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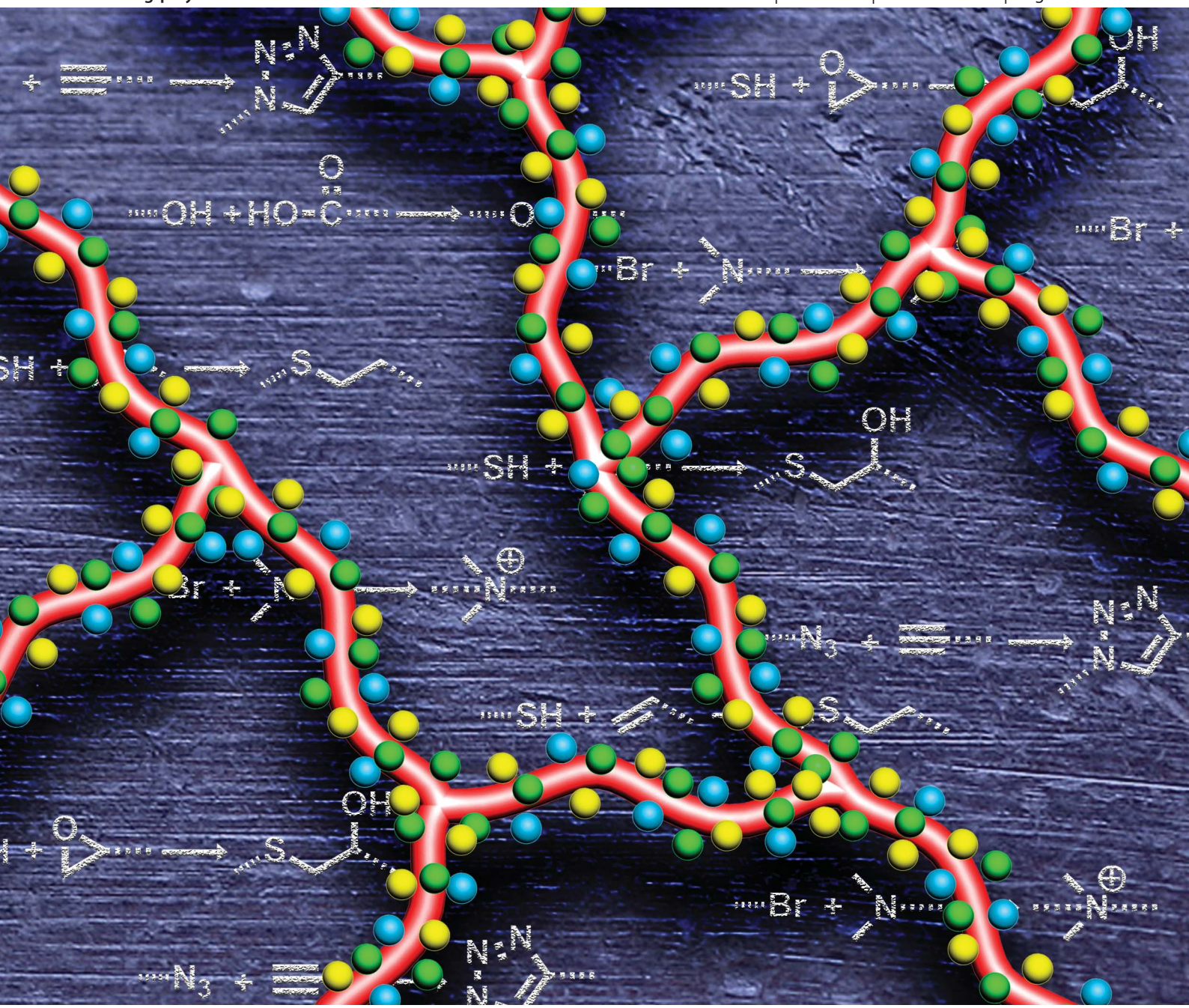

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Chao Gao *et al.*

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High-density and hetero-functional group engineering of segmented hyperbranched polymers *via* click chemistry†

Sipei Li, Jin Han and Chao Gao*

A new kind of segmented hyperbranched polymers (SHPs), hyperbranched poly(glycidyl methacrylate)s (HPGMAs), were synthesized *via* reversible addition–fragmentation chain transfer self-condensing vinyl polymerization (RAFT-SCVP). HPGMAs were efficiently functionalized on the whole scaffold *via* a collection of click chemistries, including the azidation of oxirane, thiol–epoxy click chemistry, thiol–ene click chemistry, copper-catalyzed azide–alkyne cycloaddition (CuAAC), and Menschutkin chemistry, affording SHPs with hetero-functional groups including hydroxyl + azide, dual hydroxyl, triple hydroxyl, hydroxyl + tertiary amine, hydroxyl + alkene, hydroxyl + carboxyl, alkene + azide, alkyne + azide, hydroxyl + alkyne, dual hydroxyl + alkene *etc.*, all at ~100% conversion. "Thiol–epoxy + thiol–ene" sequential dual click and "thiol–epoxy + Menschutkin chemistry + CuAAC" triple click strategies were presented, making functional group transformation readily accessible. Hydrophilic dendritic brushes, hydrophobic dendritic brushes and amphiphilic dendritic hetero-brushes were synthesized. Esterification of SHP containing hydroxy and azido groups with 1-pyrenebutyric acid yielded clickable fluorescent macromolecules, which showed a very strong excimer emission.

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Introduction

Conventional hyperbranched polymers (CHPs) synthesized *via* AB_2, latent AB_2, $A_2 + B_3$, or an asymmetric monomer-pair approach can be easily functionalized due to their abundant functional groups.[1] However, the compact structure of CHPs makes it extremely difficult to fully functionalize both the linear and terminal units, and the total conversion is usually less than 70% (Fig. 1).[2] Recently, segmented hyperbranched polymers (SHPs),[3–6] a novel subclass of dendritic polymers with long linear chains between every two branching points, are drawing increasing attentions, since the low steric congestion of sparsely branched backbones offers the opportunity of 100% conversion during functionalization (Fig. 1). In a previous report, we developed a versatile and simple method to synthesize SHPs by a combination of reversible addition–fragmentation chain transfer polymerization and self-condensing vinyl polymerization (RAFT-SCVP).[7] Indeed, full scaffold mono-functionalization of the SHPs was achieved at a 100% conversion.[7] This raises further interesting questions: (1) what if the functional group density were further improved, (2) how can hetero-functional groups be introduced on the full scaffold, and (3) how can such hetero-moieties be utilized to construct macromolecules with complex architecture and multi-functions?

Here, we extended the RAFT-SCVP method to synthesize SHPs with an epoxide group at each repeat unit by the copolymerization of glycidyl methacrylate (GMA) and the chain transfer

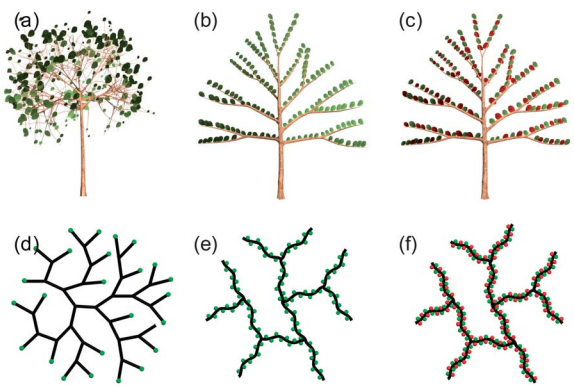

Fig. 1 (a) Densely branched tree. (b) Sparsely branched tree. (c) Hybrid sparsely branched tree. (d) Conventional hyperbranched polymer (CHP) has high steric congestion that hinders post-functionalization in the core. (e) Segmented hyperbranched polymer (SHP) makes full post-functionalization accessible due to the low steric congestion. (f) Segmented hyperbranched polymer with hetero-functionality and high functional group density.

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† Electronic supplementary information (ESI) available: Experimental conditions for thiol–epoxy click chemistry, ^{1}H NMR evolution spectra for real-time analysis, real-time analysis information for copolymerization at feed ratio of 5 and 15, FTIR spectra SHP 6 and 7, ^{1}H NMR spectra for SHP 12 and 13, absolute molecular weights of SHP-1 and solubility information of all the functional SHPs in chloroform, DMF and water. See DOI: 10.1039/c2py20951a

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monomer (CTM) of 2-((2-(((dodecylthio)carbonothioyl)thio)-2-methylpropanoyl)oxy)ethyl acrylate (ACDT). The epoxide groups were functionalized *via* azidation and thiol–epoxy chemistry to gain high-density hetero-functional SHPs. Further modifications at the hetero-sites demonstrated an ultrahigh conversion (~100%), with various reactions and sequential click chemistries affording a series of complex polymers including hydrophobic, hydrophilic and amphiphilic dendritic brushes. In addition, intense excimer-emission at low concentration was discovered on a high-density pyrene-functionalized SHP.

Experimental section

Materials

2-((2-(((Dodecylthio)carbonothioyl)thio)-2-methylpropanoyl)oxy)-ethyl acrylate (ACDT), mono-alkynyl poly(ethylene glycol) (PEG-Alk) (M_n = 350) and 1-(allyloxy)-3-azidopropan-2-ol were prepared according to previous reports.[7–9] Glycidyl methacrylate (GMA, 97%), sodium azide (99.5%), propyl mercaptan (98%), 2,2-dimethoxy-2-phenylacetophenone (DMPA, 99%), CuBr (98%), 4-pentenoic acid (97%), 4-pentynoic acid (95%), 2,2′-azobisisobutyronitrile (AIBN) were purchased from Sigma-Aldrich Corporation. 3-Mercaptopropionic acid (98%), 1-octadecanethiol (97%), propargyl bromide (99%), *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDCI, 98.5%), 4-dimethylaminopyridine (DMAP, 99%) and 1-pyrenebutyric acid were purchased from Aladdin Chemical Co., China. 1,1,4,7,7-Pentamethyldiethylenetriamine (PMDETA, 98%), 3-mercapto-1,2-propanediol (90%) and *N*,*N*′-dicyclohexylcarbodiimide were (DCC, 99%) were purchased from Alfa Aesar. Allyl mercaptan (≥80%) were purchased from TCI Shanghai. 2-Mercaptobenzothiazole (99%), chloroform-d (99.8 atom%D), stabilized with silver foil, dimethyl sulfoxide-d_6 (99.9 atom%D) were purchased from J&K chemical. 2-Mercaptoethanol (≥99%) was purchased from Boyun Reagent. 3-(Dimethylamino)-1-propanethiol was purchased from Atomax Chemicals Co. Ltd. Palmitic acid, triethylamine (TEA), dimethylformamide (DMF), 1,4-dioxane, chloroform, dichloromethane and other organic solvents were purchased from Sinopharm Chemical Reagent Co. Ltd. GMA was passed through a column of basic alumina before use and all the other materials were used as received.

Instrumentation

Gel permeation chromatography (GPC) was recorded on a Perkin Elmer HP 1100, using THF as the eluent at a flow rate of 1 mL min^{-1}, RI-WAT 150 CVt+ as the detector and linear polystyrene for calibration at 40 °C for characterization of apparent molecular weights. Light scattering data were recorded through gel permeation chromatography with a multiple angle laser scattering detection (GPC-MALLS) system using LiBr/DMF (0.05 mol L^{-1}) as the eluent at a flow rate of 1 mL min^{-1} and linear poly(methyl methacrylate) as calibration at 60 °C for the characterization of absolute molecular weights. The detection system consisted of a RI detector (Dawn DSP Laser Photometer, Wyatt Technology) and multiangle laser light scattering detector (OPTILAB DSP Interferometric Refractometer, Wyatt Technology). ^{1}H NMR (400 MHz) spectroscopy was carried out on a Varian Mercury plus 400 NMR spectrometer using $CDCl_3$ or DMSO-d_6 as solvent. Fourier transform infrared (FTIR) spectra were recorded on a PE Paragon 1000 spectrometer (film or KBr disk). Fluorescence spectra were measured with a RF-5301PC fluorophotometer (Shimadzu Corp.).

Synthesis of hyperbranched poly(glycidyl methacrylate) (HPGMA) *via* RAFT-SCVP (SHP-1)

A series of polymerizations at different feed ratios (γ, [GMA] : [ACDT]) and monomer concentrations were conducted at 75 °C as denoted in Table 1. In a typical polymerization procedure (γ = 30 : 1, [GMA] = 10 M), ACDT (0.4 g, 1 equiv.), GMA (3.7 g, 30 equiv.) and AIBN (11 mg, 0.077 equiv.) were dissolved in 2.6 mL 1,4-dioxane in a 10 mL round bottom flask sealed with a rubber stopper. After the solution was bubbled for 30 min in an ice bath for complete deoxygenation, the polymerization was triggered in a 75 °C thermostatic oil bath. After being vigorously stirred for 2 h, the reaction was instantly quenched into liquid nitrogen. After thawing, the solution was diluted with another 8 mL 1,4-dioxane and precipitated into 200 mL freezing methanol. The precipitates were dried *in vacuo* at 45 °C to afford 3.5 g dried HPGMA with a yield of 86%. The sample of entry 5 in Table 1 was used for subsequent modifications. The as-obtained HPGMA was subjected to GPC and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, CDCl3): 4.30 ($COOCH_2CHO$, $COOCH_2CH_2OCO$), 3.73 ($COOCH_2CHO$), 3.20 ($COOCH_2CHO$, $S{=}CSCH_2(CH_2)_{10}CH_3$), 2.80 and 2.66 (–$CH_2O$– in epoxide ring), 2.2–1.4 (main chain proton), 1.24 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 0.98 (methyl protons on main chain), 0.8 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of hyperbranched poly(2-hydroxy-3-azidopropyl methacrylate) (HPHAzMA or SHP-2) *via* azidation of HPGMA

The azidation was conducted according to previous publications on linear poly(glycidyl methacrylate) (PGMA).[10,11] The azidation could be catalyzed by either ammonium chloride or sodium bicarbonate. In a typical procedure, SHP-1 (1.3 g, 1 equiv.), sodium azide (1.47 g, 3 equiv.) and ammonium chloride (1.37 g, 3 equiv.) were mixed in 21 mL DMF in a 50 mL round bottom flask sealed with a rubber stopper and stirred in an ice bath for 30 min to prevent possible side reactions. Then the flask was immersed and stirred in a 50 °C thermostatic oil bath for 24 h. The solution was then precipitated into 200 mL deionized water. The precipitates were dried *in vacuo* at 40 °C overnight to give 1.5 g HPHAzMA (SHP-2) at a yield of 91%. ^{1}H NMR (400 MHz, DMSO-d_6): 5.44 (hydroxy proton), 3.87 ($COOCH_2CH(OH)CH_2N_3$), 3.35 ($COOCH_2CH(OH)CH_2N_3$), 2.20–1.40 (main chain proton), 1.23 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 0.92 (methyl protons on main chain), 0.76 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of hydrophilic dendritic brushes (SHP-3)

In a typical procedure, a 10 mL Schlenck flask was charged with SHP-2 (50 mg, 1 equiv.), PEG-Alk (270 mg, 2 equiv.), PMDETA (56 μL, 1 equiv.) and 2 mL DMF and deoxygenated by a pure N_2 purge for 15 min under stirring. Then CuBr (23 mg, 0.625 equiv.) was added into the flask under the protection of a N_2 purge. After another 15 min deoxygenation, the sealed flask

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Table 1 Selected conditions and results for RAFT-SCVP of ACDT and GMA

Entry	γ^a	$[GMA]^b$ (mol L^{-1})	Time (h)	$M_n{}^c$	$M_w{}^c$	$M_p{}^c$	PDI^c
1	30	5	65	42 700	173 700	112 900	4.06
2	30	5.5	38	35 500	90 100	99 200	2.53
3	30	6.5	20	31 600	96 300	104 800	3.04
4	30	6.5	11.5	39 600	86 000	98 900	2.17
5	30	10	2.5	18 200	31 100	27 500	1.71
6	30	20	1.67	19 900	40 000	33 800	2.01
7	15	1	45	9200	15 200	14 100	1.66
8	15	3	9	15 000	33 200	29 000	2.21
9	15	5	5	16 700	35 200	30 200	2.11
10	5	1	21	10 100	21 300	14 800	2.10
11	5	2	6	7400	12 300	8800	1.66
12	5	3.5	4	7500	12 400	9800	1.65
13	5	6.5	2	7700	13 200	11 200	1.70

^{a} Feed molar ratio of GMA to ACDT. ^{b} Concentration of initial GMA. ^{c} Number-averaged molecular weight (M_n), weight-averaged molecular weight (M_w), peak value of M_n (M_p), and polydispersity index (PDI) determined by GPC.

was put into a 50 °C thermostatic oil bath. After 32 h, the reaction was stopped and passed through a column of neutral alumina to remove copper. The obtained solution was precipitated into 20 mL diethyl ether twice. After being dried *in vacuo* at 40 °C overnight, the product of hydrophilic dendritic brush was obtained and characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, $CDCl_3$): 7.91 (methine proton on triazole ring), 4.19 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 3.66 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 3.63 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 3.36 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 2.62 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 1.24 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 0.81 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of hydrophobic dendritic brushes (SHP-4)

In a typical procedure, SHP-2 (0.8 g, 1 equiv.), palmitic acid (2.1 g, 2 equiv.) and DMAP (0.1 g, 0.2 equiv.) were mixed with 8 mL DMF in a 25 mL round bottom flask in an ice bath. A solution of EDCI (1.58 g, 2 equiv.) in 5 mL DMF was then added dropwise into the flask. The mixture was stirred for 30 min before being put into a 60 °C thermostatic oil bath. After 36 h of reaction, the solution was poured into 80 mL deionized water to remove excess EDCI and any byproducts. The precipitate was dehydrated in a vacuum freeze-drier and redissolved in 3 mL chloroform. The solution was then precipitated in 30 mL DMF. The final precipitate was dried *in vacuo* at 55 °C overnight to give the product of clickable hydrophobic dendritic brush with a yield of 63%. The product was subject to FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, CDCl3): 5.18 (methine proton near azido group), 4.40–3.80 ($COOCH_2CH2OCO$, $COOCH_2CHCH_2N_3$), 3.60–3.50 ($CHCH_2N_3$), 2.37 ($OCOCH_2CH_2(CH_2)_{13}CH_3$), 1.65 ($OCOCH_2CH_2(CH_2)_{13}CH_3$), 1.31 ($OCOCH_2CH_2(CH_2)_{13}CH_3$ and $S{=}CSCH_2(CH_2)_{10}CH_3$) 1.04 (methyl protons on main chain), 0.90 ($OCOCH_2CH_2(CH_2)_{13}CH_3$ and $S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of amphiphilic dendritic hetero-brushes (SHP-5)

In a typical procedure, SHP-4 (80 mg, 1 equiv.), PEG-Alk (240 mg, 2.5 equiv.) and PMDETA (37.12 μL, 1 equiv.) were mixed with 3 mL chloroform in a 10 mL Schlenck flask and purged with N_2 for 15 min. Afterwards, CuBr (16 mg, 0.625 equiv.) was added under the protection of a N_2 purge. After another 15 min deoxygenation, the sealed flask was stirred at 40 °C for 36 h. The solution was then precipitated into 15 mL diethyl ether. The obtained precipitate was dried *in vacuo* at 40 °C overnight. The product of amphiphilic dendritic hetero-brush (SHP-5) was characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, $CDCl_3$): 8.11 (methine proton on triazole ring), 3.66 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 3.34 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 2.67 ($NCCH_2OCOCH_2CH_2COOCH_2CH_2(OCH_2CH_2)_nOCH_3$), 1.26 ($OCOCH_2CH_2(CH_2)_{13}CH_3$ and $S{=}CSCH_2(CH_2)_{10}CH_3$), 0.85 ($OCOCH_2CH_2(CH_2)_{13}CH_3$ and $S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of SHPs with azide + alkene orthogonal functionality (SHP-6)

In a typical procedure, SHP-2 (50 mg, 1 equiv.), 4-pentenoic acid (129 mg, 5 equiv.), DCC (265.75 mg, 5 equiv.) and DMAP (15.7 mg, 0.5 equiv.) were dissolved in 2 mL DMF in a 10 mL round bottom flask containing a Teflon-coated stir-bar. After being purged with N_2 for 20 min, the flask was sealed and stirred at room temperature for 40 h. After filtration, the solution was then precipitated into 20 mL ethanol. The precipitate was redissolved in 0.5 mL chloroform and precipitated into 10 mL ethanol again. After being dried *in vacuo* at room temperature for 30 min, the product was characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, $CDCl_3$): 5.85 ($CH_2CH{=}CH_2$), 5.20–5.04 ($CHCH_2N_3$ and $CH_2CH{=}CH_2$), 4.40–3.80 ($COOCH_2CH_2OCO$, $COOCH_2CHCH_2N_3$), 3.70–3.30 ($COOCH_2CHCH_2N_3$), 2.70–2.30 ($OCOCH_2CH_2CH{=}CH_2$), 1.27 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 1.04 (methyl protons on main chain), 0.84 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of SHPs with azide + alkyne hetero functionality (SHP-7)

In a typical procedure, SHP-2 (53.5 mg, 1 equiv.), 4-pentynoic acid (159 mg, 5 equiv.), DCC (284.4 mg, 5 equiv.) and DMAP (16.8 mg, 0.5 equiv.) were dissolved in 2 mL DMF in a 10 mL round bottom flask containing a Teflon-coated stir-bar. After being purged with a

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nitrogen flow in an ice bath, the solution was left to react for 36 h at room temperature. After filtration to remove undissolved DCU, the solution was precipitated into a 10-fold excess of ethanol. The centrifuged precipitate was redissolved in 0.5 mL chloroform and precipitated into a 10-fold excess of hexane. The product was dried *in vacuo* at room temperature for 10 min and characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, $CDCl_3$): 5.25 ($CHCH_2N_3$), 4.17–4.05 ($COOCH_2CH_2OCO$, $COOCH_2CHCH_2N_3$), 2.66–2.56 ($OCOCH_2CH_2C{\equiv}CH$), 2.11 ($CH_2{\equiv}CH$), 1.27 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 1.04 (methyl protons on main chain), 0.84 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Synthesis of SHPs with azide + pyrene hetero functionality (SHP-8)

In a typical procedure, SHP-2 (50 mg, 1 equiv.), 1-pyrenebutyric acid (150 mg, 2 equiv.), EDCI (100 mg, 2 equiv.) and DMAP (7 mg, 0.2 equiv.) was dissolved in 1.5 mL DMF in a 10 mL round bottom flask containing a Teflon-coated stir-bar. After 36 h of reaction at 60 °C, the solution was poured into 20 mL deionized water to remove excess EDCI and any byproducts. The precipitate was dehydrated in a vacuum freeze-drier and redissolved in 1 mL chloroform. The solution was then precipitated in 30 mL ethyl acetate. The purification was repeated ten times to completely remove excess 1-pyrenebutyric acid. The final precipitate was dried *in vacuo* at 55 °C overnight. The product of SHP-8 was characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, $CDCl_3$): 8.5–7.3 (aromatic hydrogens on the pyrene moiety), 5,07 ($CHCH_2N_3$), 4.3–3.5 ($COOCH_2CH_2OCO$, $COOCH_2CHCH_2N_3$), 3.4–3.0 (pyrene–$CH_2CH_2CH_2COOCH$, $COOCH_2CHCH_2N_3$, $SCH_2(CH_2)_9CH_3$), 2.31 (pyrene–$CH_2CH_2CH_2COOCH$), 1.97 (pyrene–$CH_2CH_2CH_2COOCH$), 1.27 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 1.04 (methyl protons on main chain), 0.87 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

Thiol–epoxy click chemistry on SHP-1

A series of functional thiols were selected to click with SHP-1 in the presence of TEA as catalyst. In the general procedure, a 10 mL round bottom flask, immersed in an ice-water bath, was charged with SHP-1 (1 equiv.), solvent (20 equiv.), functional thiol (2 equiv.) and TEA (2 equiv.) under a nitrogen purge. After 30 min of cooling, the flask was transferred into a 40 °C thermostatic oil bath and reacted for 24 h. The product was purified *via* precipitation and dried *in vacuo*. Final products (SHP-9 to SHP-15 in Scheme 2) were characterized *via* ^{1}H NMR analysis to investigate conversion. Solvents and precipitating agents varied according to different thiols (Table S1†).

"Thiol–epoxy + thiol–ene" sequential click chemistry on SHP-1

SHP-14 with pendant hydroxyl + alkene functionality was further reacted with thiols by thiol–ene click chemistry. Typically, SHP-14 (20 mg), functional thiol (20 equiv.) and DMPA (0.02 equiv.) were mixed into a sealed round bottom flask containing a Teflon-coated stir-bar in DMF (~2 mL). The solution was purged with nitrogen for 30 min before irradiated under a 365 nm UV lamp for 12 h. Afterwards, the solution was precipitated into a 10-fold excess of diethyl ether. The product was dried *in vacuo* at room temperature for 1 h and subject to ^{1}H NMR analysis.

"Thiol–epoxy + Menschutkin + CuAAC" sequential click chemistry on SHP-1

SHP-15 with pendent tertiary amine + hydroxyl hetero functionality was subsequently reacted with propargyl bromide and 1-(allyloxy)-3-azidopropan-2-ol. 1 mL DMF and SHP-15 (50 mg, 1 equiv.) were added to a 10 mL round bottom flask immersed in an ice-bath. Propargyl bromide (43.25 mg, 2 equiv.) was added dropwise into the solution. The flask was sealed with a rubber septum and stirred at room temperature for 24 h. Afterwards, the solution was precipitated into 10 mL diethyl ether. The precipitate was dried *in vacuo* at room temperature overnight. The obtained product of SHP-15a was characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, DMSO-d_6): 5.22 (hydroxy proton), 4.60 ($CH_2C{\equiv}CH$), 4.11 ($CH_2C{\equiv}CH$), 3.89 ($OCOCH_2CH(OH)CH_2$), 3.21 ($N(CH3)_2$), 2.66 ($SCH_2CH_2CH_2N(CH_3)_2$ and $CH_2SCH_2CH_2CH_2N(CH_3)_2$), 2.06 ($SCH_2CH_2CH_2N(CH_3)_2$). 1.23 ($S{=}CSCH_2(CH_2)_{10}CH_3$), 0.82 ($S{=}CSCH_2(CH_2)_{10}CH_3$).

1 mL DMF, SHP-15a (50 mg, 1 equiv.), 1-(allyloxy)-3-azidopropan-2-ol (40.26 mg, 2 equiv.), PMDETA (27 μL, 1 equiv.) were added to a 10 mL Schlenck flask. The flask was purged with nitrogen for 15 min. Afterwards, CuBr (9.23 mg, 0.5 equiv.) was instantly added into the flask under the protection of a nitrogen purge. After another 15 min deoxygenation, the flask was sealed and left to stir for 24 h at room temperature. The solution was then precipitated into 10 mL diethyl ether. The precipitate was redissolved in 0.5 mL DMF and precipitated again into 10 mL diethyl ether. The as-obtained product of SHP-15b was dried *in vacuo* at room temperature for 1 h and characterized by FTIR and ^{1}H NMR analyses. ^{1}H NMR (400 MHz, DMSO-d_6): 8.43 (methine proton on triazole ring), 5.89 ($OCH_2CH{=}CH_2$), 5.53–5.24 (hydroxy proton, $OCH_2CH{=}CH_2$, $N(CH_3)_2CH_2N$), 4.10–3.65 ($OCH_2CH{=}CH_2$, $COOCH_2CH(OH)CH_2$), 3.40 ($CH_2OCH_2CH{=}CH_2$), 3.08 ($N(CH_3)_2$), 2.75–2.53 ($CH_2SCH_2CH_2CH_2$), 2.13 ($SCH_2CH_2CH_2$).

Results and discussion

Synthesis of HPGMAs (SHP-1) *via* RAFT-SCVP of GMA and ACDT

To obtain a multifunctional scaffold of SHP, we selected GMA possessing a highly reactive epoxy group as a co-monomer to conduct RAFT-SCVP with ACDT (Scheme 1).[7,12,13] A series of copolymerizations at different γ values, feed ratios of [GMA] to [ACDT], and monomer concentrations were conducted to investigate their influence. The results are summarized in Table 1. Generally, a higher monomer concentration accelerates the copolymerization. For example, to reach a similar number-averaged molecular weight (M_n) (*ca.* 1.8–1.9 kg mol^{-1}) for polymerizations at γ 30, it takes 2.5 h at [GMA] 10 M and 1.67 h at [GMA] 20 M. Besides, a higher γ value leads to a larger M_n. When polymerized at the same GMA concentration of 6.5 M, M_ns of HPGMAs increase from 7.7 kg mol^{-1} to 39.6 kg mol^{-1} as the γ increases from 5 to 30. When polymerized at the same GMA concentration of 5 M, the M_n of HPGMAs increase from

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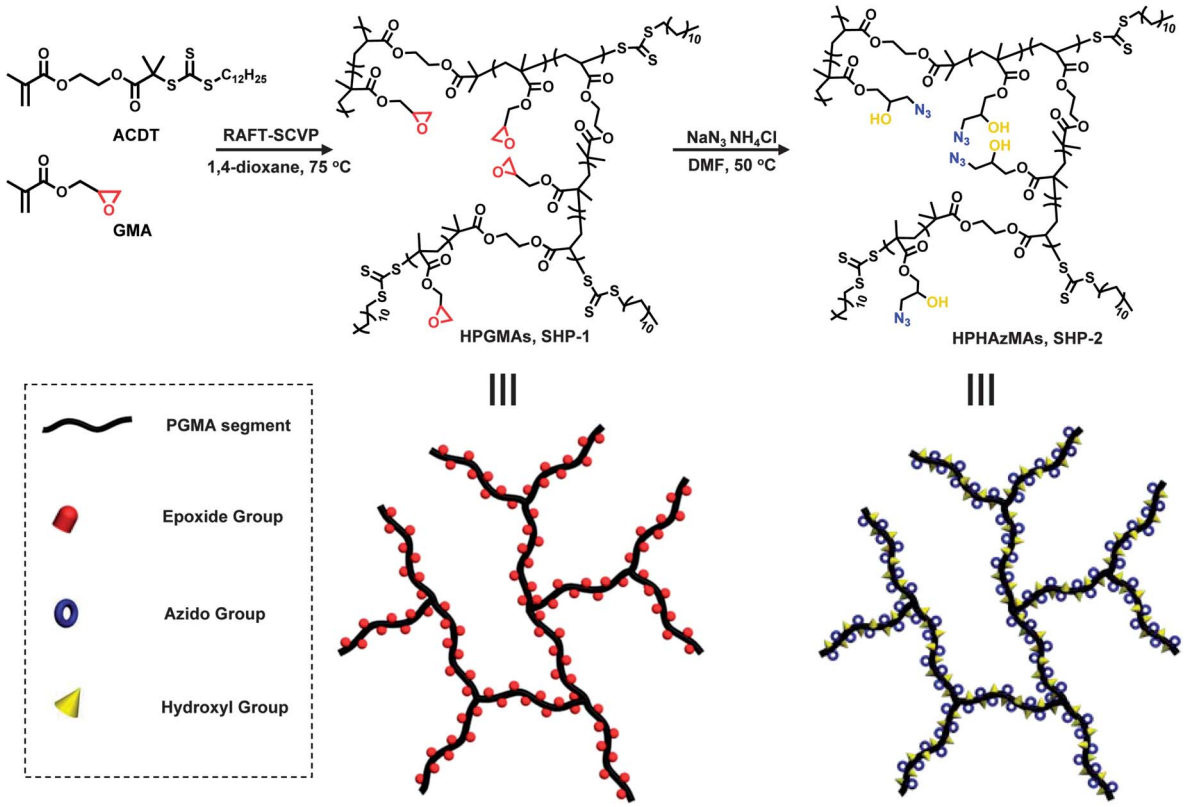

Scheme 1 Synthesis of HPGMAs (SHP-1) *via* RAFT-SCVP and HPHAzMAs (SHP-2) *via* azidation.

16.7 kg mol^{-1} to 42.7 kg mol^{-1} as the γ increases from 15 to 30. On the whole, the M_n of HPGMA at $\gamma = 5$ only fluctuate around 7 kg mol^{-1}, the M_n of HPGMA at $\gamma = 15$ fluctuates around 15 kg mol^{-1} and the M_n of HPGMA at $\gamma = 30$ ranges from 20 kg mol^{-1} to 40 kg mol^{-1}. To detect the possible absolute molecular weights, typical samples were characterized through the GPC-MALLS system (Table S2†), and it was found that the molecular weights are obviously larger than the apparent values.

Fig. 2a is the ^{1}H NMR spectrum of HPGMA polymerized at $\gamma = 30$ and [GMA] of 10 M. The disappearance of the double bond signal at 5–6 ppm indicates the complete consumption of the two kinds of co-monomers. The two peaks at 4.3 and 3.8 ppm represent the signal of the methene protons near the oxirane ring. The mono peak at 3.2 ppm is the signal of the methine proton on the oxirane ring. The two mono peaks at 2.8 and 2.6 ppm are the signals of the methene on the oxirane ring.

Real-time analysis for RAFT-SCVP of HPGMAs (SHP-1)

To further understand the microscopic mechanism and to achieve segment regularity, we conducted kinetics studies of copolymerizations at $\gamma = 30$, 15, and 5. The method is to sample a moderate amount of reacting solution for instant ^{1}H NMR and GPC analyses without precipitation. On the ^{1}H NMR spectra of samples at each time point, signals of double bonds at 6.4–5.5 ppm gradually grew weaker and the methyl proton signal of GMA shifted to 1.08 ppm as the polymerization proceeded (Fig. S1–S3†). The combination of these two kinds of signal change enables the calculations for the conversion of GMA (C_{GMA}), conversion of ACDT (C_{ACDT}) and total conversion of GMA and ACDT (C_{total}) at each time point. The trend of

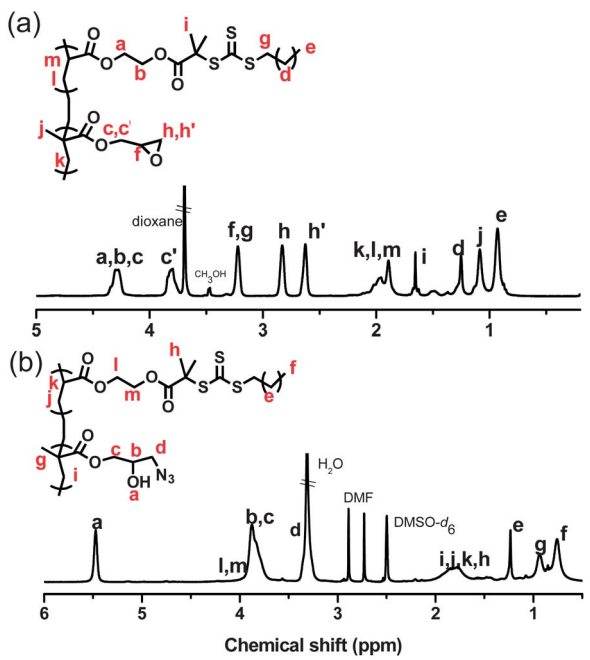

Fig. 2 (a) ^{1}H NMR spectrum of HPGMAs (SHP-1). (b) ^{1}H NMR spectrum of HPHAzMAs (SHP-2).

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molecular weight growth was monitored by GPC characterization. Notably, although the data only represent the apparent value given the nature of GPC calibration, we consider them suitable for horizontal comparison.

The study for $\gamma = 30$ was conducted at an initial [GMA] of 6.5 M (Fig. 3a and Table 2). After 20 min of polymerization, polymers with a M_n of 8.7 kg mol^{-1} formed at a C_{total} of 19.1%. Afterwards, M_n gradually grew to 20.7 kg mol^{-1} as the C_{total} rose to 97.3% at 6.5 h, during which the GPC curves kept within monomodal distributions. During the later 5.5 h, the C_{total} hardly increased while the M_n rapidly expanded to 31.1 kg mol^{-1} (Fig. 3b). This behavior was in accordance with the polycondensation nature of SCVP.[7,13] After 6.5 h of polymerization, a shoulder peak appeared on the GPC curves, indicating the part coupling between the formed macromolecules because of the high viscosity. Notably, at each time point during the whole process, C_{GMA} and C_{ACDT} increase almost at the same rate and the actual unit ratio "*m*" of GMA to ACDT in the polymer kept constant around 30, equal to the feed ratio γ. This fact means that the segments formed in SHPs at this feed ratio are relatively regular and between every two branching points there are approximately 30 GMA units. In this case, the resulting SHP has a similar architecture to HyperMacs synthesized from narrow-polydispersed AB_2 macromonomers.[3,7] For comparison, we also performed investigations on the kinetics of copolymerizations with $\gamma = 5$ and 15 (Tables S3 and S4, Fig. S1–S5†). Generally, the actual "*m*" is obviously higher than the corresponding γ and changes randomly, suggesting that the activity of GMA is greater than that of ACDT and the segment distribution of the resulting SHP is broad. Therefore, we use the SHP at $\gamma = 30$ for the following multi-functionalization.

Azidation of HPGMAs and synthesis of dendritic brushes

Azidation of GMA using sodium azide, a sort of click chemistry,[14] has been utilized to introduce hydroxyl + azide hetero-functionality for linear PGMA backbones.[10,11] Here, this chemistry is introduced to a hyperbranched system. The generated HPHAzMA (SHP-2) was characterized by ^{1}H NMR and FTIR analyses. In the FTIR spectrum, a strong absorbance representing the valence vibration of azido group at 2112 cm^{-1} was observed (Fig. 4a). In the ^{1}H NMR spectrum, compared to that of HPGMAs, the peaks representing the methene protons next to the ester group, the methine proton and methene protons on the oxirane at 4.3 ppm, 3.8 ppm, 3.2 ppm, 2.8 ppm, 2.6 ppm totally disappeared. Newly emerged signal peaks were observed at 5.4 ppm, 3.8 ppm, 3.5 ppm representing the hydroxy proton, methine proton/methene protons near the ester group and the methene protons near the azido group (Fig. 2b), denoting complete ring opening. Due to the orthogonality of the adjacent hydroxy and azido groups, the HPHAzMAs could undergo esterification and CuAAC[15] independently. Potentially, the azido group could be transformed into an amino group *via* Staudinger reduction,[16] and might extend the SHPs' applicability into biosystems *via* Staudinger conjugation.[17]

Based on the orthogonality of HPHAzMAs (SHP-2), two kinds of dendritic brushes, *i.e.*, a hydrophilic dendritic brush (SHP-3) and a hydrophobic dendritic brush (SHP-4) were synthesized, either by CuAAC or EDCI esterification. Moreover, a kind of amphiphilic dendritic hetero-brush (SHP-5), was synthesized for the fist time. The synthesis protocol is depicted in Scheme 2. The hydrophilic dendritic brush (SHP-3) was synthesized *via* CuAAC between HPHAzMAs and PEG-Alk. In the ^{1}H NMR spectrum (Fig. 4b), the signal at 3.62 ppm represents the methene protons of the PEG backbone and the peak at 7.91 ppm represents the methine proton of the formed triazole ring. In the FTIR spectrum of SHP-4 (Fig. 4a), the valence vibration absorbance at ~2100 cm^{-1} completely disappeared, indicating 100% conversion of the click coupling. Likewise, SHP-4 was synthesized *via* EDCI esterification between HPHAzMAs and palmitic acid. The reaction temperature was maintained at 60 °C for higher reactivity. In its ^{1}H NMR spectrum (Fig. 4c), the previous hydroxy proton at 5.4 ppm disappeared and a new peak

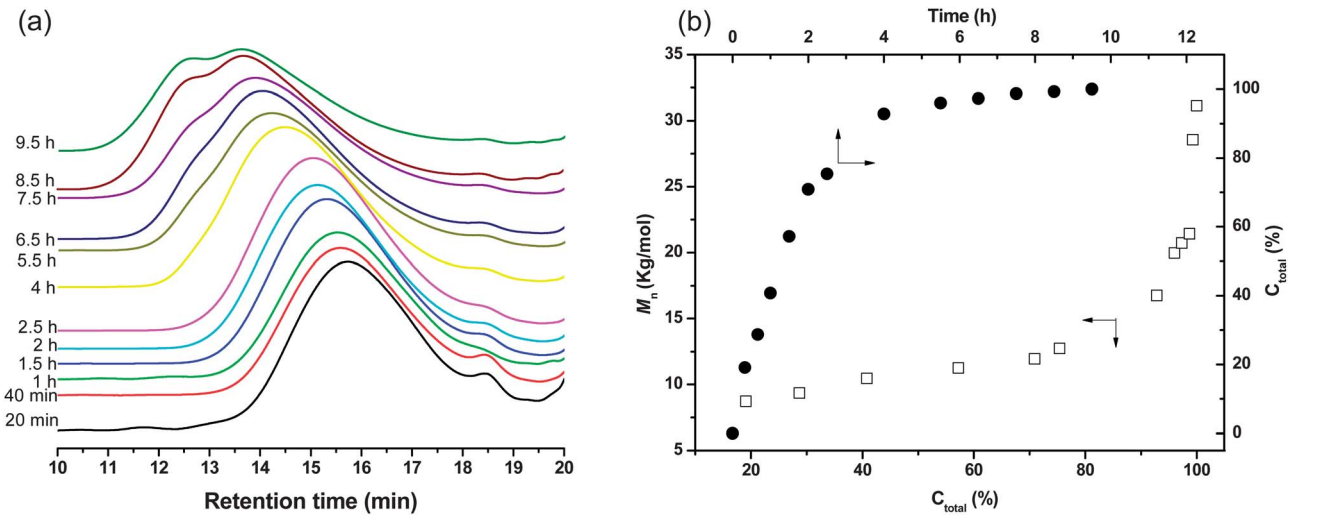

Fig. 3 Polymerization results for RAFT-SCVP of GMA and ACDT at a feed ratio of 30 : 1. (a) GPC traces of HPGMAs at different reaction times. The samples for ^{1}H NMR and GPC measurements were characterized without purification. (b) Hollow black squares (□): molecular weight (M_n) as a function of total vinyl group convertion (C_{total}); filled black circles (●): C_{total} as a function of polymerization time.

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Table 2 Synthesis of HPGMAs by RAFT-SCVP of ACDT and GMA at a feed ratio of 30

Entry	Time (h)	C_{GMA}[a] (%)	C_{ACDT}[a] (%)	C_{total}[b] (%)	m[c]	DB[d]	M_n[e]	M_w[e]	M_p[e]	PDI[e]
1	0	—	—	—	—	—	—	—	—	—
2	0.33	19.2	16.3	19.1	35.4	0.0275	8700	12 200	12 100	1.39
3	0.67	28.9	24.6	28.7	35.2	0.0276	9300	13 700	13 400	1.46
4	1	41.0	35.7	40.8	34.5	0.0282	10 400	14 500	13 900	1.39
5	1.5	57.7	49.5	57.2	35.1	0.0278	11 200	16 300	15 500	1.45
6	2	71.2	63.2	70.9	33.8	0.0287	11 900	18 100	17 100	1.51
7	2.5	75.6	69.3	75.4	32.7	0.0296	12 700	19 200	17 900	1.51
8	4	93.0	89.2	92.8	30.0	0.0310	16 700	27 100	24 700	1.61
9	5.5	96.2	92.3	96.0	30.0	0.0310	19 900	33 300	29 100	1.67
10	6.5	97.4	94.2	97.3	31.0	0.0312	20 700	37 800	32 300	1.83
11	7.5	98.7	97.3	98.7	30.4	0.0318	21 400	42 700	35 200	1.99
12	8.5	99.3	98.2	99.3	30.3	0.0319	28 500	57 400	40 900	2.01
13	9.5	100	100	100	29.9	0.0322	31 100	65 100	42 400	2.09

[a] Conversions of GMA (C_{GMA}) and ACDT (C_{ACDT}) determined from ^{1}H NMR analysis. [b] Total conversion of vinyl groups, $C_{total} = (30 \times C_{GMA} + C_{ACDT})/31$. [c] Unit ratio of GMA to ACDT in polymers, calculated from ^{1}H NMR results. [d] Degree of branching (DB) calculated from ^{1}H NMR results.[5] [e] Number-averaged molecular weight (M_n), weight-averaged molecular weight (M_w), peak value of M_n (M_p), and polydispersity index (PDI) determined by GPC.

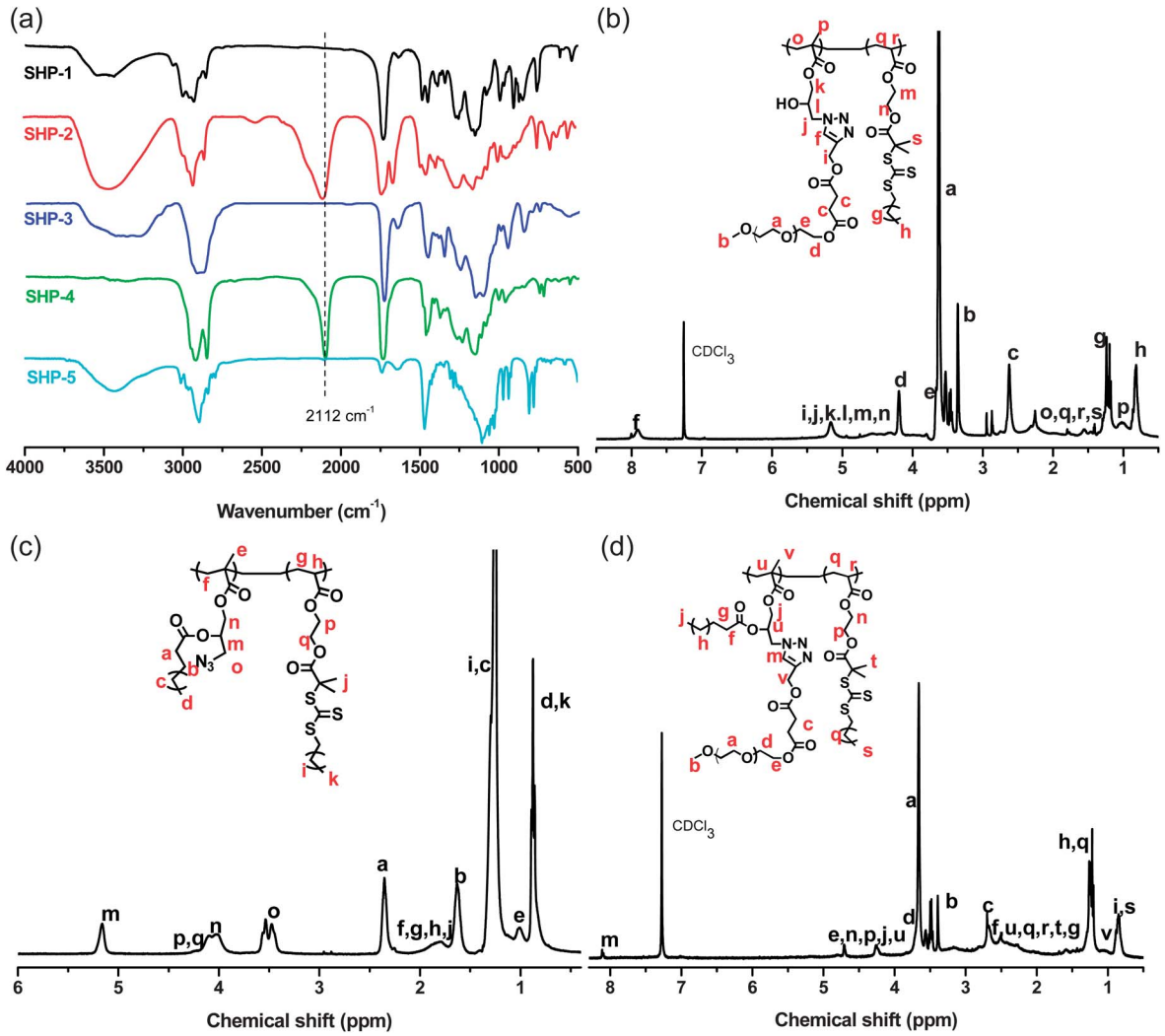

Fig. 4 (a) FTIR spectra of SHP-1, SHP-2, SHP-3, SHP-4 and SHP-5. (b) ^{1}H NMR spectrum of hydrophilic dendritic brushes (SHP-3). (c) ^{1}H NMR spectrum of hydrophobic dendritic brushes (SHP-4). (d) ^{1}H NMR spectrum of amphiphilic dendritic hetero-brushes (SHP-5).

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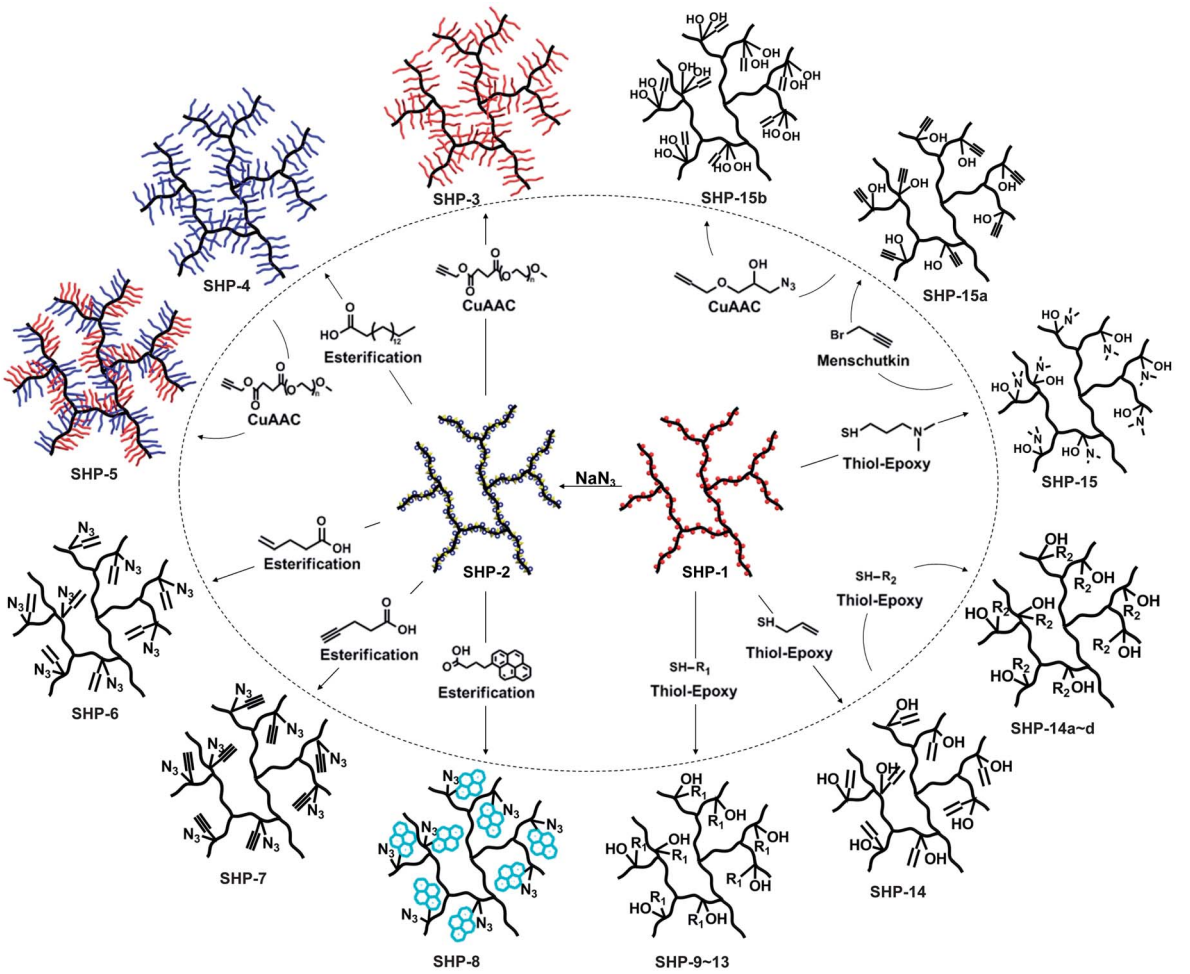
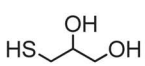
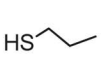
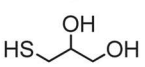
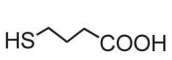
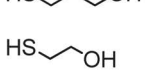
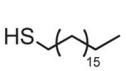
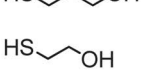
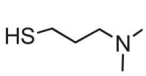
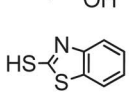
appeared at 5.18 representing the methine proton near the ester group. The double peak at ~4.1 ppm represents the methene group that belongs to the GMA part. The double peak at ~3.5 ppm represents the methene group near the azide. The integration ratio of these three signals is exactly 1 : 2 : 2, indicating 100% conversion for the esterification. Signals at 2.37 ppm, 1.65 ppm, 1.32 ppm and 0.9 ppm belong to the aliphatic chains. In the FTIR spectrum (Fig. 4a), absorbance at ~2100 cm^{-1} represents the remaining azido group after esterification and the absorbance at ~3500 cm^{-1} almost disappeared, indicating the consumption of the hydroxyl group. Previously, linear hetero-brushes[11,18] and hyperbranched hetero-brushes[19] have been reported. Herein, we report the first synthesis of amphiphilic dendritic hetero-brushes (SHP-5) *via* CuAAC chemistry between SHP-3 and PEG-Alk. Its FTIR spectrum and ^1H NMR spectrum are displayed in Fig. 4a and d. The signal at 3.66 ppm represents the methene protons of PEG backbones, the peak at 8.12 ppm represents the methine proton of the triazole ring and the signals at 1.2 and 0.9 ppm represent the aliphatic chains (Fig. 4d). In the FTIR spectrum, the absorbance at ~2100 cm^{-1} completely disappeared, indicating the full consumption of the azido group.

SHPs with azide + alkene hetero-functionality (SHP-6)

Thiol–ene click chemistry[20] has been demonstrated recently as a powerful tool in the chemical synthesis and functionalization of biomacromolecules. To orthogonally employ thiol–ene and



$HS-R_1$	Code	$HS-R_1$	Code	$HS-R_2$	Code	$HS-R_2$	Code
	SHP-9		SHP-12		SHP-14a		SHP-14c
	SHP-10		SHP-13		SHP-14b		SHP-14d
	SHP-11						

Scheme 2 High-density, hetero-functional group engineering of segmented hyperbranched polymers (SHPs).

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CuAAC chemistries to functionalize polymers is an interesting yet challenging topic. Recently, Hawker and coworkers reported alkene + azide chain-end-functionalized linear polymers, alkene–alkyne backbone-functionalized linear polymers, and dendrimers using both thiol–ene chemistry and CuAAC.[21] In this work, we synthesized SHPs with alkene + azide hetero-functionality at each unit of the scaffold (SHP-6), by esterification of SHP-2 and 4-pentenoic acid. In the ^{1}H NMR spectrum of SHP-6 (Fig. 5a), the signals ranging from 6.0 ppm to 4.9 ppm represent the double bond protons and the methine proton near the ester group. The peak at 4.0 ppm represents the methene protons next to the ester group of the GMA part. The signal at 3.4 ppm represents the signal of the methene protons close to the azido group. The double peak at 2.5 ppm represents the methene protons near the ester group of the pentenoic moiety. The integration ratio of "**b**" to "**a** + **c**" equals 1 : 3, and the integration ratio of "**a** + **c**" to "**d** + **h** + **i**" equals 3 : 2, indicating 100% conversion by the esterification. In the FTIR spectrum of SHP-6 (Fig. S6†), the absorbance at ~2100 cm^{-1} indicates the existence of the azido group after esterification and no side reactions between the alkene and azide moieties.

SHPs with azide + alkyne hetero-functionality (SHP-7)

The introduction of complimentary click functional groups for polymer materials is currently an area of great interest because of the self-crosslinkability under mild conditions for the polymer materials.[22] Similar to the case of SHP-6, we synthesized SHPs with full-scaffold alkyne + azide hetero-functionality (SHP-7) *via* esterification of SHP-2 and 4-pentynoic acid. In the ^{1}H NMR spectrum of SHP-7 (Fig. 5b), the peak signal "**d**" at 5.25 ppm represents the methine proton near the ester bond and the signal "**e**" at 4.17–4.05 ppm represents the methene protons beside "**d**". The signal "**a**" at 2.11 ppm represents the alkynyl proton. A conversion of 100% was achieved again since the integration ratio of "**e**" to "**d**" exactly equals 2. In the FTIR spectrum of SHP-7 (Fig. S6†), the adsorption peak at ~2100 cm^{-1} is still strong, and a new peak appeared at ~3300 cm^{-1} assigned to the alkynyl group, indicating that SHP-7 was prepared successfully.

SHPs with azide + pyrene hetero-functionality (SHP-8)

Due to its distinct photochemical and physical properties,[23] pyrene has long been regarded as the fruit fly for photochemists. One key challenge nowadays is to design novel topological structures for improving pyrene's photochemical properties.[24] The pyrene moiety is easy to form excimer, making it popular for use in sensors and probes.[25] Taking advantage of both SHPs' hyperbranched structure and accessible functionalization on the full scaffold, we synthesized clickable and fluorescent macromolecules (SHP-8) *via* esterification of SHP-2 and 1-pyrenebutyric acid at a high conversion (Scheme 2). Fig. 6a shows the ^{1}H NMR spectrum of SHP-8. The peaks around 8.5–7.5 ppm represent the aromatic protons on the pyrene ring, peak "**e**" represents the methine proton near the ester unit, and peaks "**c**" and "**g**" represent the methyl protons next to the pyrene ring and the azide unit, respectively. The integration ratio of "**e**" to "**c** + **g**" is around 1 : 4, denoting the high conversion (~100%) of the esterification. The intact peak at ~2100 cm^{-1} in the FTIR spectrum shown in Fig. 6b indicates the existence of the azido group after esterification. The emission spectra of SHP-8 at various concentrations are displayed in Fig. 7a. The peaks at 377 nm (M_1) and 398 nm (M_2) are from the monomer emission, and the peak at 475 nm (E) is from the dynamic excimer emission.[26] Interestingly, strong dynamic excimer emission but weak monomer emission was observed for SHP-8 in DMF even at the extremely diluted pyrene concentration of 7.0×10^{-9} M. Fig. 7b shows the photograph of SHP-8 before and after excitation at 365 nm, exhibiting that SHP-8 emits visible strong blue light at a

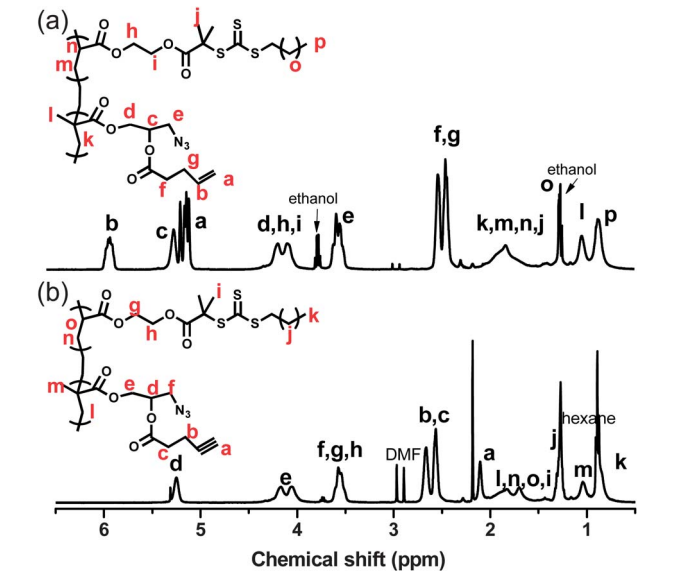

Fig. 5 ^{1}H NMR spectra of SHP-6 (a) and SHP-7 (b).

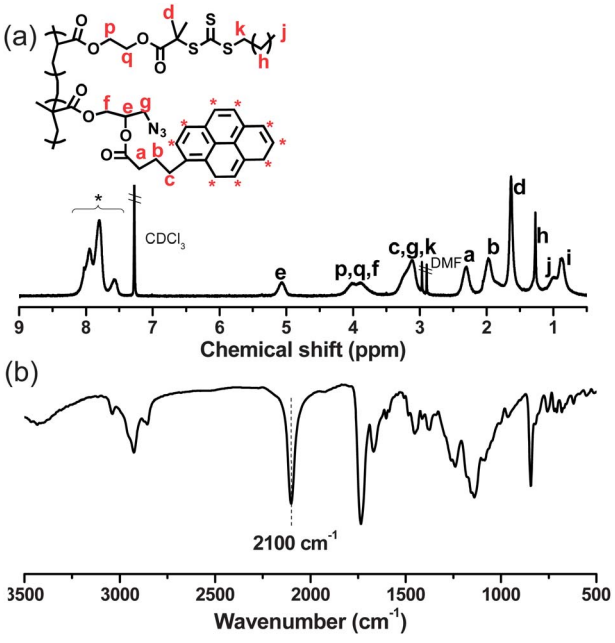

Fig. 6 (a) ^{1}H NMR spectrum of SHP-8. (b) FTIR spectrum of SHP-8.

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concentration of 1.5×10^{-4} M. On the contrary, the precursor of 1-pyrenebutyric acid only has weak static excimer emission[27] at about 425 nm and strong monomer emission at 398 nm, and exhibits no dynamic excimer emission. The emission intensity plots of SHP-8 at 475 nm and 377 nm are displayed in Fig. 7c. Generally both the excimer and monomer emission intensity increase linearly with concentration while the slope for the fitted line at 475 nm (240.0) is much steeper than the slope at 377 nm (36.8). The excimer intensity quickly reached 864 at 3.5×10^{-7} M (note: a higher concentration would lead to a stronger emission intensity and exceeded the maximum of our instrument) while the monomer intensity slowly reached 146. These data declared that high-density immobilization of pyrene on a SHP could result in dramatic red-shift of emission wavelength by about 80–100 nm. The intensity ratio of excimer (475 nm) to monomer (377 nm), I_E/I_{M_1}, is a well-recognized feature for the degree of excimer emission enhancement (Fig. 7c). SHP-8 at a very low pyrene concentration of 7×10^{-9} M has an I_E/I_{M_1} value of 1.73, and as the concentration increased to 3.5×10^{-7} M (still quite low!), the I_E/I_{M_1} value arose to as high as 5.9. According to the increasing trend of the intensity *vs.* concentration plot, I_E/I_{M_1} should become larger at higher concentration. Previously, pyrene-functionalized dendrimers also showed strong dynamic excimer emission with I_E/I_{M_1} of 2.19 at a much higher pyrene concentration of 1.5×10^{-6} M due to the crowded microenvironment.[28] Our results indicate that the microenvironment of SHPs is more crowded and more favorable for excimer formation than those conventional dendritic polymers, promising the wide applications of the fluorescent and clickable SHP.

Hetero functionalization *via* thiol–epoxy click chemistry

As has been explained in a previous review,[20] the mechanism of thiol–epoxy chemistry[29,30] is a nucleophilic ring-opening reaction and could be summarized in three sequential steps: (1) thiolation of the thiols by a base catalyst, (2) alkoxidation of the oxirane ring under attack by thiolate, (3) protonation of the alkoxide. We extended this click chemistry to a hyperbranched system for hetero-functionalization. Seven kinds of thiols were selected to react with HP-1, allyl mercaptan, 1-octadecanethiol, 2-mercaptobenzothiazole, 2-mercaptoethanol, 3-mercapto-1,2-propanediol, propyl mercaptan and 3-(dimethylamino)-1-propanethiol (Scheme 2). The reactions were carried out in mild conditions with TEA as catalyst at 40 °C in organic solvents and the products were characterized by ^{1}H NMR analysis (Fig. 8, S7 and S8†). The absence of the oxirane signals on the ^{1}H NMR spectra proved the 100% conversion of the reaction. Successful attachments of the electron donating 1-octadecanethiol and propyl mercaptan indicate the extremely high reactivity of thiol–epoxy chemistry. *Via* reaction with 2-mercaptoethanol or 3-mercapto-1,2-propanediol, SHPs with higher hydroxyl density (SHP-9 and SHP-10) were synthesized. *Via* reaction with 2-mercaptobenzothiazole, SHPs with a hydroxyl group and a functional benzothiazole ring on each of the repeat units was obtained (SHP-11) with potential application in nonlinear optics (NLO).[31] *Via* reaction with allyl mercaptan and 3-(dimethylamino)-1-propanethiol, SHP-14 and SHP-15 with hydroxyl + alkene and hydroxyl + tertiary amine hetero functionality were gained, which allows sequential click chemistry functionalization by either thiol–ene chemistry or the Menschutkin reaction.[7]

Hetero functionalization of SHPs *via* multiple and sequential click chemistries

The growing demand for more sophisticated polymer design calls for a facile method of multi-step functionalization and functionality transformation. Reports on post-modification *via*

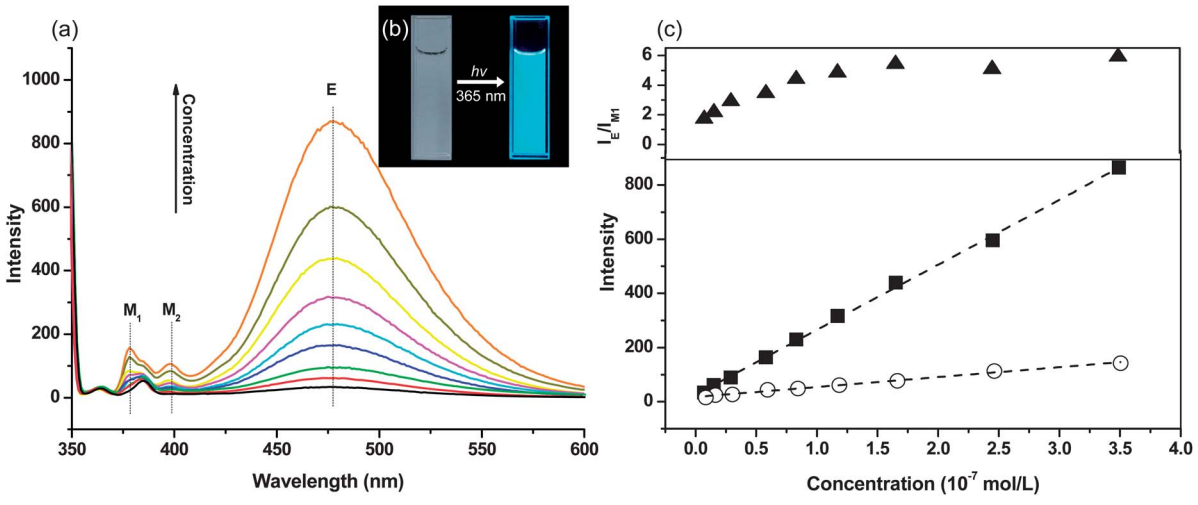

Fig. 7 (a) Fluorescence emission spectra of SHP-8 at pyrene concentration from 7.0×10^{-9} to 3.5×10^{-7} M excited at 344 nm. M_1 and M_2 are monomer emission peaks and E is the excimer emission peak. (b) Photographs of SHP-8 solutions at 1.5×10^{-4} M before and after excitation at 365 nm. (c) Filled black squares (■): pyrene concentration *versus* fluorescence emission intensity at 475 nm of SHP-8. Hollow black circles (○): pyrene concentration *versus* fluorescence emission intensity at 377 nm of SHP-8. Filled black triangle (▲): pyrene concentration *versus* I_E/I_{M_1}.

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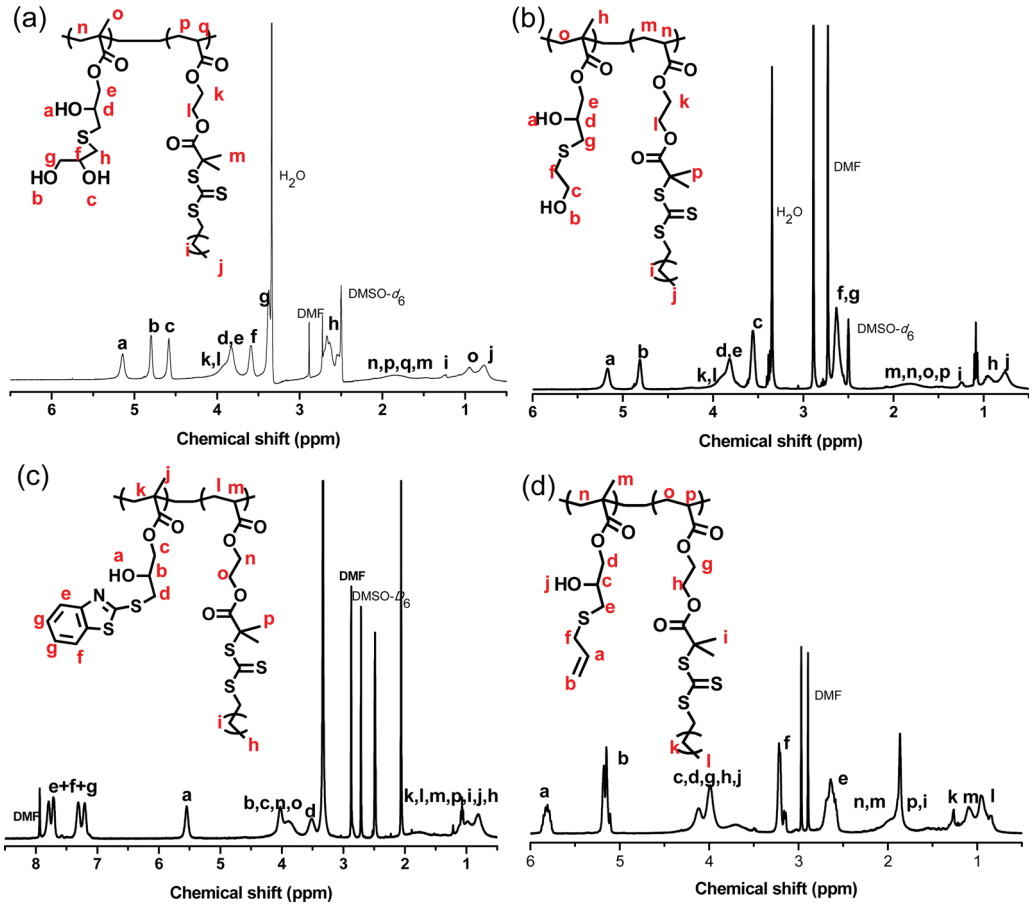

Fig. 8 ^{1}H NMR spectra of SHP-9 (a), SHP-10 (b), SHP-11 (c), and SHP-14 (d).

sequential click chemistry (SCC) at the backbone of linear polymers have been reported.[32] Here, we realized multi-step hetero-functionalization on SHPs *via* two different SCC approaches, "thiol–epoxy + thiol–ene" dual click and "thiol–epoxy + Menschutkin + CuAAC" triple click.

In the dual click chemistry protocol, allyl mercaptan is firstly clicked onto SHP-1 *via* thiol–epoxy click chemistry to generate SHP-14. Subsequently, a collection of functional thiols, including 3-(dimethylamino)-1-propanethiol, 2-mercaptoethanol, 3-mercapto-1,2-propanediol and 3-mercaptopropionic acid, are clicked onto SHP-14 *via* photoradical thiol–ene chemistry (Scheme 2).[33,34] The products were characterized by ^{1}H NMR analysis (Fig. 9). The disappearance of signals ranging from ~5 to ~6 ppm indicates the complete conversion of allyl groups. Possible ring-formation and self-crosslinking were kept to a minimum by keeping the thiols in 20-fold excess for the reaction. Accordingly, the alkenyl groups of SHP-14 were fluently transformed into two hydroxyls, one hydroxyl, carboxyl and tertiary amine groups (SHP-14a–d, Scheme 2).

In the triple click chemistry approach, SHP-1 is firstly clicked with 3-(dimethylamino)-1-propanethiol at a conversion of 100% to form SHP-15. The following reaction of SHP-15 and propargyl bromide *via* Menschutkin quaternization[35] yields SHP-15a. In the FTIR spectrum of SHP-15a (Fig. 10a), an absorption peak at ~2100 cm^{-1} appeared, indicating the successful conjugation of propargyl moiety. In the ^{1}H NMR spectrum of SHP-15a (Fig. 10c), the signal of *N*-methyl groups completely shifted from 2.1 to 3.2 ppm at 100% conversion. This step not only transforms the tertiary amine into an alkyne, but also results in

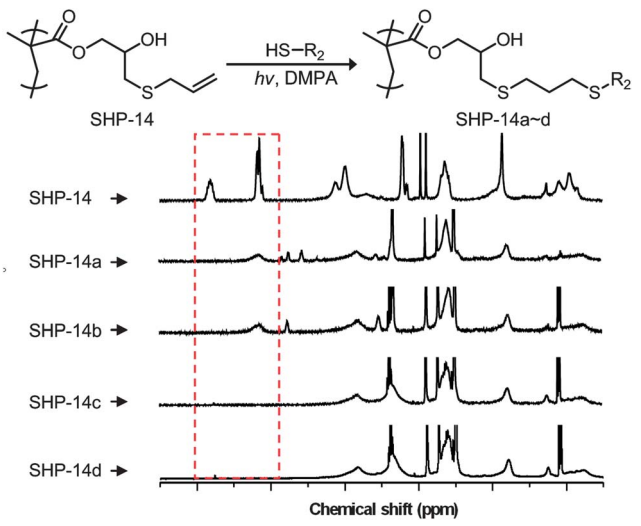

Fig. 9 Hetero-functionalization of SHPs *via* the "thiol–epoxy + thiol–ene" sequential click approach and the ^{1}H NMR spectra of SHP-14a–d.

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a cationic, hydroxy scaffold that is useful in gene-carriers and bio-conjugation.[36] SHP-15a was then reacted with tri-functional 1-(allyloxy)-3-azidopropan-2-ol *via* CuAAC click chemistry, affording SHP-15b with two hydroxy groups and an alkene group on the repeat units. A 100% conversion was achieved again since the alkyne absorption peak at ~2100 cm^{-1} completely disappeared from the corresponding FTIR spectrum (Fig. 10a). The two hydroxyls could be further esterified and the alkene could undergo thiol–ene chemistry, making higher-density functionality possible.

Conclusions

SHPs with an epoxy group at each repeating unit were readily synthesized *via* RAFT-SCVP. With the aid of various highly efficient conjugation chemistries, including "thiol–epoxy + thiol–ene" dual click and "thiol–epoxy + Menschutkin chemistry + CuAAC" triple click approaches, SHPs with high-density hetero-functionality of hydroxyl + azide, dual hydroxyl, triple hydroxyl, hydroxyl + tertiary amine, hydroxyl + alkene, hydroxyl + carboxyl, alkene + azide, alkyne + azide, hydroxyl + alkyne, dual hydroxyl + alkene, *etc.* were obtained. Such sequential click approaches provide a versatile toolbox for post-modification and fabrication of complex macromolecules. Based on the hetero-functional scaffolds, hydrophobic dendritic brushes, hydrophilic dendritic brushes and amphiphilic dendritic hetero-brushes were constructed. By combining their hyper-branched nature and accessible full-scaffold functionalizability, we designed and achieved a new kind of clickable, pyrene-based blue-emitting macromolecules with a very high I_E/I_{M_1} value at low concentration. The resulting polymers with unique topology and special hetero-functionality promise broad applications in bio-conjugation and fine synthesis of multifunctional materials.

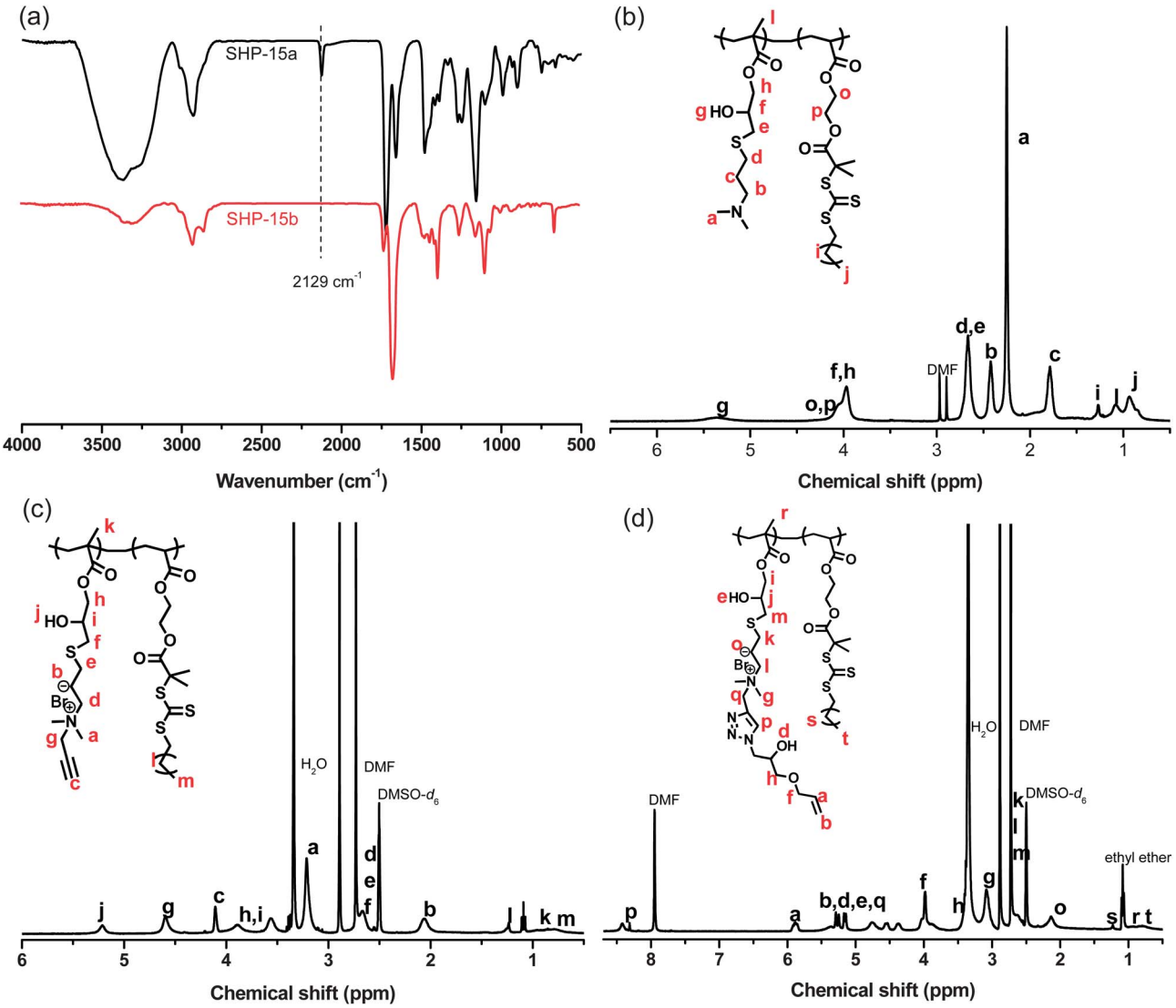

Fig. 10 FTIR spectra of SHP-15a (black curve) and SHP-15b (red curve) (a), and ^{1}H NMR spectra of SHP-15 (b), SHP-15a (c), and SHP-15b (d).

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Notes and references

1 C. Gao and D. Yan, *Prog. Polym. Sci.*, 2004, **29**, 183; D. Yan, C. Gao and H. Frey, *Hyperbranched Polymers: Synthesis, Properties and Applications*, John Wiley & Sons, Hoboken, NJ, 2011; M. Adeli, *Novel Polymers and Nanoscience*, Transworld Research Network, Kerala, India, 2008.

2 B. I. C. R. Voit, *Chimie*, 2003, **6**, 821; M. Calderón, M. A. Quadir, S. K. Sharma and R. Haag, *Adv. Mater.*, 2010, **22**, 190; C. M. Paleos, D. Tsiourvas and Z. Sideratou, *Mol. Pharm.*, 2007, **4**, 169; X. Yu, Z. Liu, J. Janzen, I. Chafeeva, S. Horte, W. Chen, R. K. Kainthan, J. N. Kizhakkedathu and D. E. Brooks, *Nat. Mater.*, 2012, **11**, 468; M. Jikei and M. Kakimoto, *Prog. Polym. Sci.*, 2001, **26**, 1233; Y. Han, C. Gao and X. He, *Sci. China: Chem.*, 2012, **55**, 604.

3 References regarding SHPs synthesized from HyperMacs approach: L. R. Hutchings, J. M. Dodds and S. J. Roberts-Bleming, *Macromolecules*, 2005, **38**, 5970; L. R. Hutchings, *Soft Matter*, 2008, **4**, 2150; L. R. Hutchings, J. M. Dodds and S. J. Roberts-Bleming, *Macromol. Symp.*, 2006, **240**, 56; L. R. Hutchings, J. M. Dodds, D. Rees, S. M. Kimani, J. J. Wu and E. Smith, *Macromolecules*, 2009, **42**, 8675; J. M. Dodds and L. R. Hutchings, *Macromol. Symp.*, 2010, **291–292**, 26; L. Z. Kong, M. Sun, H. M. Qiao and C. Y. Pan, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 454; S. Hilf, F. Wurm and F. M. Kilbinger, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 6932; D. Konkolewicz, C. K. Poon, A. Gray-Weals and S. Perrier, *Chem. Commun.*, 2011, **47**, 239; J. M. Dodds, E. de Luca, L. R. Hutchings and N. Clarke, *J. Polym. Sci., Part B: Polym. Phys.*, 2007, **45**, 2762; N. Clarke, E. de Luca, J. M. Dodds, S. M. Kimani and L. R. Hutchings, *Eur. Polym. J.*, 2008, **44**, 665.

4 References regarding SHPs synthesized from SCVP-ATRP approach: H. Mori, A. H. E. Müller and P. F. W. Simon, in *Hyperbranched Polymers: Synthesis, Properties and Applications*, ed. D. Yan, C. Gao and H. Frey, John Wiley & Sons, Hoboken, NJ, 2011, ch. 5; A. Pfaff and A. H. E. Müller, *Macromolecules*, 2011, **44**, 1266; S. Muthukrishnan, G. Jutz, X. Andre, H. Mori and A. H. E. Müller, *Macromolecules*, 2005, **38**, 9; S. Muthukrishnan, D. P. Erhard, H. Mori and A. H. E. Müller, *Macromolecules*, 2006, **39**, 2743; C. Gao, S. Muthukrishnan, W. Li, J. Yuan, Y. Xu and A. H. E. Müller, *Macromolecules*, 2007, **40**, 1803; H. Mori, D. C. Seng, H. Lechner, M. Zhang and A. H. E. Müller, *Macromolecules*, 2002, **35**, 9270; S. Muthukrishnan, H. Mori and A. H. E. Müller, *Macromolecules*, 2005, **38**, 3108; H. Mori, A. Walther, X. André, M. G. Lanzendörfer and A. H. E. Müller, *Macromolecules*, 2004, **37**, 2054; M. Rikkou-Kalourkoti, K. Matyjaszewski and C. S. Patrickios, *Macromolecules*, 2012, **45**, 1313; C. Cheng, K. L.Wooley and E. Khoshdel, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 4754; C. Gao and X. Zheng, *Soft Matter*, 2009, **5**, 4788.

5 References regarding SHPs synthesized from SCVP-RAFT approach: C. B. Zhang, Y. Zhou, Q. Liu, S. X. Li, S. Perrier and Y. L. Zhao, *Macromolecules*, 2011, **44**, 2034; A. P. Vogt, S. R. Gondi and B. S. Sumerlin, *Aust. J. Chem.*, 2007, **60**, 396; A. P. Vogt and B. S. Sumerlin, *Macromolecules*, 2008, **41**, 7368; S. Carter, S. Rimmer, A. Sturdy and M. Webb, *Macromol. Biosci.*, 2005, **5**, 373; S. Carter, B. Hunt and S. Rimmer, *Macromolecules*, 2005, **38**, 4595; S. Carter, S. Rimmer, R. Rutkaite, L. Swanson, J. P. A. Fairclough, A. Sturdy and M. Webb, *Biomacromolecules*, 2006, **7**, 1124.

6 References regarding SHPs synthesized from A_2 + B_3 macromonomer approach: A. R. Fornof, T. E. Glass and T. E. Long, *Macromol. Chem. Phys.*, 2006, **207**, 1197; S. Unal, I. Yilgor, J. P. Sheth, G. L. Wilkes and T. E. Long, *Macromolecules*, 2004, **37**, 7081; S. Unal and T. E. Long, *Macromolecules*, 2006, **39**, 2788; M. G. McKee, T. Park, S. Unal, I. Yilgor and T. E. Long, *Polymer*, 2005, **46**, 2011; S. Unal, G. Ozturk, K. Sisson and T. E. Long, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 6285; A. J. Duncan, J. M. Layman, M. P. Cashion, D. J. Leo and T. E. Long, *Polym. Int.*, 2010, **59**, 25.

7 J. Han, S. Li and C. Gao, *Macromolecules*, 2012, **45**, 4966.

8 H. He, Y. Zhang, C. Gao and J. Wu, *Chem. Commun.*, 2009, 1655.

9 K. Iskin, G. Yilmaz and Y. Yagci, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 2417.

10 N. V. Tsarevsky, S. A. Bencherif and K. Matyjaszewski, *Macromolecules*, 2007, **40**, 4439; Y. Zhang, H. He and C. Gao, *Macromolecules*, 2008, **41**, 9581.

11 C. Li, Z. Ge, J. Fang and S. Liu, *Macromolecules*, 2009, **42**, 2916; X. Lian, D. Wu, X. Song and H. Zhao, *Macromolecules*, 2010, **43**, 7434.

12 G. Moad, E. Rizzardo and S. H. Thang, *Aust. J. Chem.*, 2005, **58**, 379; G. Moad, E. Rizzardo and S. H. Thang, *Aust. J. Chem.*, 2006, **59**, 669; G. Moad, E. Rizzardo and S. H. Thang, *Polymer*, 2008, **49**, 1079.

13 J. M. J. Frechet, M. Henmi, I. Gitsov, S. Aoshima, M. R. Leduc and R. B. Grubbs, *Science*, 1995, **269**, 1080; C. J. Hawker, J. M. J. Frechet, R. B. Grubbs and J. Dao, *J. Am. Chem. Soc.*, 1995, **117**, 10763.

14 A. Padwa and S. Murphree, *ARKIVOC*, 2006, 6; R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.

15 W. H. Binder and R. Sachsenhofer, *Macromol. Rapid Commun.*, 2007, **28**, 15; P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Frechét, K. B. Sharpless and V. Fokin, *Angew. Chem., Int. Ed.*, 2004, **43**, 3928.

 This journal is © The Royal Society of Chemistry 2013

Published on 28 November 2012. Downloaded by Zhejiang University on 26/02/2014 07:21:04.

16 M. Vaultier, N. Knouzi and R. Carrié, *Tetrahedron Lett.*, 1983, **24**, 763; P. T. Nyffeler, C. Liang, K. Koeller and C. Wong, *J. Am. Chem. Soc.*, 2002, **124**, 10773.
17 E. Saxon and C. R. Bertozzi, *Science*, 2000, **287**, 2007; M. Köhn and R. Breinbauer, *Angew. Chem., Int. Ed.*, 2004, **43**, 3106.
18 L. Gu, Z. Shen, S. Zhang, G. Lu, X. Zhang and X. Huang, *Macromolecules*, 2007, **40**, 4486; J. Wu and C. Gao, *Macromolecules*, 2010, **43**, 7139; Y. Li, J. Zou, B. P. Das, M. Tsianou and C. Cheng, *Macromolecules*, 2012, **45**, 4623.
19 Y. Han and C. Gao, *Sci. China: Chem.*, 2010, **53**, 2461.
20 C. E. Hoyle, A. B. Lowe and C. Bowman, *Chem. Soc. Rev.*, 2010, **39**, 1355.
21 L. M. Campos, K. L. Killops, R. Sakai, J. M. Paulusse, D. Damiron, E. Drockenmuller, B. W. Messmore and C. J. Hawker, *Macromolecules*, 2008, **41**, 7063; P. Antoni, M. J. Robb, L. Campos, M. Montanez, A. Hult, E. Malmström, M. Malkoch and C. J. Hawker, *Macromolecules*, 2010, **43**, 6625; M. J. Robb, L. A. Connal, B. F. Lee, N. A. Lynd and C. J. Hawker, *Polym. Chem.*, 2012, **3**, 1618.
22 J. M. Spruell, M. Wolffs, F. A. Leibfarth, B. C. Stahl, J. Heo, L. A. Connal, J. Hu and C. J. Hawker, *J. Am. Chem. Soc.*, 2011, **133**, 16698.
23 J. B. Birks, *Photophysics of Aromatic Molecules*, Wiley, New York, 1970; M. M. Mok, R. Thiagarajan, M. Flores, D. C. Morse and T. P. Lodge, *Macromolecules*, 2012, **45**, 4818; S. W. Hong, K. H. Kim, J. Huh, C. Ahn and W. H. Jo, *Chem. Mater.*, 2005, **17**, 6213; K. Paek, S. Chung, C. Cho and B. J. Kim, *Chem. Commun.*, 2011, **47**, 10272; C. Gao, D. Yan, B. Zhang and W. Chen, *Langmuir*, 2002, **18**, 3708; C. Gao, D. Yan and W. Chen, *Macromol. Rapid Commun.*, 2002, **23**, 465.
24 T. M. Figueira-Durate and K. Müllen, *Chem. Rev.*, 2011, **111**, 7260.
25 M. Montalti, A. Credi, L. Prodi and M. T. Gandolfi, *Handbook of photochemistry*, Taylor & Francis, New York, 3rd edn, 2005.
26 J. B. Birks, *Rep. Prog. Phys.*, 1975, **38**, 903.
27 Y. Niko and G. Konishi, *Macromolecules*, 2012, **45**, 2327; S. Chen, J. Duhamel, G. J. Bahun and A. Adronov, *J. Phys. Chem. B*, 2011, **115**, 9921; G. J. Bahun and A. Adronov, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1016.
28 L. A. Baker and R. M. Crooks, *Macromolecules*, 2000, **33**, 9034.
29 Y. C. Yuan, M. Z. Rong, M. Q. Zhang, J. Chen, G. C. Yang and X. M. Li, *Macromolecules*, 2008, **41**, 5197; R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.
30 S. De and A. Khan, *Chem. Commun.*, 2012, **48**, 3130; A. Brändle and A. Khan, *Polym. Chem.*, 2012, **3**, 3224; S. De, C. Stelzer and A. Khan, *Polym. Chem.*, 2012, **3**, 2342; M. Benaglia, A. Alberti, L. Giorgini, F. Magnoni and S. Tozzi, *Polym. Chem.*, 2013, **4**, 124.
31 J. Song, C. Huang, K. Nagata, J. Z. Yeh and T. Narahashi, *J. Pharmacol. Exp. Ther.*, 1997, **282**, 707; P. Hrobárik, I. Sigmundova, P. Zahradnik, P. Kasak, V. Arion, F. Edith and K. Clays, *J. Phys. Chem. C*, 2010, **114**, 22289; S. Alavez, M. C. Vantipalli, D. J. S. Zucker, I. M. Klang and G. J. Lithgow, *Nature*, 2011, **472**, 226.
32 J. D. Flores, N. J. Treat, A. W. York and C. L. McCormick, *Polym. Chem.*, 2011, **2**, 1976; S. Hecht, *J. Polym. Sci., Part A: Polym. Chem.*, 2003, **41**, 1047; Z. Dong and Z. Ye, *Macromolecules*, 2012, **45**, 5020; J. Han, B. Zhao, Y. Gao, A. Tang and C. Gao, *Polym. Chem.*, 2011, **2**, 2175; J. Han, B. Zhao, A. Tang, Y. Gao and C. Gao, *Polym. Chem.*, 2012, **3**, 1918.
33 C. E. Hoyle and C. N. Bowman, *Angew. Chem., Int. Ed.*, 2010, **49**, 1540; C. E. Hoyle, T. Y. Lee and T. Roper, *J. Polym. Sci., Part A: Polym. Chem.*, 2004, **42**, 5301; M. L. Conte, M. J. Robb, Y. Hed, A. Marra, M. Malkoch, C. J. Hawker and A. Dondoni, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 4468.
34 Y. Geng, D. E. Discher, J. Junstynska and H. Schlaad, *Angew. Chem.*, 2006, **118**, 7740; Z. Hordyjewicz-Baran, L. You, b. Smarsly, R. Sigel and H. Schlaad, *Macromolecules*, 2007, **40**, 3901; S. P. S. Koo, M. M. Stamenović, R. A. Prasath, A. J. Inglis, F. E. Du Prez, C. Barner-Kowollik, W. V. Camp and T. Junkers, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1699; R. L. A. David and J. A. Kornfield, *Macromolecules*, 2008, **41**, 1151; A. Gress, A. Volkel and H. Schlaad, *Macromolecules*, 2007, **40**, 7928; J. Lutz and H. Schlaad, *Polymer*, 2008, **49**, 817; Y. Geng, D. E. Discher, J. Justynska and H. Schlaad, *Angew. Chem., Int. Ed.*, 2006, **45**, 7578; N. Gupta, B. F. Lin, L. M. Campos, M. D. Dimitriou, S. T. Hikita, N. D. Treat, M. V. Tirrell, D. O. Clegg, E. J. Kramer and C. J. Hawker, *Nat. Chem.*, 2009, **2**, 138; J. D. Flores, N. J. Treat, A. W. York and C. L. McCormick, *Polym. Chem.*, 2011, **2**, 1976.
35 H. Sun, J. Han and C. Gao, *Polymer*, 2012, **53**, 2884; S. Wang, F. Shiraishi and K. Nakano, *Chem. Eng. J.*, 2002, **87**, 261; J. D. Reinheimer, J. D. Harley and W. W. Meyers, *J. Org. Chem.*, 1963, **28**, 1575.
36 H. Sun and C. Gao, *Biomacromolecules*, 2010, **11**, 3609; X. Wang, Y. He, J. Wu, C. Gao and Y. Xu, *Biomacromolecules*, 2010, **11**, 245; L. Zhou, C. Gao, W. Xu, X. Wang and Y. Xu, *Biomacromolecules*, 2009, **10**, 1865; C. Gao, Y. Xu, D. Yan and W. Chen, *Biomacromolecules*, 2003, **4**, 704.