Facile synthesis and self-assembly of multihetero-arm hyperbranched polymer brushes†

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A facile methodology was presented for scalable synthesis of hyperbranched-star polymers with tens of hydrophilic and hydrophobic hetero-arms, in merely two steps starting from monomers. Self-condensing atom transfer radical polymerization (SC-ATRP) of a clickable initiator-monomer (click-inimer), 3-azido-2-(2-bromo-2-methylpropanoyloxy)propyl methacrylate, resulted in a hyperbranched polymer with azido and bromo multihetero-groups. Subsequently orthogonal one-pot "grafting onto" azide-alkyne click coupling and "grafting from" ATRP with the core of hyperbranched polymer afforded targeted miktoarm globular binary brushes. The brushes could readily assemble into superstructures of 150–300 nm spheres and micro-scale sheets. Furthermore, hyperbranched copolymer possessing azido, hydroxyl and bromo trihetero-groups were synthesized by self-condensing atom transfer radical copolymerization of the click-inimer and 2-hydroxyethyl methacrylate (HEMA). Hyperbranched trinity brushes were then facilely prepared *via* a one-pot multigrafting strategy by a combination of click chemistry, esterification, and ATRP. The trinity brushes could assemble into superstructures of micron-scale dendritic tubes.

1. Introduction

Biomacromolecules possessing a multitype of functional side groups are very important for many bioprocesses and biosystems since each type of group can perform unique functions independently. To obtain mimetic polymers is of crucial importance for access of multifunctional materials and biomimetic machines. However, despite their high reputation for numerous functional groups, hyperbranched polymers (HPs) with multihetero-groups that are compatible after further modification is yet to be reported.[1–3]

Based on a core/backbone of multifunctional polymer, star or comb-like molecular brushes can be constructed *via* either "grafting from" approach that enables *in situ* polymerization of monomer initiated from the core or "grafting onto" approach that permits direct reaction between terminal-functionalized polymers and the core.[4–6] Because of their unique structures, special properties, and possible biomimetic applications, molecular brushes with side heterochains (or miktoarms) have drawn increasing attention recently.[7–12] Owing to the incompatibility of different functional groups during grafting, multistep reactions are generally required for the target of complex brushes with hetero-arms, which seriously limits their availability and further applications. Alternatively, miktoarm molecular brushes can be accessed by copolymerization of different macromonomers *via* the "grafting through" approach.[13–15] However, it is hard to achieve such brushes with a high degree of polymerization (DP) owing to the strong steric hindrance of macromolecules. Moreover, trinary hetero-arm and more complex molecular brushes have rarely been addressed. These problems always shrivel desirable macromolecular designs and thus greatly confine the development of functional polymer science and relevant subjects.

Except for the synthesis, self-assembly or micellization of miktoarm (or Janus) brushes represents another promising direction since the dynamic assembly nature associated with the complicated molecular structure of miktoarm brushes could illuminate biomimetics.[16] However, this research is still in its infancy, and normally only spherical micelles have been observed for the reported miktoarm cylindrical brushes.[17,18]

To meet these challenges, herein, we present an efficient methodology to readily achieve binary and ternary-functional HPs by one-step self-condensing atom transfer radical polymerization (SC-ATRP) or copolymerization, and then binary and trinary miktoarm globular molecular brushes *via* one-pot orthogonal multigrafting by a combination of "grafting onto" click chemistry and "grafting from" ATRP, since both azide-alkyne click chemistry[19–30] and ATRP[31–33] have been widely demonstrated as powerful and facile techniques in material design and synthesis. Furthermore, we investigated the unique dynamic self-assembly behaviors of the resulting miktoarm molecular brushes.

2. Experimental

2.1 Materials

All raw materials of monomers and reagents were purchased from Aldrich, except for those specially mentioned. All solvents

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were purchased from Sinopharm Chemical Reagent Co., LtdS (Shanghai).

2.2 Instrumentation and characterization

Fourier-transform infrared (FTIR) spectra were recorded on a PE Paragon 1000 spectrometer, and all the samples were prepared as KBr pellets. ^{1}H NMR spectra were obtained using a Varian Mercury Plus 400 MHz spectrometer. Molecular weights were determined by gel permeation chromatography (GPC) using PE series 200, with a RI-WAT 150CV+ as a detector, using BrLi/DMF (0.01 mol/L) as the eluent at a flow rate of 1 mL/min and polystyrene as standards at 70 °C. Scanning electron microscopy (SEM) images were recorded using an LEO 1550VP field-emission microscope, and the samples were dropped onto silicon surfaces and sputter-coated with a thin gold layer. Transmission electron microscopy (TEM) analysis was conducted on a JEOL JEL2010 field-emission electron microscope at 200 kV. AFM images were recorded with a Digital Instrument (DI) Nanoscope IIIa scanning probe microscope, mounted with Si_3N_4 tips. The sample solution or suspension was dropped onto a freshly-peeled mica surface, and then used to do AFM measurements after evaporation of solvent under vacuum.

2.3 Synthesis of 3-azido-2-hydroxypropyl methacrylate

To a round-bottom flask sodium azide (20 g, 0.31 mol), sodium bicarbonate (15 g, 0.18 mol), water (250 mL) and THF (50 mL) were added. The flask was closed with a rubber plug and backfilled with nitrogen. To this solution, glycidyl methacrylate (GMA, 20 mL) was added with a nitrogen-purged syringe and the reaction was carried out at room temperature for 48 hours in the darkness. Then, the mixture was extracted with dichloromethane (5 × 100 mL). The organic mixture was dried with magnesium sulfate overnight. After filtration, the solvent of dichloromethane was removed by a rotary evaporator under reduced pressure, affording 3-azido-2-hydroxypropyl methacrylate (AzMA) (20.25 g, yield 74.4%). ^{1}H NMR ($CDCl_3$, δ, ppm): H_2C=C 6.15/6.18, 5.64/5.66; –CH(OH)– 5.07/4.06; –OCOCH_2– 4.24/3.82; –CH_2N_3 3.43/3.55; –OH 2.87; –CH_3 1.96.

2.4 Synthesis of 3-azido-2-(2-bromo-2-methylpropanoyloxy)propyl methacrylate

The as-prepared AzMA (10 g, 54 mmol) was dissolved in a Schlenk flask containing a mixture of anhydrous dichloromethane (60 mL) and triethylamine (20 mL). Then, α-bromoisobutyryl bromide (13.1 g, 56.8 mmol) dissolved in dichloromethane (20 mL) was added dropwise to the flask at 0–5 °C in 1 h under nitrogen atmosphere. The mixture was stirred at room temperature for 24 h. The insoluble salt was removed by filtration, and the solution was washed by 1M HCl, 1M NaOH and water 5 times. The organic mixture was dried with magnesium sulfate overnight. After filtration, the solvent of dichloromethane was removed by a rotary evaporator and then a pump under reduced pressure, giving rise to 3-azido-2-(2-bromo-2-methylpropanoyloxy)propyl methacrylate (AzBrMA) (10.5 g, yield 58.2%). ^{1}H NMR ($CDCl_3$, δ, ppm): H_2C=C 6.13/6.18, 5.62/5.66; –CH(OCO)– 5.27; –OCOCH_2– 4.40/4.33; –CH_2N_3 3.57; =C–CH_3 1.95; –C(CH_3)$_2$Br 1.94.

2.5 Synthesis of hyperbranched poly(AzBrMA)

Hyperbranched poly(AzBrMA), HPAzBrMA, was synthesized by self-condensing atom transfer radical polymerization (SC-ATRP) of the clickable initiator-monomer (click-inimer) AzBrMA. Typically, ethyl acetate (3 mL) and AzBrMA (3.0 g, 8.75 mmol) were added to a 25 mL Schlenk flask with a magnetic bar, which was deoxygenated by bubbling with nitrogen for at least 30 min. *N*,*N*,*N*′,*N*″,*N*″-Pentamethyldiethylenetriamine (PMDETA, 18 μL, 0.0875 mmol) and CuBr (12.5 mg, 0.0875 mmol) were added into the mixture under nitrogen flow. The reaction was carried out at 60 °C for 24 h. The viscosity of the mixture was too high to be stirred with the magnetic bar. The mixture was then diluted with THF, and precipitated in ether three times. The final product of HPAzBrMA was obtained after drying in a vacuum oven overnight at room temperature (2.12 g, yield 70.6%).

2.6 Synthesis of monoalkyne-terminated poly(ethylene glycol) (PEG-Alk)

PEG-Alk was synthesized according to the previous protocol with the raw material of monohydroxyl-terminated PEG (PEG-OH) (M_n = 750 g/mol).[28] ^{1}H NMR ($CDCl_3$, δ, ppm): ≡CCH_2O 4.68; –CH_2OCO 4.32; –OCH_2CH_2O– 3.62; –OCOCH_2CH_2OCO– 2.66; HC≡C 2.48.

2.7 Synthesis of binary brushes with bihetero-arms *via* a "one-pot" approach

To a 25 mL Schlenk flask, HPAzBrMA (60 mg, with azido 0.175 mmol and bromo 0.175 mmol), PEG-Alk (175 mg, with alkyne 0.197 mmol), CuBr (12 mg, 0.085 mmol), PMDETA (16 μL, 0.085 mmol), THF (1 mL) and DMF (0.5 mL) were added under nitrogen flow. The reaction was carried out at room temperature for 1 h. Then, deoxygenated monomer MMA (3.0 g, 30 mmol) was injected into the mixture by a nitrogen-purged syringe and the reaction was further carried out for 24 hours at room temperature. After polymerization, the copper catalyst was removed by passing it through an alkaline alumina column and the resulting polymer was precipitated in methanol and ether alternately for at least five times. The binary polymer brush of HPAzBrMA-star-PEG/PMMA was then obtained after drying under vacuum at room temperature overnight (514.9 mg).

2.8 Synthesis of hyperbranched poly(AzBrMA-co-HEMA)

Hyperbranched poly(AzBrMA-co-HEMA), HP(AzBrMA-co-HEMA), was synthesized by self-condensing atom transfer radical copolymerization of AzBrMA and 2-hydroxyethyl methacrylate (HEMA). AzBrMA (1.0 g, 2.9 mmol), HEMA (0.38 g, 2.9 mmol), PMDETA (5.8 μL, 0.029 mmol), CuBr (4.2 mg, 0.029 mmol) and ethyl acetate (1 mL) were added into a 25 mL Schlenk flask under nitrogen flow. The reaction was carried out at 50 °C for 4 hours. The mixture was diluted with DMF and precipitated in ether several times. The final product of HP(AzBrMA-co-HEMA) was obtained after drying in a vacuum oven overnight at room temperature (529.4 mg, yield 38.3%).

2.9 Synthesis of trinity polymer brushes with trihetero-arms *via* a "one-pot" approach

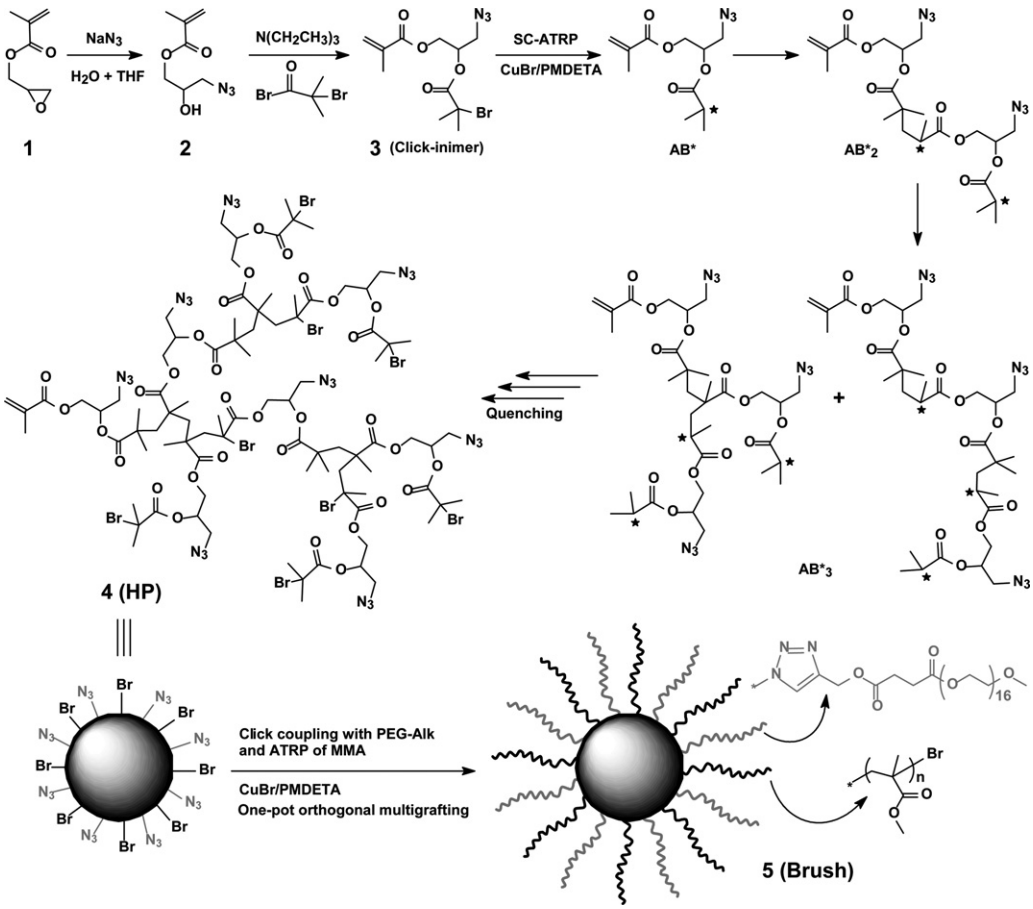
To a 25 mL Schlenk flask, HP(AzBrMA-co-HEMA) (50 mg), PEG-Alk (88 mg), palmitic acid (C16, 49 mg), *N*,*N*′-dicyclohexylcarbodimide (DCC, 40.5 mg), 4-(dimethylamino)pyridine (DMAP, 5 mg) and DMF (2 mL) were added under nitrogen flow. CuBr (5.4 mg, 0.037 mmol) and PMDETA (7.5 μL, 0.037 mmol) were added into the mixture. The reaction was carried out for 24 hours at room temperature and *tert*-butyl acrylate (*t*BA, 467 mg, 3.6 mmol) was injected by a nitrogen-purged syringe. After another 24 hours of polymerization, the copper catalyst was removed by passing through an alkaline alumina column and the resulting polymer was precipitated in methanol. The collected solid was then dialyzed over chloroform with a membrane (cut off 5000), producing a trinity polymer brush of HP(AZMA-co-HEMA)-star-PEG/C16/P*t*BA after removal of solvent (133.6 mg).

3. Results and discussion

3.1 Synthesis and micellization of binary polymer brushes

Scheme 1 depicts the protocol for synthesis of a hyperbranched polymer with binary functional groups and globular molecular brushes with amphiphilic hetero-arms. At first, we designed a clickable self-initiating monomer (click-inimer), 3-azido-2-(2-bromo-2-methylpropanoyloxy)propyl methacrylate (AzBrMA, **3**), in which the bromo group can initiate ATRP of methacrylate, and azido grants further click coupling with alkynes. SC-ATRP of **3** results in initially activated inimer AB* and condensed oligomers of AB^*_2, AB^*_3, *etc.*, and finally hyperbranched polymer **4** containing both bromo and azido groups at repeated units. Subsequent click coupling with monoalkyne-terminated poly(ethylene glycol) (PEG-Alk) and ATRP of methyl methacrylate (MMA) on **4** by either one-pot or separated steps give rise to the miktoarm globular brush **5**. Only two-pot reactions are performed to achieve such a complex architecture if starting from a monomer, and two steps could even be simplified as a one-pot reaction if required. The hetero-arms can be replaced with lots of desired blocks, indicating the versatility and compatibility of this methodology.

The click-inimer **3** was synthesized by reaction of glycidyl methacrylate (**1**) with sodium azide in the mixed solvents of water and tetrahydrofuran (THF) at room temperature without any phase-transfer catalyst (to give **2**), followed by reaction with α-bromoisobutyryl bromide. The commercial availability of reagents associated with the simple process grants the cost-effectively scalable synthesis of the click-inimer. Since Fréchet *et al.* reported a self-condensing vinyl polymerization (SCVP) approach to produce irregularly dendritic or hyperbranched polymers in 1995,[34] various HPs have been prepared from inimers possessing vinyl and halide (*e.g.*, Br, Cl) groups,



Scheme 1 The protocol for facile synthesis of a biheterofunctional hyperbranched polymer and multihetero-arm globular brushes.

especially by the SC-ATRP.[1,35–37] The SC-ATRP of AzBrMA was carried out in ethyl acetate with the catalyst/ligand system of CuBr/*N*,*N*,*N*′,*N*″,*N*‴-pentamethyldiethylenetriamine (PMDETA) at 60 °C, affording **4** with the weight-average molecular weight (M_w) of 45 580 and polydispersity index (PDI) of 2.24 (see Fig. 1B). The polymerization kinetics was monitored by gel permeation chromatography (GPC) and ^{1}H NMR measurements (see ESI).† In the NMR spectra, we find that the intensity of vinyl protons decreases as the polymerization time increases. The GPC results show that the main peaks of polymeric species continuously move toward larger molecular weights associated with the rise of intensity. The correlation between conversion of vinyl groups and molecular weight is exponential (Fig. 1A), which is in accordance with those found in the conventional cases of SC-ATRP.[35,36] The GPC elution curves and kinetics show both natures of self-condensing and vinyl polymerization and thus demonstrated the successful formation of hyperbranched macromolecules.[34–39]

The resulting hyperbranched polyAzBrMA **4** was further characterized by FTIR and ^{1}H NMR (Fig. 1). In the FTIR spectrum, the characteristic absorption peak of the azido group is strongly observed at 2106 cm^{-1} (Fig. 1C). In the ^{1}H NMR spectrum (Fig. 1D), protons of azidomethylene and bromoisobutyryl are clearly found as signals at *ca.* 3.5 and 1.92 ppm, respectively. These data indicate that polymer **4** contains a large amount of both azido and bromo groups. Therefore, we readily obtained the designed multifunctional clickable macroinitiator.

Based on the core of **4**, multifunctional molecular brushes can be constructed by bonding other polymeric chains *via* either the "grafting from" or "grafting onto" strategy. Generally, "grafting from" works better than "grafting onto" in terms of high grafting efficiency and controllability. Nevertheless, Matyjaszewski and coworkers found that click "grafting onto" could also work well in the synthesis of molecular brushes, especially for more flexible grafts like PEG.[25] Herein, we employed both strategies in a one-pot reaction to prepare polymer brushes with hetero-arms by a combination of click chemistry and *in situ* ATRP. PEG and PMMA were selected as hydrophilic and hydrophobic chains, respectively. The grafting reaction was carried out in the mixed solvents of THF and DMF at room temperature with the same catalyst system of CuBr/PMDETA by addition of PEG-Alk for click coupling and subsequent MMA for ATRP. We studied the kinetics of the click reaction between PEG-Alk with **4**, and found that the M_w of the resulting polymer did not increase considerably after 1 h, indicating that the click reaction was very fast and

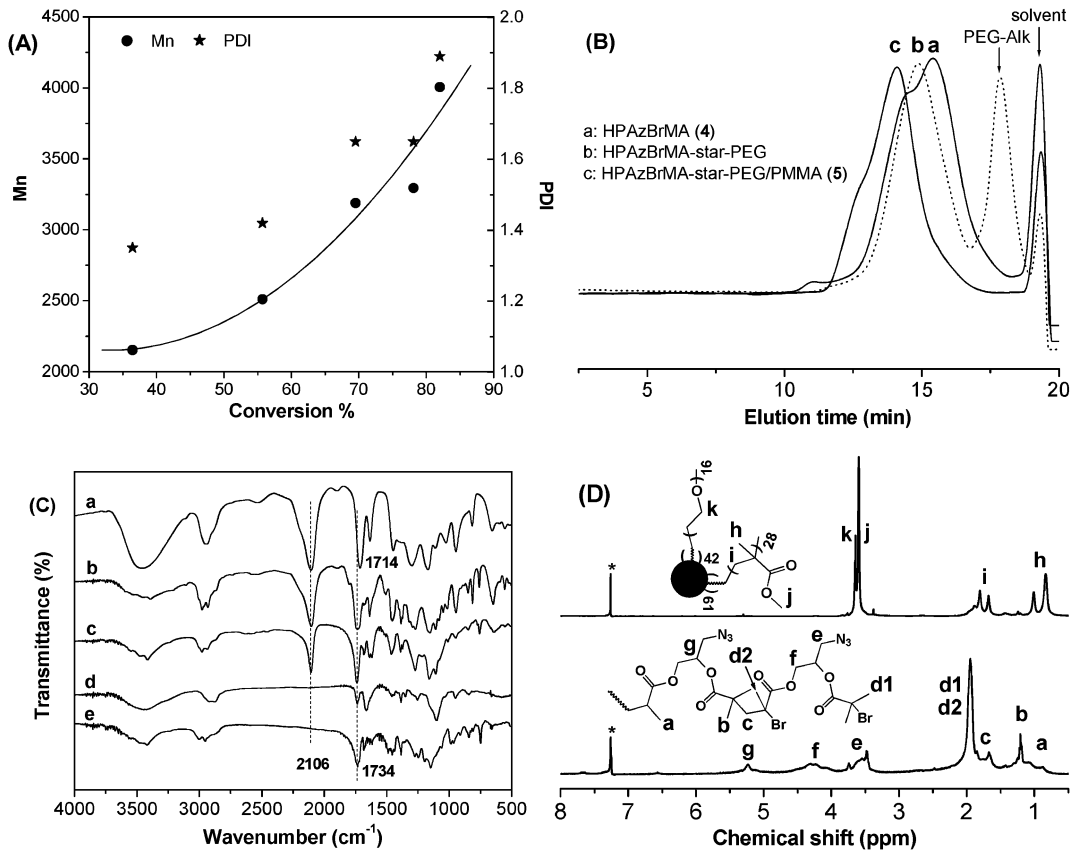
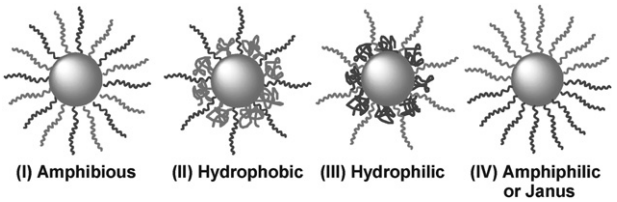


Fig. 1 (A) The number-average molecular weight (M_n) and PDI *vs.* vinyl conversion for the samples taken from the reaction system at given times for the SC-ATRP of AzBrMA. (B) GPC curves of hyperbranched polyAzBrMA **4**, HPAzBrMA-star-PEG (after one hour click coupling), and binary polymer brush **5**. (C) FTIR spectra of 3-azido-2-hydroxypropyl methacrylate, AzMA (a), 3-azido-2-(2-bromo-2-methylpropanoyloxy)propyl methacrylate, AzBrMA (b), hyperbranched polyAzBrMA **4** (c), HPAzBrMA-star-PEG (d, the sample taken from the reaction system after one hour click coupling), and hyperbranched binary brush of HPAzBrMA-star-PEG/PMMA **5** (e). (D) ^{1}H NMR spectrum of hyperbranched polyAzBrMA **4** (bottom) and globular binary brush with hetero-arms of PEG and PMMA; The * denotes the signal of solvent of $CHCl_3$.

became exhausted before 1 h. Therefore we added MMA to the reaction system after one hour of click coupling in order to win relatively high grafting efficiency as well for the "grafting onto" moiety.

The polymer brush **5** was characterized by GPC, FTIR and ^{1}H NMR (Fig. 1). GPC measurements show that the M_w increases from 45 580 for the clickable macrointiator to 204 500 for the final product, and the sample taken from the reaction system after one hour of click coupling had a M_w of 97 150 and PDI of 1.70 (Table 1). The tandem significant increase of molecular weights indicated that both "grafting onto" and "grafting from" strategies are highly efficient in the synthesis of hetero-arm brushes. From the IR spectra (Fig. 1C), the peak found at 2106 cm^{-1}, assigned to azido absorption, disappears after click coupling, further confirming the high efficiency of click grafting. In the ^{1}H NMR spectrum of final product **5** (Fig. 1D), the peaks at 0.7–1.1 ppm (–CH_3 of PMMA backbone), 3.59 ppm (–OCH_3 of PMMA side groups), and 3.64 ppm (–OCH_2CH_2O– of PEG chain) are clearly observed, demonstrating both PMMA and PEO chains were grafted successfully on to core **4**. However, the proton signals of the core molecule cannot be detected any more, indicating the high grafting efficiency and high molecular weight of the final brushes. The total apparent M_n of PEG arms is *ca.* 36 900, corresponding to 42 arms with conversion of *ca.* 69% for the click coupling, and the average degree of polymerization (DP) for the PMMA grafts is calculated to be *ca.* 28 with supposed initiating efficiency of 100% (61 arms). The real molecular weight of the PEG arms and final brushes may be higher than the apparent ones measured by GPC, suggesting that the click coupling efficiency could be higher than 69%. In fact, the azido absorption peak cannot be detected from the corresponding FTIR spectrum after click coupling, indicating that the click efficiency almost approached 100%, because the azido peak is quite sensitive in the FTIR spectrum and a tiny concentration such as the terminal azido group of a linear polymer should be detectable.

The resulting dendritic brushes with hetero-arms may reversibly change their chain state according to the surrounding conditions to amphibious, hydrophobic, hydrophilic, and amphiphilic (see Scheme 2). So the brushes could readily undergo micellization into larger superstructures by unbalancing the amphibious state *via* the addition of poor solvent of either hydrophobic or hydrophilic arms (Fig. 2 and ESI†).



Scheme 2 Cartoon for possible change states of globular molecular brushes with binary hetero-arms.

The unimolecular micelle structures of brush **5** can be directly visualized as nanodots in diameters of 8–20 nm under atomic force microscope (AFM) (Fig. 2A,B). As expected, the amphiphilic brush **5** is extremely easy to self-assemble into larger micelles by addition of only a drop of water into its DMF solution which unbalances the original state to form a new balance (Fig. 2C,D).[40–42] Fig. 2 (E,F) shows the 3D and phase images of assembled micelles with diameters of 150–300 nm in DMF/H_2O (2 : 1 by volume), and we can clearly find the fluctuant mound or turtleback-like morphology on each micelle which was caused by the compact packing of individual unimolecular micelles (Fig. 2G). This indicates the ultra-strong interaction between unimolecular micelles due to their numerous multivalency arms united by one skeleton (Fig. 2H), which is essentially different from the self-assembly of conventional linear block copolymers that generally results in discrete brush-like surface morphology. In addition, we can even recognize and count the unimolecular micelles that formed bigger spheres from the phase image because of the big size of the 3D macromolecules (several to tens of molecules per each top view surface of assembled micelles), which is also quite unique for the assembly of the multiarm brushes and is rarely accessible in cases of linear copolymers. This result also implies that organic molecular machines and devices could be fabricated directly by AFM manipulation depending on the easily viewable size and multifunctional arms of hyperbranched brushes. The aggregation and assembled structures were also monitored and confirmed by dynamic light scattering (DLS, ESI†) and scanning electron microscopy (SEM, ESI†).

We also tried the addition of methanol into the same DMF solution of brush **5**, and found different aggregated morphology. The AFM observations showed that when a small quantity of

Table 1 Selected results for the globular molecular brushes with multihetero-arms

Polymer	$M_{w,GPC}$[a]	$M_{n,GPC}$[a]	PDI[a]	MW_{NMR}[b]	Arms	DP_{arm}[c]
HPAzBrMA **4**	45 580	20 350	2.24	—	—	—
HPAzBrMA-*star*-PEG	97 150	57 250	1.70	—	PEG: 42	—
Binary brush **5**	204 500	78 050	2.62	230 850	PEG: 42 PMMA: 61	PMMA: 28
HP(AzBrMA-*co*-HEMA) **7**	40 500	11 940	3.39	—	—	—
Trinity brush **8**	158 800	40 160	3.95	71 930	PEG: 14 C16: 28 P*t*BA: 24	P*t*BA: 13

[a] The weight-average molecular weight (M_w), number-average molecular weight (M_n), and polydispersity index (PDI) of polymers measured by gel permeation chromatography (GPC) using BrLi/DMF (0.01 mol/L) as the eluent and polystyrene as standards at 70 °C. [b] Molecular weight calculated from ^{1}H NMR spectrum on the basis of $M_{n,GPC}$ of corresponding precursor polymer. [c] Average degree of polymerization (DP) of arms for the globular molecular brushes *via* a "grafting from" ATRP approach.

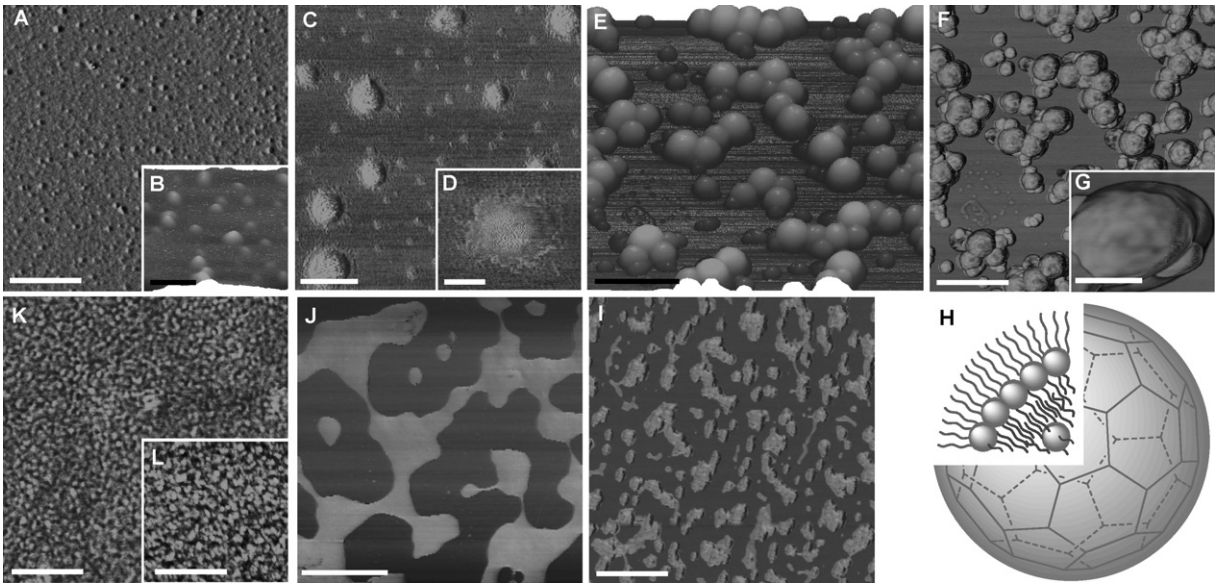


Fig. 2 AFM phase (A) and amplified 3D pattern (B) of binary brush **5** from diluted DMF solution, AFM phase (C, D) images of **5** when tiny amount of water was added to the DMF solution, AFM 3D pattern (E) and phase images (F, G) of the assembled spherical particles of **5** in DMF/H_2O (2/1 by volume), cartoon of an assembled micelle of **5** (H) showing the multivalent and densely packed arms of the same polymer, AFM phase images of micelles of **5** in DMF/methanol with volume ratio of 10/1 (I) and 2/1 (J), local amplified AFM phase image of J (K) showing the unimolecular micelle structure, and AFM phase image of **5** from concentrated DMF solution (L). The scale bars are 250 nm (A), 50 nm (B), 1 μm (C), 250 nm (D), 500 nm (E), 500 nm (F), 100 nm (G), 2.5 μm (I), 5 μm (J), 250 nm (K, L).

methanol (methanol/DMF = 1/10) was added, irregular micelles with sizes from hundreds of nanometers to several microns formed (Fig. 2I). As a larger quantity of methanol was added, the micelles further aggregated rapidly and finally formed giant sheets (methanol/DMF = 1/2) (Fig. 2J). The boundary of the micelles was identified easily on the phase image, and thus we can see clearly the micellar unimolecules composed in the sheet when zoomed in (Fig. 2K, L). This indicates that complex superstructures can be accessed by the hierarchical aggregation of molecules and as-formed micelles through continual unbalancing.

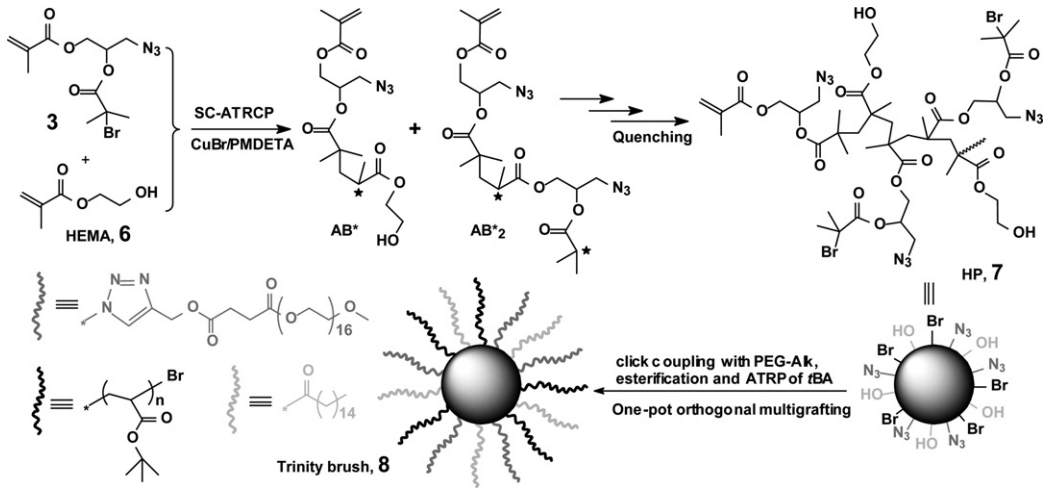
The SC-ARTP described above showed us a facile approach to binary functional HPs, and the one-pot orthogonal multigrafting strategy showed us a convenient and effective avenue to miktoarm molecular brushes which could be readily assembled into spherical micelles in diameters of 150–300 nm. Questions appear: could trinary functional HPs and more complex brushes be accessed by the same methodology? What is the assembly result for the trinity brushes if possible? These questions will be addressed in the following section.

3.2 Synthesis and self-assembly of trinity polymer brushes

Scheme 3 depicts the synthesis protocol for the globular brushes with tri-hetero arms (trinity brushes) from the core of the ternary-functional hyperbranched polymer. Self-condensing atom transfer radical copolymerization (SC-ATRCP) of the click-inimer (**3**) and 2-hydroxyethyl methacrylate (HEMA, **6**) initially affords AB*, AB^*_2 and other oligomers, and finally hyperbranched copolymer possessing azido, hydroxyl and bromo groups (**7**).[43,44] Subsequent one-pot click coupling of alkyne-terminated poly(ethylene oxide) (PEG-Alk), esterification of palmitic acid (C16) and ATRP of *tert*-butyl acrylate (*t*BA) gives the target trinity molecular brush **8**.

The SC-ATRCP of **3** and **6** was carried out in ethyl acetate at 50 °C for 4 h in the presence of CuBr/PMDETA, affording hyperbranched poly(AzBrMA-*co*-HEMA) **7** with the weight-average molecular weight (M_w) of 40 500 and PDI of 3.39 (see Fig. 3A and Table 1). The unit ratio of **3** to **6** calculated from the ^{1}H NMR spectrum of the copolymer is close to 1/1.3. Hence, the copolymer contains *ca.* 24 azido, 24 bromo and 31 hydroxyl groups. Subsequently, the hyperbranched copolymer was used as a multifunctional core to graft trine arms by a combination of azide-alkyne click chemistry, esterification and ATRP in a one-pot. PEG-Alk, palmitic acid and *t*BA were chosen as building materials, as PEG is hydrophilic, palmitoyl is hydrophobic and P*t*BA is intervenient after grafting. GPC measurements showed that the final polymer brush poly(AzBrMA-*co*-HEMA)-star-PEG/C16/P*t*BA (**8**) had a M_w of 158 800 and PDI of 3.95, demonstrating the significant increase in molecular weight for the trinity brush (Fig. 3A and Table 1).

The products were further characterized by FTIR and ^{1}H NMR measurements. In the FTIR spectrum of **7** (Fig. 3C), the azido absorption peak is strongly observed at 2108 cm^{-1}, whereas it disappears after click coupling for the trinity brush **8**, indicating the high click grafting efficiency. Meanwhile, the hydroxyl absorption band of **7** was clearly found at 3200–3800 cm^{-1}, while it almost vanishes after esterification for **8**, showing the high conversion of hydroxyl groups in the one-pot multigrafting. In the ^{1}H NMR spectrum of **8** (Fig. 3D), all of the proton signals of core **7**, PEG, C16 and P*t*BA moieties can be detected, respectively, suggesting that the trihetero-arms have been successfully linked on the HP core. Calculated from the integration values of ^{1}H NMR, trinity brush **8** contains *ca.* 14 PEG arms with a click



Scheme 3 Synthesis protocol for ternary-functional hyperbranched polymer and trihetero-arm (trinity) molecular brushes.

conversion of *ca.* 58% and 28 palmitoyl groups with 90% of esterification conversion, and the average DP of P*t*BA chains is *ca.* 13 with a supposed initiating efficiency of 100% (Table 1). The detailed influence parameters and optimization of grafting conditions are in progress, and will be reported later. It is noteworthy that the calculated values of brush arms from the ^{1}H NMR spectrum may have certain errors compared to the real ones because the solubilities of different organic moieties of core and arms are different from each other in a solvent. Owing to the possible local micellization in a solvent, how to get the accurate arm numbers for such a kind of complex molecular brush is still an open question for discussion in future work.

A complex molecular structure is always associated with versatile functions and unique self-assembly behaviors.[45–51] Therefore we also investigated the self-assembly behavior of the trinity brush **8**, by addition of water into its DMF solution. In order to probe the mechanism of the self-assembly, we observed the process in terms of assembling time (see Fig. 4A–G, ESI†). When water was injected into the DMF solution (H_2O : DMF = 1 : 2 by volume), a drop of sample at given time was taken out to observe under an optical microscope. At the first 60 minutes, we found several sheets floating in the mixed solution without a regular shape. After 3 h, we observed the intermediate state with rolled sheets and a few straight or branched tubes. Thereby,

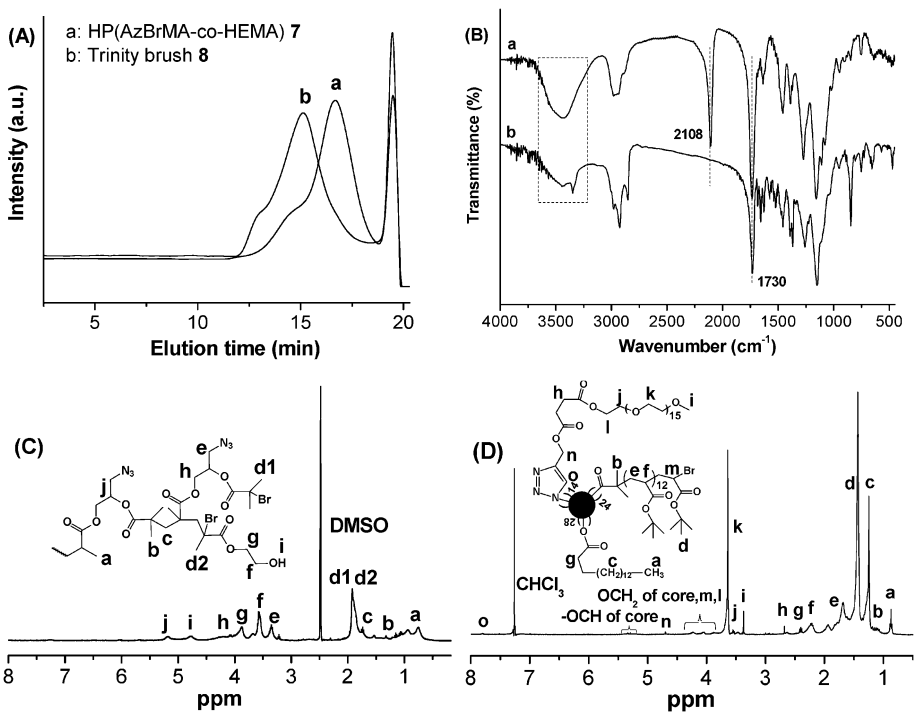


Fig. 3 (A) GPC curves of hyperbranched poly(AzBrMA-*co*-HEMA) **7** (a) and trinity brush **8** (b). (B) FTIR spectra of hyperbranched poly(AzBrMA-*co*-HEMA) **7** (a) and the trinity brush **8** (b). (C) ^{1}H NMR spectrum of hyperbranched poly(AzBrMA-*co*-HEMA) **7** in DMSO-d_6. (D) ^{1}H NMR spectrum of the trinity brush **8** in $CDCl_3$.

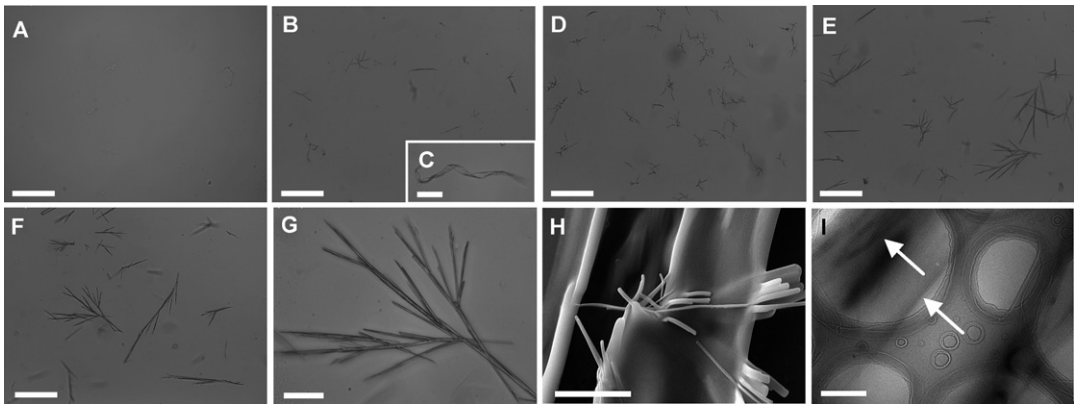


Fig. 4 Optical microscope images of trinity brush **8** in DMF/water (2/1 by volume) for 15 min (A), 3 h (B, C), 4 h (D), and 24 h (E–G). SEM image of assembled brush **8** showing the unclosed tube structure and possible branching sites (H). TEM image of assembled brush **8** showing the tube walls were constructed with parallel-aligned small fibers (indicated by the arrows) (I). The scale bars are 100 μm (A), 200 μm (B), 60 μm (C), 200 μm (D–F), 50 μm (G), 1 μm (H), and 500 nm (I).

we found some of the sheets rolled up to form the short straight tubes which aggregated together to construct the dendritic tubes. More and more dendritic tubes formed after 4 h with the disappearance of the sheets. After 24 h, the dendritic tubes grew larger, up to several hundreds of microns with a branch length of tens of microns. Under the optical microscope, we could find many tubes and most of them were branched with a few linear ones. This indicates that the self-assembly of the trinity brush is a slowly dynamic hierarchical process. Such a slowly "growing" process might possibly be used to mimic the formation, development and evolution of some biosystems.[52]

According to these observations, we proposed an assumption to explain the mechanism of the formation of the branched tubes (Fig. 5). At first, as the water was added into the mixture, the hydrophobic hyperbranched core of **8** collapsed and the three kinds of arms rearranged in the mixture: the hydrophilic PEG arms came together to extend in the solution outside the unimolecular micelles and the hydrophobic C16 and P*t*BA chains also gathered and collapsed entad. Because the fraction of hydrophilic moiety is too small to cover and stabilize the unimolecular micelles, aggregation of micelles occurs, forming sheet structures initially and rolled tubes subsequently so as to keep a new balance by the release of interface energy. The uncovered hydrophobic sides or ends of tubes can recognize each other and then stick together with the principle of "similitude and compatibility", which possibly results in branched structures. The SEM image showed the possible branching site of the unclosed tube where smaller fibres were stretching out from the main one, giving further evidence of our speculation (Fig. 4H, ESI†). The TEM image showed that the tube walls were constructed with parallel-aligned fibers of small micelles, also agreeing with the mechanism (Fig. 4I, ESI†).

The aggregation process was further traced with ^{1}H NMR measurements in a deuterated DMF/water system (Fig. 6, ESI†). It shows that the integration ratio of hydrophobic arms of C16 and P*t*BA to hydrophilic arms of PEG decreases exponentially with the time, indicating that (1) the self-assembly process is dynamic, and (2) the hydrophobic arms tend to be covered gradually by the hydrophilic ones with the assembly going further. This data also confirmed the dynamic assembly process and the phase-separated structures shown in Fig. 4.

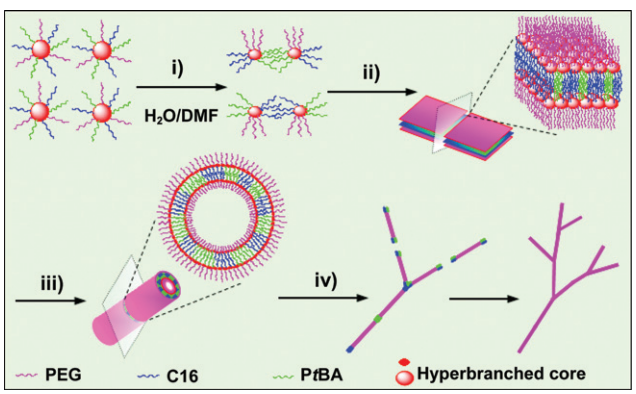


Fig. 5 Supposed mechanism for the dynamic self-assembly of a trinity molecular brush: (i) molecular aggregation into large micelles, (ii) micelle aggregation into sheet structures, (iii) rolling up of the micellar sheets into tubules, (iv) tubule aggregation into dendritic tubes. Process (ii), (iii) and (iv) may occur simultaneously. The illustrations are not drawn to scale.

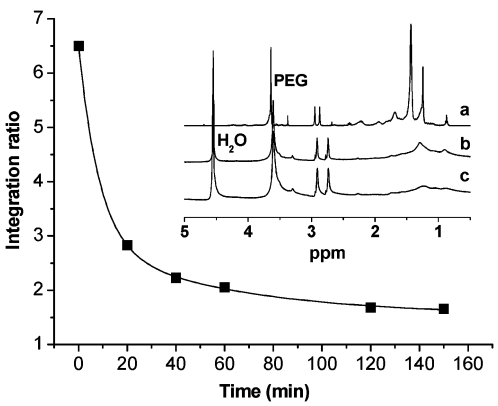


Fig. 6 The integration ratio of hydrophobic arms of C16 and P*t*BA to hydrophilic arms of PEG for the trinity brush **8** in DMF-d_7/D_2O as a function of time after the addition of D_2O into DMF-d_7 solution. The inset shows the ^{1}H NMR spectra of **8** in DMF-d_7 (a), in DMF-d_7 + D_2O for 20 min (b) and 150 min (c), respectively.

4. Conclusions

Hyperbranched polymers with multihetero-functional groups can be facilely prepared by self-condensing atom transfer radical polymerization and copolymerization. The orthogonal one-pot multi-grafting strategy showed us a quick, convenient and efficient avenue to miktoarm molecular brushes. The grafting tools could be extended to many other chemical reactions and controlled/living polymerizations. Moreover, dynamic self-assembled superstructures can be easily obtained by the unbalancing of amphiphilic brushes. All of these features will pave the way to complicated macromolecules, open the door of supermolecular chemistry of complex brushes, and promise the potential application of molecular brushes in biomimetic chemistry.

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Notes and references

1 C. Gao and D. Yan, *Prog. Polym. Sci.*, 2004, **29**, 183.
2 B. Voit, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 2679.
3 A. P. Goodwin, S. S. Lam and J. M. J. Fréchet, *J. Am. Chem. Soc.*, 2007, **129**, 6994.
4 S. S. Sheiko, B. S. Sumerlin and K. Matyjaszewski, *Prog. Polym. Sci.*, 2008, **33**, 759.
5 M. Zhang and A. H. E. Müller, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 3461.
6 I. Luzinov, S. Minko and V. V. Tsukruk, *Soft Matter*, 2008, **4**, 714.
7 D. Neugebauer, Y. Zhang, T. Pakula and K. Matyjaszewski, *Polymer*, 2003, **44**, 6863.
8 D. Wu, Y. Yang, X. Cheng, L. Liu, J. Tian and H. Zhao, *Macromolecules*, 2006, **39**, 7513.
9 X. Luo, G. Wang, X. Pang and J. Huang, *Macromolecules*, 2008, **41**, 2315.
10 M. Xie, J. Dang, H. Han, W. Wang, J. Liu, X. He and Y. Zhang, *Macromolecules*, 2008, **41**, 9004.
11 C. Liu, Y. Zhang and J. Huang, *Macromolecules*, 2008, **41**, 325.
12 K. Ranganathan, R. Deng, R. K. Kainthan, C. Wu, D. E. Brooks and J. N. Kizhakkedathu, *Macromolecules*, 2008, **41**, 4226.
13 V. Heroguez, Y. Gnanou and M. Fontanille, *Macromolecules*, 1997, **30**, 4791.
14 D. Neugebauer, Y. Zhang, T. Pakula and K. Matyjaszewski, *Macromolecules*, 2005, **38**, 8687.
15 D. Neugebauer, J. Rydz, I. Goebel, P. Dacko and M. Kowalczuk, *Macromolecules*, 2007, **40**, 1767.
16 S. Lee and N. D. Spencer, *Science*, 2008, **319**, 575.
17 L. Gu, Z. Shen, S. Zhang, G. Lu, X. Zhang and X. Huang, *Macromolecules*, 2007, **40**, 4486.
18 J. Yin, Z. S. Ge, H. Liu and S. Y. Liu, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 2608.
19 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004.
20 C. J. Hawker and K. L. Wooley, *Science*, 2005, **309**, 1200.
21 A. P. Goodwin, S. S. Lam and J. M. J. Fréchet, *J. Am. Chem. Soc.*, 2007, **129**, 6994.
22 P. Wu, M. Malkoch, J. N. Hunt, R. Vestberg, E. Kaltgrad, M. G. Finn, V. V. Fokin, K. B. Sharpless and C. J. Hawker, *Chem. Commun.*, 2005, 5775.
23 N. V. Tsarevsky, B. S. Sumerlin and K. Matyjaszewski, *Macromolecules*, 2005, **38**, 3558.
24 H. F. Gao and K. Matyjaszewski, *Macromolecules*, 2006, **39**, 4960.
25 H. F. Gao and K. Matyjaszewski, *J. Am. Chem. Soc.*, 2007, **129**, 6633.
26 N. V. Tsarevsky, S. A. Bencherif and K. Matyjaszewski, *Macromolecules*, 2007, **40**, 4439.
27 X. Jiang, E. B. Vogel, M. R. Smith and G. L. Baker, *Macromolecules*, 2008, **41**, 1937.
28 Y. Zhang, H. He and C. Gao, *Macromolecules*, 2008, **41**, 9581.
29 H. He, Y. Zhang, C. Gao and J. Wu, *Chem. Commun.*, 2009, 1655.
30 Y. Zhang, H. He, C. Gao and J. Wu, *Langmuir*, 2009, **25**, 5814.
31 T. E. Patten, J. H. Xia, T. Abernathy and K. Matyjaszewski, *Science*, 1996, **272**, 866.
32 J. Wang and K. Matyjaszewski, *J. Am. Chem. Soc.*, 1995, **117**, 5614.
33 W. A. Braunecker and K. Matyjaszewski, *Prog. Polym. Sci.*, 2007, **32**, 93.
34 J. M. J. Fréchet, M. Henmi, I. Gitsov, S. Aoshima, M. R. Leduc and R. B. Grubbs, *Science*, 1995, **269**, 1080.
35 M. W. Weimer, J. M. J. Fréchet and I. Gitsov, *J. Polym. Sci., Part A: Polym. Chem.*, 1998, **36**, 955.
36 K. Matyjaszewski, S. G. Gaynor, A. Kulfan and M. Podwika, *Macromolecules*, 1997, **30**, 5192.
37 H. Mori, D. C. Seng, M. F. Zhang and A. H. E. Müller, *Langmuir*, 2002, **18**, 3682.
38 K. Matyjaszewski, S. G. Gaynor and A. H. E. Müller, *Macromolecules*, 1997, **30**, 7034.
39 A. H. E. Müller, D. Y. Yan and M. Wulkow, *Macromolecules*, 1997, **30**, 7015.
40 Y. Zhou and D. Yan, *Chem. Commun.*, 2009, 1172.
41 D. Yan, Y. Zhou and J. Hou, *Science*, 2004, **303**, 65.
42 L. Cheng, G. Z. Zhang, L. Zhu, D. Y. Chen and M. Jiang, *Angew. Chem., Int. Ed.*, 2008, **47**, 10171.
43 H. Mori, D. C. Seng, H. Lechner, M. F. Zhang and A. H. E. Müller, *Macromolecules*, 2002, **35**, 9270.
44 S. Muthukrishnan, H. Mori and A. H. E. Müller, *Macromolecules*, 2005, **38**, 3108.
45 L. Zhang and A. Eisenberg, *Science*, 1995, **268**, 1728.
46 L. Zhang, K. Yu and A. Eisenberg, *Science*, 1996, **272**, 1777.
47 J. C. M. van Hest, D. A. P. Delnoye, M. W. P. L. Baars, M. H. P. van Genderen and E. W. Meijer, *Science*, 1995, **268**, 1592.
48 J. D. Hartgerink, E. Beniash and S. I. Stupp, *Science*, 2001, **294**, 1684.
49 Z. B. Li, E. Kesselman, Y. Talmon, M. A. Hillmyer and T. P. Lodge, *Science*, 2004, **306**, 98.
50 H. G. Cui, Z. Y. Chen, S. Zhong, K. L. Wooley and D. J. Pochan, *Science*, 2007, **317**, 647.
51 C. B. Tang, E. M. Lennon, G. H. Fredrickson, E. J. Kramer and C. J. Hawker, *Science*, 2008, **322**, 429.
52 X. Wang, G. Guerin, H. Wang, Y. Wang, I. Manners and M. A. Winnik, *Science*, 2007, **317**, 644.

