly(ethylene oxide) corona. *Macromolecules* **2003**, *36*, 8253–8259.
- Feng, X.; Taton, D.; Borsali, R.; Chaikof, E. L.; Gnanou, Y. pH Responsiveness of dendrimer-like poly(ethylene oxide)s. *J. Am. Chem. Soc.* **2006**, *128*, 11551–11562.
- Matmour, R.; Lepoittevin, B.; Joncheray, T. J.; El-khoury, R. J.; Taton, D.; Duran, R. S.; Gnanou, Y. Synthesis and investigation of surface properties of dendrimer-like copolymers based on polystyrene and poly(*tert*-butylacrylate). *Macromolecules* **2005**, *38*, 5459–5467.
- Feng, X.; Taton, D.; Chaikof, E. L.; Gnanou, Y. Fast access to dendrimer-like poly(ethylene oxide)s through anionic ring-opening polymerization of ethylene oxide and use of nonprotected glycidol as branching agent. *Macromolecules* **2009**, *42*, 7292–7298.
- Feng, X.; Taton, D.; Chaikof, E. L.; Gnanou, Y. Toward an easy access to dendrimer-like poly(ethylene oxide)s. *J. Am. Chem. Soc.* **2005**, *127*, 10956–10966.
- Kong, L. Z.; Pan, C. Y. Preparation of dendrimer-like copolymers based on polystyrene and poly(L-lactide) and formation of hollow microspheres. *Polymer* **2008**, *49*, 200–210.
- Zhao, Y.; Shuai, X.; Chen, C.; Xi, F. Synthesis of star block copolymers from dendrimer initiators by combining ring-opening polymerization and atom transfer radical polymerization. *Macromolecules* **2004**, *37*, 8854–8862.
- Teertstra, S. J.; Gauthier, M. Dendrigraft polymers: Macromolecular engineering on a mesoscopic scale. *Prog. Polym. Sci.* **2004**, *29*, 277–327.
- Trollsås, M.; Kelly, M. A.; Claesson, H.; Siemens, R.; Hedrick, J. L. Highly branched block copolymers: Design, synthesis, and morphology. *Macromolecules* **1999**, *32*, 4917–4924.
- Stancik, C. M.; Pople, J. A.; Trollsås, M.; Lindner, P.; Hedrick, J. L.; Gast, A. P. Impact of core architecture on solution properties of dendrimer-like star copolymers. *Macromolecules* **2003**, *36*, 5765–5775.
- Trollsås, M.; Hedrick, J. L. Dendrimer-like star polymers. *J. Am. Chem. Soc.* **1998**, *120*, 4644–4651.
- Hedrick, J. L.; Trollsås, M.; Hawker, C. J.; Athoff, B.; Claesson, H.; Heise, A.; Miller, R. D. Dendrimer-like star block and amphiphilic copolymers by combination of ring opening and atom transfer radical polymerization. *Macromolecules* **1998**, *31*, 8691–8705.
- Percec, V.; Barboiu, B.; Grigoras, C.; Bera, T. K. Universal iterative strategy for the divergent synthesis of dendritic macromolecules from conventional monomers by a combination of living radical polymerization and irreversible TER minator multifunctional initiator (TERMINI). *J. Am. Chem. Soc.* **2003**, *125*, 6503–6516.
- Matmour, R.; Gnanou, Y. Combination of an anionic terminator multifunctional initiator and divergent carbanionic polymerization: Application to the synthesis of dendrimer-like polymers and of asymmetric and miktoarm stars. *J. Am. Chem. Soc.* **2008**, *130*, 1350–1361.
- Orfanou, K.; Iatrou, H.; Lohse, D. J.; Hadjichristidis, N. Synthesis of well-defined second (G-2) and third (G-3) generation dendritic polybutadienes. *Macromolecules* **2006**, *39*, 4361–4365.
- Bender, J. T.; Knauss, D. M. Dendritic polystyrene with hydroxyl-functionalized branch points by convergent living anionic polymerization. *Macromolecules* **2009**, *42*, 2411–2418.
- Hutchings, L. R.; Roberts-Bleming, S. J. DendriMacs. Well-defined dendritically branched polymers synthesized by an iterative convergent strategy involving the coupling reaction of AB₂ macromonomers. *Macromolecules* **2006**, *39*, 2144–2152.
- Altintas, O.; Demirel, A. L.; Hizal, G.; Tunca, U. Dendrimer-like miktoarm star terpolymers: A₃-(B-C)₃ via click reaction strategy. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 5916–5928.
- Urbani, C. N.; Bell, C. A.; Whittaker, M. R.; Monteiro, M. J. Convergent synthesis of second generation AB-type miktoarm dendrimers using “click” chemistry catalyzed by copper wire. *Macromolecules* **2008**, *41*, 1057–1060.
- Bell, C. A.; Jia, Z.; Kulis, J.; Monteiro, M. J. Modulating two copper(I)-catalyzed orthogonal “click” reactions for the one-pot synthesis of highly branched polymer architectures at 25 °C. *Macromolecules* **2011**, *44*, 4814–4827.
- Matsuo, A.; Watanabe, T.; Hirao, A. Synthesis of well-defined dendrimer-like branched polymers and block copolymer by the iterative approach involving coupling reaction of living anionic polymer and functionalization. *Macromolecules* **2004**, *37*, 6283–6290.
- Hirao, A.; Matsuo, A.; Watanabe, T. Precise synthesis of

- dendrimer-like star-branched poly(methyl methacrylate)s up to seventh generation by an iterative divergent approach involving coupling and transformation reactions. *Macromolecules* **2005**, *38*, 8701–8711.
- 34 Hirao, A.; Watanabe, T. Precise synthesis and characterization of fourth-generation dendrimer-like star-branched poly(methyl methacrylate)s and block copolymers by iterative methodology based on living anionic polymerization. *Macromolecules* **2009**, *42*, 682–693.
 - 35 Yoo, H. S.; Watanabe, T.; Matsunaga, Y.; Hirao, A. Precise synthesis of dendrimer-like star-branched poly(*tert*-butyl methacrylate)s and their block copolymers by a methodology combining α -terminal-functionalized living anionic polymers with a specially designed linking reaction in an iterative fashion. *Macromolecules* **2012**, *45*, 100–112.
 - 36 Deffieux, A.; Schappacher, M.; Hirao, A.; Watanabe, T. Synthesis and AFM structural imaging of dendrimer-like star-branched polystyrenes. *J. Am. Chem. Soc.* **2008**, *130*, 5670–5672.
 - 37 Zhang, H.; He, J.; Zhang, C.; Ju, Z.; Li, J.; Yang, Y. Continuous process for the synthesis of dendrimer-like star polymers by anionic polymerization. *Macromolecules* **2012**, *45*, 828–841.
 - 38 Zhang, H.; Zhu, J.; He, J.; Qiu, F.; Zhang, H.; Yang, Y.; Lee, H.; Chang, T. Easy synthesis of dendrimer-like polymers through a divergent iterative “end-grafting” method. *Polym. Chem.* **2013**, *4*, 830–839.
 - 39 Wang, Y.; Qi, G.; He, J. Unimolecular micelles from layered amphiphilic dendrimer-like block copolymers. *ACS Macro Lett.* **2016**, *5*, 547–551.
 - 40 Natalello, A.; Tonhauser, C.; Berger-Nicoletti, E.; Frey, H. A combined DPE/epoxide termination strategy for hydroxyl end-functional poly(2-vinylpyridine) and amphiphilic AB₂-miktoarm stars. *Macromolecules* **2011**, *44*, 9887–9890.
 - 41 Zheng, K.; He, J. Thermally “switchable” nanoreactor from amphiphilic dendrimer-like copolymer with dense hydrophilic shell. Manuscript in preparation.
 - 42 Ruckenstein, E.; Zhang, H. Well-defined graft copolymers based on the selective living anionic polymerization of the bifunctional monomer 4-(vinylphenyl)-1-butene. *Macromolecules* **1999**, *32*, 6082–6087.
 - 43 Wang, X.; He, J.; Yang, Y. Synthesis of ABCD-type miktoarm star copolymers and transformation into zwitterionic star copolymers. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 4818–4828.
 - 44 Gauthier, M.; Li, J.; Dockendorff, J. Arborescent polystyrene-graft-poly(2-vinylpyridine) copolymers as unimolecular micelles synthesis from acetylated substrates. *Macromolecules* **2003**, *36*, 2642–2648.
 - 45 Kee, R. A.; Gauthier, M. Arborescent polystyrene-graft-poly(2-vinylpyridine) copolymers: Synthesis and enhanced polyelectrolyte effect in solution. *Macromolecules* **2002**, *35*, 6526–6532.
 - 46 Kee, R. A.; Gauthier, M. Arborescent polystyrene-graft-poly(*tert*-butyl methacrylate) copolymers: Synthesis and enhanced polyelectrolyte effect in solution. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2335–2346.
 - 47 Chu, B.; Liu, T. Characterization of nanoparticles by scattering techniques. *J. Nanopart. Res.* **2000**, *2*, 29–41.
 - 48 Li, L.; He, C.; He, W.; Wu, C. Formation kinetics and scaling of “defect-free” hyperbranched polystyrene chains with uniform subchains prepared from seesaw-type macromonomers. *Macromolecules* **2011**, *44*, 8195–8206.
 - 49 Trollsås, M.; Atthof, B.; Wüsch, A.; Hedrick, J. L. Constitutional isomers of dendrimer-like star polymers: Design, synthesis, and conformational and structural properties. *Macromolecules* **2000**, *33*, 6423–6438.