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Fast bulk click polymerization approach to linear and hyperbranched alternating multiblock copolymers†

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A novel bulk click polymerization (BCP) approach was determined to prepare alternative multiblock copolymers (AMCs). Poly(ε-caprolactone) (PCL) and polyethylene glycol (PEG) were first modified into azide and alkyne terminated macromonomers by esterification, respectively. Subsequent azide–alkyne click polymerization of the two macromonomers in bulk without any solvents using CuBr/*N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA) as a catalyst system afforded AMCs with higher degrees of polymerization (DPs) than those obtained *via* solution polymerization (SP) in the control experiments. Through this approach, within 1 h (normally 5 min), AMCs were obtained with high DPs of up to 16, as revealed by gel permeation chromatography (GPC). Studies on the thermal properties of the AMCs showed that the alternating structure confined the crystallizations of the PCL and PEG blocks. The solution self-assembly behavior of the amphiphilic AMCs was investigated for the first time, and interesting structures such as globules, fibers, and worms were observed by means of atomic force microscopy (AFM). Additionally, hyperbranched AMCs were also prepared *via* an $A_2 + B_3$ strategy.

Introduction

Due to the synergies of different functional blocks, multiblock copolymers have been extensively investigated to create novel functions.[1] For instance, combinations of blocks with different rigidities, compatibilities, and glass transition temperatures have resulted in thermoplastic elastomer polymers,[2] polymer plasticizers or compatilizers,[3–5] and shape-memory materials,[6–8] respectively. In this regard, alternative multiblock copolymers (AMCs) composed of different polar blocks have received increasing attention, since they can serve as emulsion agents,[3,9] phase transfer catalysts,[9] protein-adsorption-resistant materials,[10] biodegradable thermal-sensitive hydrogels for wound healing[11–16] and support matrices for drug release and cell growth.[17–20]

So far, four general strategies have been developed to prepare AMCs. The first strategy is condensation copolymerization of macromonomers possessing reactive terminal groups, such as hydroxyl, amino, and carboxyl groups. In such a process, *N*,*N*′-dicyclohexylcarbodimide (DCC)[11,12,17–19] or acyl chloride intermediates[4,7,21] were generally employed, and strictly well-defined alternating multiblocks can be achieved in the resulting AMCs. The second strategy is based on chain extension of reactive macromolecules with small chain extension agents such as 1,6-hexanediisocyanate (HDI) and tolylene-2,4-diisocyanate (TDI).[2,3,8,10,13] The third strategy denotes the self-condensation polymerization of di- or tri-block copolymer precursors with self-reactive terminal groups.[22,23] For example, di-thiol terminated macromonomers could be oxidized into AMCs *via* the formation of disulfide bonds. The last strategy signifies RAFT polymerization with poly(chain transfer units) as the chain transfer agent. In the RAFT polymerization process, monomers are consecutively inserted into poly(chain transfer units) chains to form polymer blocks.[24–26] However, it is difficult to quickly access AMCs *via* these strategies due to the relatively slow polycondensations tried thus far.

Recently, the emerging click chemistry proposed by Sharpless *et al.*, has been demonstrated to be an efficient and fast ligation technology for preparation of complex-structured polymers and modification of material surfaces.[27] In the research field of multiblock copolymers (MCs), Matyjaszewski *et al.* prepared azide terminated PS-*b*-PEO-*b*-PS triblock copolymers and then employed them to react with small dialkyne molecules to form MCs.[28] Zhu *et al.* improved this method by assembling PEO-*b*-PPO-*b*-PEO into micelles in water, followed by a click reaction to prepare MCs.[29] However, a long time (24–48 h) was still needed to fulfill the click-polycondensation in solvents. Hence, the quick and simple preparation of AMCs with high block values is still a big challenge.

Herein, we present a fast bulk click polymerization approach (BCP) to prepare AMCs without any solvents. Linear AMCs with high block values can be readily prepared in several minutes.

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The resulting AMCs can self-assemble into interesting structures such as giant fibers and worms.

Experimental

Materials

Polyethylene glycol (PEG, M_n = 1500 and 4600), poly(ε-caprolactone) diol (PCL-diol, M_n = 1250 and 2000) and poly(ε-caprolactone) triol (PCL-triol, M_n = 900) were purchased from Aldrich. Propargyl alcohol (99%), succinic anhydride (98%), *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA, 98%), *N*,*N*-(dimethylamino) pyridine (DMAP, 98%) and 1,3-dicyclohexylcarbodiimide (DCC, 98%) were purchased from Alfa Aesar and used as received. 2-Chloroethanol and tetrabutyl ammonium bromide (TBAB) were acquired from Aladdin. CuBr (Aldrich, 98%) was stirred in acetic acid for 24 h, washed with methanol three times, and vacuum dried for 24 h. Dichloromethane (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF), diethyl ether, tetrahydrofuran (THF), and other organic solvents were purchased from Sinopharm Chemical Reagent Co. Ltd. Prior to use, CH_2Cl_2 was dried over CaH_2. Acetone was dried over anhydrous $MgSO_4$. Water was distilled twice before use.

Measurements

^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were acquired on a Varian Mercury Plus 400 MHz spectrometer at 20 °C. Fourier-transform infrared (FTIR) spectra were recorded on a PE Paragon 1000 spectrometer (KBr disk). Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC) using PE series 200 with RI-WAT 150CV+ as detector, DMF (containing 0.01 mol L^{-1} LiBr) as the mobile phase at a flow rate of 1 mL min^{-1} and polyethylene glycol (PEG) as a standard at 70 °C. Thermal properties of the polymers were measured on a PerkinElmer Pyris-1 differential scanning calorimetry (DSC) under N_2 at a heating and cooling rate of 10 °C min^{-1}. Atomic force microscopy (AFM) was recorded in tapping mode on a Digital Instrument Nanoscope III scanning probe microscope.

Synthesis of 4-oxo-4-(prop-2-ynyloxy) butanoic acid, 1

The compound was synthesized according to the reported procedure with some modifications.[30] To a 250 mL round-bottom flask, acetone (80 mL), propargyl alcohol (17.4 g, 0.31 mol), succinic anhydride (30.0 g, 0.3 mol), DMAP (1.22 g, 0.01 mol) were charged. The reaction system was refluxed for 24 h. Then, acetone and excess propargyl alcohol were removed *via* rotary evaporator. The solid residual was recrystallized in toluene to afford **1** as white crystals (42.16 g, 0.27 mol). ^1H NMR (400 MHz, $CDCl_3$): 4.70 (d, 2H, CH_2O), 2.68 (m, 4H, CH_2CH_2), 2.48 (t, 1H, C≡C*H*).

Synthesis of 4-(2-azidoethoxy)-4-oxobutanoic acid, 2

To a DMF (30 mL) solution of 2-chloroethanol (22.0 g, 0.27 mol), NaN_3 (21.1 g, 0.32 mol) was slowly added in portions. TBAB (3.2 g, 0.01 mol) was then added. The mixture was stirred and heated at 80 °C for 24 h. The reaction system was distilled under reduced pressure to afford a DMF solution of 2-azidoethanol. Then, 2-azidoethanol was reacted with succinic anhydride to give **2** following the above procedure for **1**. ^1H NMR (400 MHz, $CDCl_3$): 4.27 (t, 2H, $N_3CH_2CH_2$), 3.48 (t, 2H, N_3CH_2), 2.68 (m, 4H, CH_2CH_2COOH).

Synthesis of dialkyne-ended PCL, PCL1 and PCL2

Alkynyl end groups were introduced onto PCL by esterification of terminal hydroxyl groups of PCL with **1**.[31] Typically, 50.0 g of PCL-diol (M_n = 1250, 40.0 mmol) was dissolved in 1.5 L distilled CH_2Cl_2 in a 3 L Schlenk flask. Under N_2 atmosphere and magnetic stirring, DCC (19.8 g, 96.0 mmol) and DMAP (0.6 g, 4.80 mmol) were added into the flask, followed by cooling the mixture in an ice-water bath. After dissolving DCC and DMAP, **1** (15.0 g, 96.0 mmol) was added, and the mixture was stirred at room temperature for 48 h. The generated dicyclohexylurea (DCU) was removed by filtrating, then the reaction solution was washed successively with 1 M HCl aqueous solution (3 × 1.5 L), 1 M NaOH aqueous solution (3 × 1.5 L) and deionized water (3 × 1.5 L). The obtained organic solution was dried over anhydrous $MgSO_4$ overnight. After filtration, the filtrate was concentrated on a rotary evaporator and then poured into diethyl ether (0 °C). The collected solids were further purified by repeat dissolvation and precipitation and finally dried under vacuum at 40 °C overnight to give 56.0 g of **PCL1** with a yield of 92.1%. Another dialkyne-ended PCL was similarly prepared from PCL-diol (M_n = 2000) and denoted as **PCL2**.

Synthesis of diazido-ended PEG, PEG1 and PEG2

Typically, DCC (4.95 g, 24.0 mmol), DMAP (0.15 g, 1.2 mmol), PEG (M_n = 1500, 15.0 g, 10.0 mmol) and 150 mL of distilled CH_2Cl_2 were mixed in a 250 mL Schlenk flask jacketed with aluminum foil. Then, the flask was immersed in an ice-water bath followed by dropwise adding a CH_2Cl_2 (20 mL) solution of **2** (4.49 g, 24.0 mmol). After the mixture was stirred at room temperature for 48 h, the precipitated DCU was removed by filtration and the filtrate was washed successively with 1 M HCl aqueous solution (3 × 150 mL), 1 M NaOH aqueous solution (3 × 150 mL) and deionized water (3 × 150 mL). The organic layer was dried over anhydrous $MgSO_4$ overnight, concentrated on a rotary evaporator and poured into cold diethyl ether (0 °C). The precipitates were re-dissolved and precipitated three times. Being dried under vacuum at 40 °C overnight, **PEG1** (16.3 g, 90.2%) was obtained. Another diazido-ended PEG was similarly prepared from PEG-diol (M_n = 4600) and denoted as **PEG2**.

Synthesis of trialkyne-ended PCL, PCL3

The same protocol as the synthesis of **PCL1** was employed to synthesize **PCL3**. DCC (4.95 g, 24.0 mmol), PCL-triol (Mn = 900, 6.0 g, 6.7 mmol), DMAP (0.15 g, 1.2 mmol), **1** (3.74 g, 23.9 mmol) and 100 mL distilled CH_2Cl_2 were used to yield **PCL3** (4.52 g, 59.4%).

Synthesis of linear (PEG–PCL)$_n$ alternating multiblock copolymers (LAMCs) by bulk click polymerization

In protocol **BCP1**, click polymerization between melted dialkyne-ended PCLs and diazido-ended PEGs was performed at 70 °C for 5 min without stirring in the presence of CuBr/PMDETA. In protocol **BCP2**, the same procedure as **BCP1** was used, but the polymerization time was 1 h. In protocol **BCP3**, the same procedure as **BCP2** was used, but with mechanically vigorous stirring.

Synthesis of linear (PEG–PCL)$_n$ alternating multiblock copolymers (LAMCs) by conventional solution polymerization

In the control experiments of conventional solution polymerization, in protocol **SP1**, in the absence of PMDETA ligand, a CH_2Cl_2 (1 mL) solution of dialkyne-ended PCL (100 mg) and CuBr was added dropwise with a CH_2Cl_2 (1 mL) solution of diazido-ended PEG within 1 h under N_2, with a molar ratio of [dialkyne-ended PCL] : [diazido-ended PEG] : [CuBr] of 1.0 : 1.0 : 0.33. The solution was stirred magnetically at room temperature for 24 h, diluted with CH_2Cl_2, and passed through neutral alumina to remove the copper catalyst. The product of LAMC was obtained after two precipitations into diethyl ether and vacuum dried for 24 h. In another solution polymerization protocol, **SP2**, the same procedure as **SP1** was used, but in the presence of PMDETA ligand.

A series of LAMCs were thus obtained with different PCL and PEG macromonomers under different conditions, as listed in Table 1. As an example to illustrate the denominations, **(PEG1–PCL1)BCP1** means that the AMC was prepared by copolymerization of **PCL1** and **PEG1** *via* the protocol **BCP1**.

Table 1 Polymerization results of the LAMCs

Time	LAMCs[a]	M_n	M_w	PDI[b]	DP	Conv.[c]
1 h	**(PCL1–PEG1)BCP2**	14 900	22 800	1.5	5	80%
24 h	**(PCL1–PEG1)SP1**	13 800	28 700	2.1	5	80%
24 h	**(PCL1–PEG1)SP2**	54 300	78 700	1.5	18	94%
5 min	**(PCL1–PEG2)BCP1**	32 000	57 400	1.8	5	80%
1 h	**(PCL1–PEG2)BCP2**	32 000	65 800	1.6	7	86%
24 h	**(PCL1–PEG2)SP1**	41 900	66 800	1.6	7	86%
24 h	**(PCL1–PEG2)SP2**	54 700	78 800	1.4	9	89%
5 min	**(PCL2–PEG1)BCP1**	38 300	71 800	1.9	11	91%
1 h	**(PCL2–PEG1)BCP2**	55 100	94 100	1.7	16	94%
24 h	**(PCL2–PEG1)SP1**	18 800	30 800	1.6	5	80%
24 h	**(PCL2–PEG1)SP2**	35 000	69 800	2.0	10	90%
1 h	**(PCL2–PEG2)BCP2**	37 900	59 800	1.6	6	83%
1 h	**(PCL2–PEG2)BCP3**	46 200	76 600	1.7	7	86%
24 h	**(PCL2–PEG2)SP1**	17 500	28 200	1.6	3	67%
24 h	**(PCL2–PEG2)SP2**	22 600	35 600	1.6	3	67%

[a] **(PCL1–PEG1)BCP2** means the polymer was obtained by bulk click polymerization of **PCL1** and **PEG1** under the protocol of **BCP2**. **(PCL1–PEG1)SP1** means the polymer was acquired by solution polymerization of **PCL1** and **PEG1** under the protocol of **SP1**. Solution polymerization was conducted as a control experiment for comparison with bulk click polymerization. [b] Polydispersity index (M_w/M_n). [c] Conv. means the conversion of azide or alkyne groups. Reacted groups formed triazole rings between polymerized macromonomers and the amounts were associated with DP, while unreacted groups located at the two ends of polymer chains. Thus, conv. can be approximately calculated according to this equation: conv. = (DP − 1)/DP.

Synthesis of hyperbranched (PCL–PEG)$_n$ alternating multiblock copolymers (HAMCs)

Diazido-ended PEG and trialkyne-ended PCL containing equal amounts of azide and alkyne groups were copolymerized with CuBr/PMDETA as catalyst. Similarly, three protocols were used. In the bulk polymerization protocol, **BCP**, the reactions were carried out in bulk in the presence of CuBr/PMDETA at 70 °C for 0.5 h. In the solution polymerization protocol, **SP1**, in the absence of PMDETA ligand, CuBr was quickly added to a CH_2Cl_2 (2 mL) solution of diazido-ended PEG (100 mg) and trialkyne-ended PCL under N_2. The molar ratio of reagents of [diazido-ended PEG] : [trialkyne-ended PCL] : [CuBr] was 1.5 : 1.0 : 0.33. The solution was stirred magnetically at room temperature for 10 h, diluted with CH_2Cl_2, and passed through neutral alumina to remove the copper catalyst. The formed HPAMC was obtained by two precipitations into diethyl ether and vacuum dried for 24 h. In another solution polymerization protocol, **SP2**, the reactions were carried out in the presence of PMDETA ligand following the protocol **SP1**. The molar ratio of reagents of [diazido-ended PEG] : [trialkyne-ended PCL] : [CuBr] : [PMDETA] = 1.5 : 1.0 : 0.33 : 0.33. The HAMC prepared *via* copolymerization of **PEG1** and **PCL3** under protocol BCP were denoted as **HAMC-1-BCP**. Other HAMCs were denoted in the same manner. The results are presented in Table 2.

Preparation of micelles

The LAMC copolymers were dissolved in THF overnight, and then the THF solutions of the copolymers were dialyzed against distilled water to prepare micelles. The drops were spin-coated onto the surfaces of mica plates and dried under vacuum at room temperature overnight, affording the self-assembled samples of copolymers for AFM characterizations.

Results and discussion

General description of bulk click polymerization (BCP)

The reported MCs, such as poly(PS-*b*-PEO-*b*-PS) and poly(PEO-*b*-PPO-*b*-PEO), were prepared by solution polymerization.[28,29] Due to solvent dilution, concentrations of terminal reactive groups were highly reduced, leading to the decrease in DP and long reaction time caused by relatively low reactivity of end functional groups. Therefore, it would be more efficient to carry out such polymerizations

Table 2 Polymerization results of the HAMCs[a]

HAMCs	M_n	M_w	PDI	DP
HAMC-1-SP1	13 000	37 400	2.9	5
HAMC-1-SP2	21 000	77 100	3.7	8
HAMC-1-BCP	17 900[a]	62 300	3.5	7
HAMC-2-SP1	23 600	173 200	7.3	4
HAMC-2-SP2	25 500	92 800	3.6	4
HAMC-2-BCP	16 800[a]	53 800	3.2	3

[a] Partially crosslinked copolymers were obtained. It was found that there were some small crosslinked gels that could not be dissolved in CH_2Cl_2. The major part of copolymers that could be dissolved copolymers were subjected to GPC characterization.

in bulk. If so, MCs and AMCs with high DP can be possibly prepared in a short time. Besides, no organic solvent is needed in a bulk polymerization, which is quite attractive in large-scale production for the green and cost-effective features. Thus, we represent **BCP** to fast synthesize AMCs in this article.

Since bulk polymerization proceeds in a liquid state, liquid or melted macromolecular monomers are needed. PCL and PEG were chosen as monomers because they can be totally melted at a mild temperature (~60 °C). The terminal hydroxyl groups of commercial PCL and PEG were esterified to introduce azide and alkyne groups, respectively. Subsequent BCP between them quickly afforded AMCs of high DP. Moreover, hyperbranched AMCs can also be synthesized *via* BCP. The synthesis protocol is shown in Scheme 1.

Synthesis of PCL and PEG macromonomers

As illustrated in Scheme 1, the dialkyne-ended PCL and diazido-ended PEG were synthesized by esterifications of PCL with **1** and **2** in the presence of DCC and DMAP, respectively.

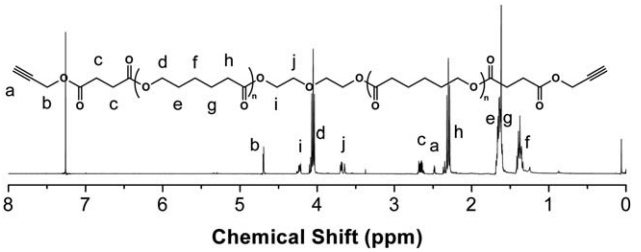
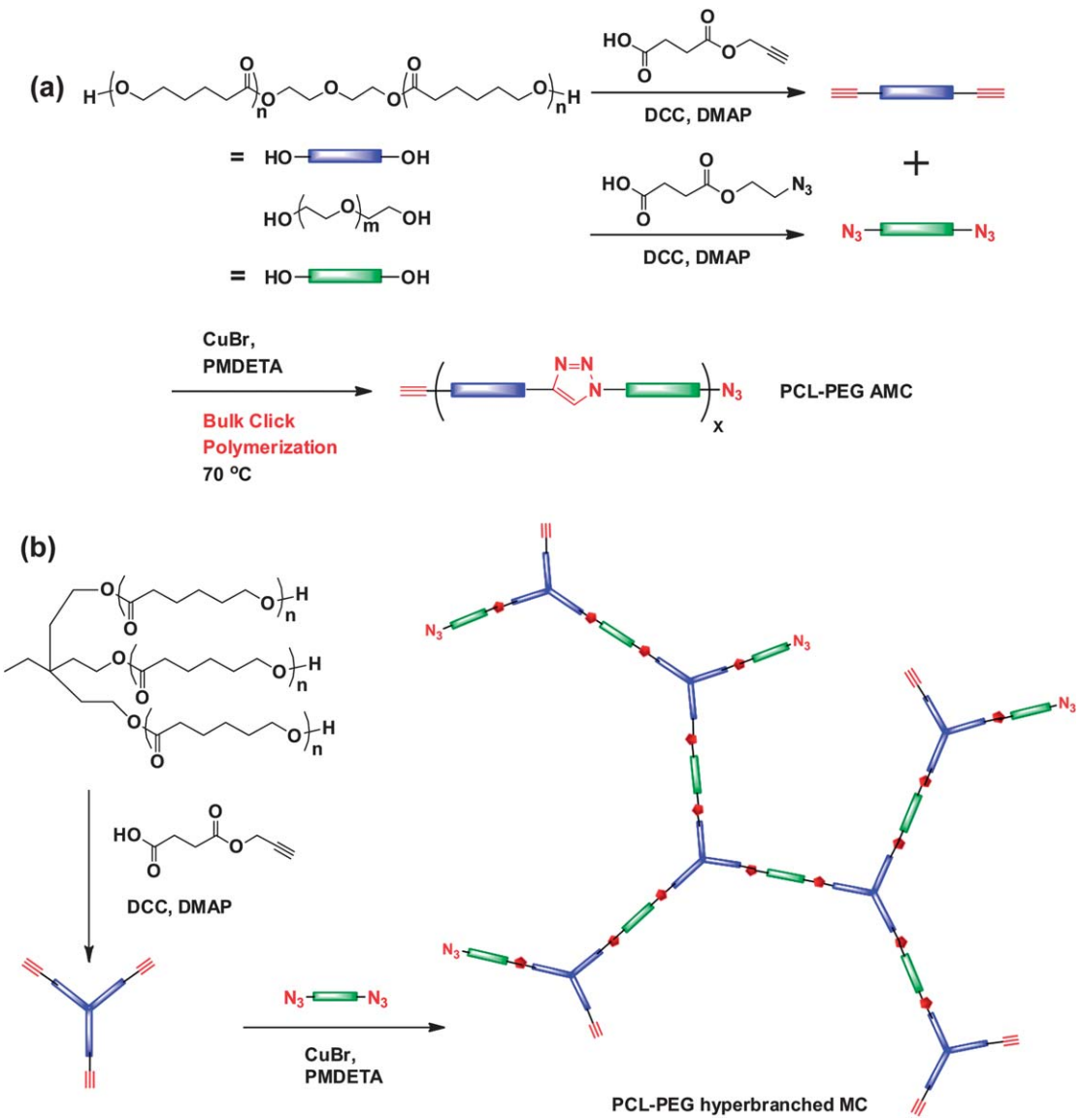


Fig. 1 ^{1}H NMR spectrum of dialkyne-ended PCL.



Scheme 1 Synthetic route for linear (a) and hyperbranched AMCs (b) *via* bulk click polymerization (BCP) and conventional solution polymerization (SP).

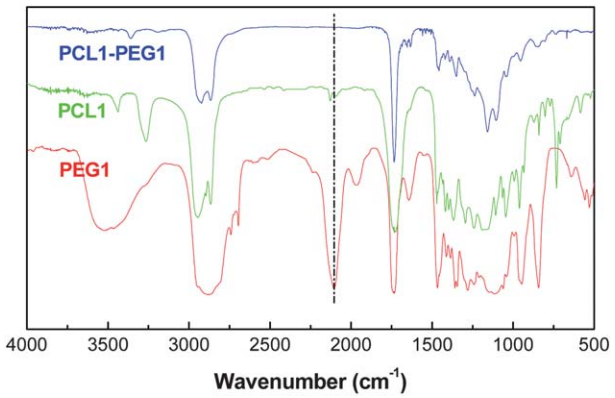


Fig. 2 FTIR spectra of **PEG1–PEG1**, **PCL1**, and **PEG1**.

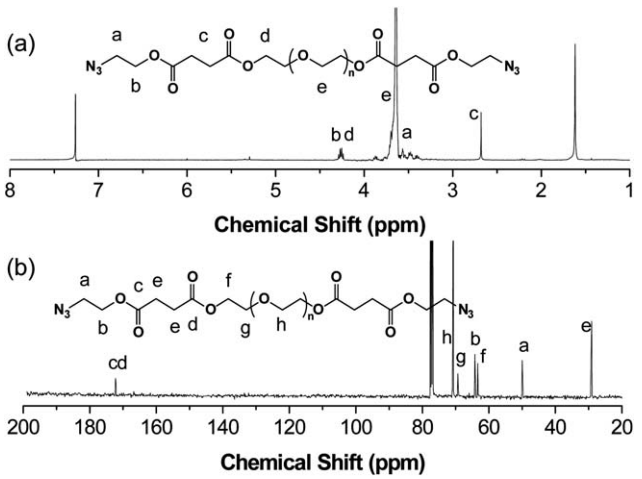


Fig. 3 ^{1}H (a) and ^{13}C (b) NMR spectra of diazido-ended PEG.

Both the macromonomers could be prepared on a large-scale as described in the experimental section. In the ^{1}H NMR (Fig. 1) and FTIR (Fig. 2) spectra of dialkyne-ended PCL, the signals of the protons in the propargyl groups were observed at 2.48 and 4.7 ppm, the signals of the protons in the $COOCH_2CH_2COO$ moiety were seen at 2.68 ppm, and the characteristic absorption bands of alkyne groups emerged at 3300 and 2150 cm^{-1}. In the MALDI-TOF mass spectra (Fig. S1 and S2†), it was found that, after the introduction of alkyne groups at both ends, the PCL polymers' molecular weights increased 276 Da which was equal to the theoretical value. These results indicated the successful preparation of dialkyne-ended PCL. In the ^{13}C NMR (Fig. 3) and FTIR (Fig. 2) spectra of diazido-ended PEG, the carbon signals of the $N_3CH_2CH_2O$ moiety were located at 49.8 and 64.1 ppm, a carbon signal ascribed to the methylene unit in the newly formed $COOCH_2$ moiety emerged at 63.3 ppm, and the azide groups exhibited a strong absorption band at 2106 cm^{-1}. MALDI-TOF MS analysis (Fig. S3 and S4†) showed that the molecular weight of each PEG chain increased to 338 Da after reaction completion. These results implied that PEG-diol was successfully functionalized with azide groups.

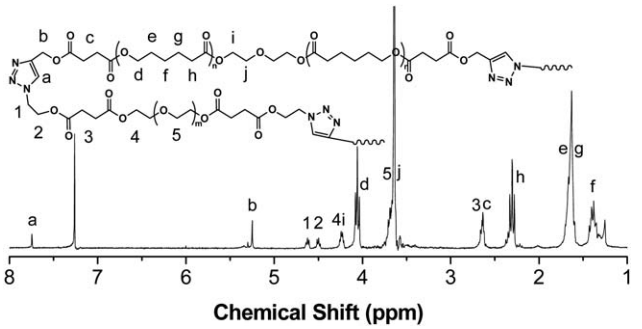


Fig. 4 ^{1}H NMR spectrum of a **PCL1–PEG1** LAMC.

Synthesis and characterization of PCL–PEG linear AMCs

PCL and PEG linear AMCs (LAMCs) were prepared *via* Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) click polymerization. Two PCL chains of different length, **PCL1** and **PCL2**, and two PEG chains of different length, **PEG1** and **PEG2**, were orthogonally copolymerized to afford four types of LAMCs, **PCL1–PEG1**, **PCL1–PEG2**, **PCL2–PEG1**, and **PCL2–PEG2**.

The ^{1}H NMR spectrum of a typical LAMC, **PCL1–PEG1**, was presented in Fig. 4. By comparing it with the spectra of dialkyne-ended PCL and diazide-ended PEG, a new signal at 7.74 ppm emerged as a characteristic single peak of the protons in the triazole rings. The single peak implied that only the 1,4-adducts were regioselectively acquired due to the catalysis of Cu(I) and the 1,5-adducts did not exist, though they could be generated together with the 1,4-adducts *via* thermal-induced Huisgen coupling.[32] Due to the ring formation, the signals of the protons in the $N_3CH_2CH_2O$-moiety originally located at 3.49 and 4.28 ppm shifted to 4.50 and 4.62 ppm, respectively, and the signal of the $-CH_2-$ proton in the propargyl group originally appearing at 4.7 ppm shifted to 5.25 ppm. In the FTIR spectrum of **PCL1–PEG1**, the characteristic bands of the azide and alkyne groups originally appearing between 2100 and 2125 cm^{-1} disappeared due to the transformation of these two groups into triazole rings. These observations revealed that the CuAAC click condensation between PCL and PEG indeed occurred, giving rise to PCL and PEG LAMCs.

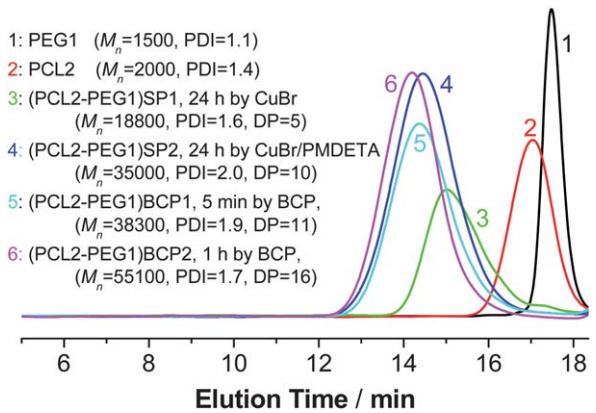


Fig. 5 GPC curves of the **PCL2–PEG1** series LAMCs.

Table 3 Polymerization results of other PCL–PEG LAMCs acquired from literatures

M_n of PCL monomer	M_n of PEG monomer	M_n	M_w	PDI	DP	Ref.
3000	3000	44 900	75 400	1.7	8	6
1250	2000	27 200	67 400	2.5	8	4
1250	1000	7700	22 800	1.6	3	4
1000	1000	12 700	29 200	2.3	6	14
3000	3000	26 400	40 500	1.5	4	7
2000	1500	38 000	—	—	11	15
1250	1000	28 000	—	—	12	15
2000	1000	37 800	—	—	12	15

The LAMCs were subjected to GPC measurements. The results and typical curves are presented in Table 1 and Fig. 5, respectively. The LAMCs displayed symmetrically unimodal peaks that came out obviously earlier than those of the PCL and PEG macromonomers, indicating that high molecular weight LAMCs without macromonomer precursors were obtained. Five protocols with different reaction conditions were tried comparatively as described in the experimental section (*e.g.*, with or without PMDETA ligands, with or without stirring, solution polymerization or bulk polymerization). Generally, LAMCs have molecular weights an order of magnitude higher than those of macromonomers (Table 1). The PDI of the obtained LAMCs varied from 1.4 to 2.1 and the highest number-average DP reached 16. By comparing the LAMCs obtained under protocol **SP1** with those under **SP2**, it was judged that the addition of PMDETA ligands could greatly enhance the molecular weights of the LAMCs. Because the melting temperatures (T_m) of PEG and PCL are about 48 and 46 °C, respectively, the copolymerization can efficiently proceed in bulk at 70 °C. The comparison between the LAMCs obtained under **SP2** and those under **BCP1** and **BCP2** revealed that BCP at 70 °C for 1 h gave LAMCs with a higher DP when higher molecular weight macromonomers were employed, mainly due to the higher concentration of terminal clickable groups. The vigorous stirring could also enhance the molecular weight and DP to some extent because of the more efficient touching of clickable groups, as suggested by the results of **(PCL2–PEG2)BCP2** and **(PCL2–PEG2)BCP3**. Notably, the DP resulted from BCP with only 5 min of polymerization approached 11, higher than that obtained by common click polymerization for 24 h in solvent. Furthermore, the sample **(PCL2–PEG1)BCP2** in the series of **PCL2–PEG1** reached the highest DP of 16 with an M_n of 55 100 and an M_w of 94 100. As a comparison, the results of PCL–PEG AMCs previously reported in the literature are listed in Table 3. Obviously, the M_n and DP of AMCs prepared by our fast BCP (within 1 h) are generally higher than previous results with 1–24 h of polymerization, and our M_n (55 100) and DP (16) maxima are also much higher than previous values (M_n = 44 900 and DP = 13). Therefore, BCP is indeed a fast and highly efficient method for preparation of AMCs.

Synthesis and characterization of PCL–PEG hyperbranched AMCs

Long-chain dendritic polymers including DendriMac and HyperMac have been identified as new dendritic polymers.[33]

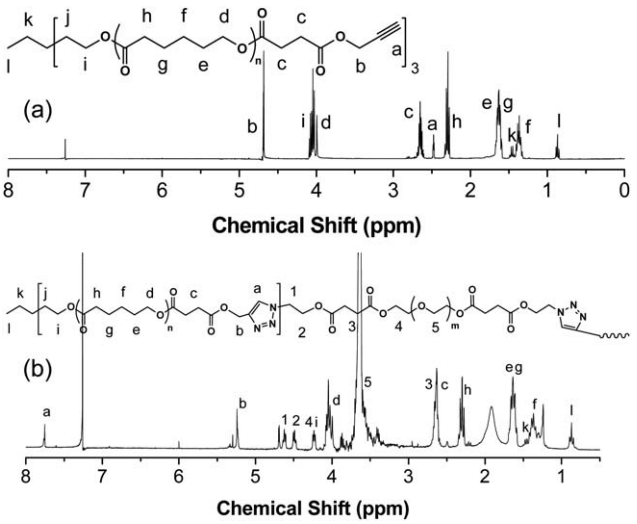


Fig. 6 ^{1}H NMR spectrum of trialkyne-ended PCL, **PCL3** (a); and **HAMC-2-SP1** (b) prepared under condition **SP1**.

Herein, based on the successful application of BCP in the fast formation of LAMCs, we also tried to prepare hyperbranched AMCs (HAMCs) or HyperMac AMCs *via* the $A_2 + B_3$ methodology.[34] A PCL macromonomer containing three terminal alkyne groups, **PCL3**, was used as a B_3 monomer. In the ^{1}H NMR spectrum of **PCL3** (Fig. 6), the propargyl groups displayed the proton signals at 2.5 and 4.7 ppm. **PEG1** and **PEG2** were used as A_2 monomers. Fig. 6b shows the ^{1}H NMR spectrum of HAMCs. Because the structure of **PCL3** is very close to **PCL1** and **PCL2**, the spectrum is similar to that of LAMCs (Fig. 4). The peak at 4.7 ppm implied the existence of unreacted propargyl groups which can be utilized for further modification with other azide compounds. Three copolymerization conditions were applied as described in the experimental section. The results are summarized in Table 2. Because the $A_2 + B_3$ reaction can easily cause crosslinking, the polymerization should be generally conducted under mild and dilute conditions. As a result, **SP1** afforded soluble HAMCs, which adopted dilute solution in the absence of PMDETA at room temperature. By the addition of

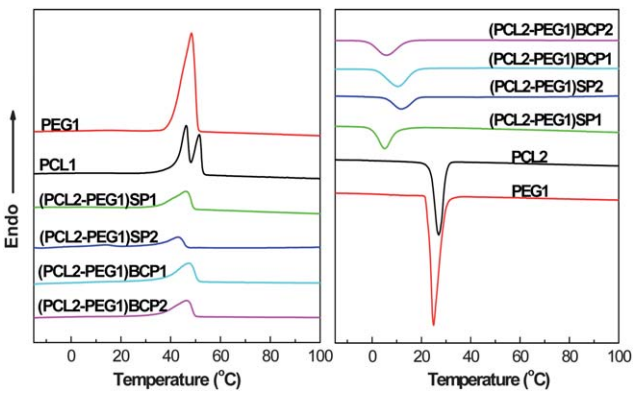


Fig. 7 The heating (left) and cooling (right) DSC thermograms of the **PCL2–PEG1** series LAMCs.

Table 4 DSC data of the macromonomers and LAMCs

LAMCs	T_m (°C)	ΔH_m (J g^{-1})	T_c (°C)	ΔH_c (J g^{-1})
PCL2	46.2	62.6	27.1	−62.6
PEG1	48.4	160.7	25.0	−153.9
(PCL2–PEG1)SP1	46.2	35.4	5.2	−37.1
(PCL2–PEG1)SP2	43.5	26.6	12.0	−28.6
(PCL2–PEG1)BCP1	47.4	31.4	10.5	−38.0
(PCL2–PEG1)BCP2	46.5	35.9	5.7	−37.2

PMDETA ligands, the molecular weights could be greatly enhanced. The bulk copolymerization at 70 °C for 0.5 h resulted in partially crosslinked polymers. The sample, **HAMC-1-SP2**, possessed the highest DP of 8. Much broader PDIs were found for the HAMCs, which is consistent with the theory and prior experimental results of hyperbranched polymers.[34,35]

Thermal properties of LAMCs

With an identical thermal operation applied to the samples, the heating and cooling DSC profiles for the macromonomers and the **PCL2–PEG1** series are shown in Fig. 7a and b, respectively. The dual melting behavior of **PCL2** is attributed to melting of the initial crystals followed by recrystallization and final melting of the crystals grown during the heating scan.[36] All the copolymers showed a single melting and a single crystallization peak probably due to the overlapping of each melting endotherm and cooling exotherm. The melting curves of the LAMCs and the control macromonomers exhibited similar melting peaks at 30–50 °C. In the cooling curve, the T_cs of the LAMCs were much lower than those of the control **PCL2** and **PEG1**, probably resulting from the confinement effect of multiblock topological structure with crystallization. Both the melting enthalpy and crystallization enthalpy values were much lower than the control **PCL2** and **PEG1**, revealing that the LAMCs exhibit a lower degree of crystallinity (Table 4).

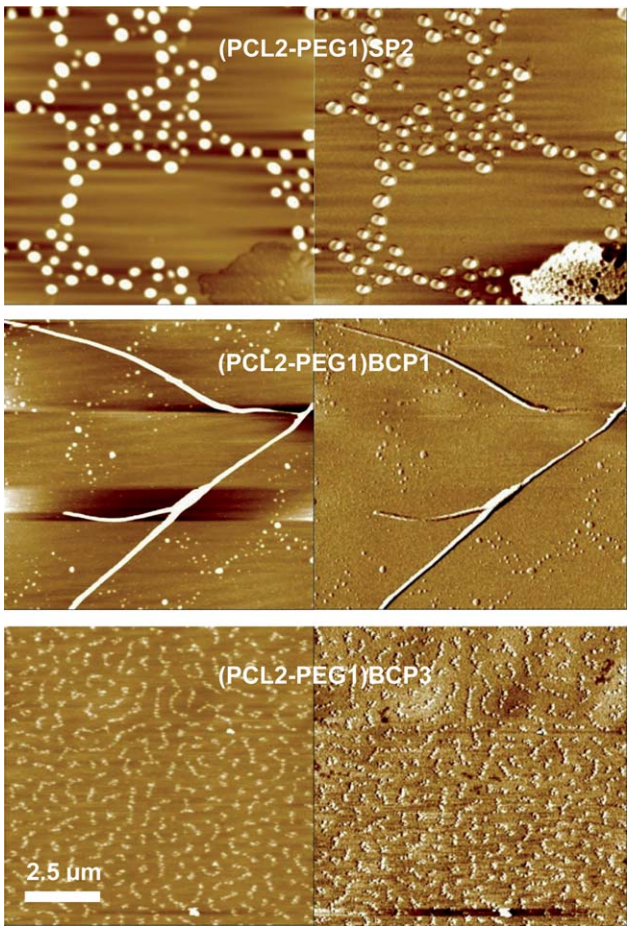


Fig. 8 AFM tapping mode height (left) and phase (right) images for **(PCL2–PEG1)SP2** (top), **(PCL2–PEG1)BCP1** (middle), and **(PCL2–PEG1)BCP3** (bottom).

Primary self-assembly behavior of PCL–PEG LAMCs

The LAMCs possess water-insoluble PCL and water-soluble PEG segments, so water is chosen as a selective solvent to induce self-assembly. With an identical operation being applied, three LAMCs, **(PCL2–PEG1)SP1**, **(PCL2–PEG1)BCP1**, and **(PCL2–PEG2)BCP3**, were employed to form micelles. The self-assembled samples were subjected to atomic force microscopy (AFM) analysis (Fig. 8). **(PCL2–PEG1) SP1** assembled into globular particles with diameters ranging from 0.3 to 0.9 μm. **(PCL2–PEG1)BCP1**, with a higher DP than **(PCL2–PEG1)SP1**, formed fibres with diameters of about 0.1 μm. **(PCL2–PEG2)BCP3**, with longer PEG chains, afforded worm-like assemblies. The involved mechanism of the formation of these structures is not clear yet. More investigations are being conducted in our lab currently, and the details will be reported later.

Conclusions

Both the bulk and solution click copolymerizations for preparing LAMCs were conducted. Consequently, the bulk click condensation of melted PCL and PEG macromonomers at 70 °C under vigorous stirring was ascertained to be much more powerful on affording LAMCs of high DP. Additionally, BCP exhibited improved rapidness and simplicity. The preparation of HAMCs *via* the bulk and solution click copolymerizations with $A_2 + B_3$ methodologies were also investigated. As a result, the bulk copolymerization proceeded very quickly and afforded partially crosslinked copolymers, while the milder solution conditions could yield soluble HAMCs. The afforded LAMCs exhibited a lower degree of crystallization compared with the PCL and PEG macromonomers. The primary observations of the solution self-assembly behaviours of these amphiphilic LAMCs revealed that they can form globules, fibres, and worm-like structures, implying that AMCs can be used as versatile self-assembly precursors to construct many supramolecular structures.

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References

1 N. Hadjichristidis, M. Pitskalis, S. Pispas and H. Iatrou, *Chem. Rev.*, 2001, **101**, 3747; N. Hadjichristidis, E. Iatrou, M. Pitsikalis and J. Mays, *Prog. Polym. Sci.*, 2006, **31**, 1068; K. Matyjaszewski, *Science*, 2011, **333**, 1104.
2 D. Cohn and A. H. Salomon, *Biomaterials*, 2005, **26**, 2297.
3 H. Q. Xie, D. Xie, X. Y. Chen and J. S. Guo, *J. Appl. Polym. Sci.*, 2005, **95**, 1295.
4 P. Ferruti, I. Mancin, E. Ranucci, C. De Felice, G. Latini and M. Laus, *Biomacromolecules*, 2003, **4**, 181.
5 F. Samperi, R. Mendichi, L. Sartore, M. Penco and C. Puglisi, *Macromolecules*, 2006, **39**, 9223.
6 M. Nagata and K. Inaki, *J. Appl. Polym. Sci.*, 2011, **120**, 3556.
7 M. Nagata and I. Kitazima, *Colloid Polym. Sci.*, 2006, **284**, 380.
8 C. Min, W. Cui, J. Bei and S. Wang, *Polym. Adv. Technol.*, 2005, **16**, 608.
9 H. Q. Xie and J. S. Guo, *Angew. Makromol. Chem.*, 1999, **264**, 82.
10 J. H. Parka, Y. W. Chob, I. C. Kwonb, S. Y. Jeongb and Y. H. Bae, *Biomaterials*, 2002, **23**, 3991.
11 J. S. Lee, Y. H. Bae, Y. S. Sohn and B. Jeong, *Biomacromolecules*, 2006, **7**, 1729.
12 M. K. Joo, Y. S. Sohn and B. Jeong, *Macromolecules*, 2007, **40**, 5111.
13 J. W. Lee, F. J. Hua and D. S. Lee, *J. Controlled Release*, 2001, **73**, 315.
14 S. J. Bae, M. K. Joo, Y. Jeong, S. W. Kim, W. K. Lee, Y. S. Sohn and B. Jeong, *Macromolecules*, 2006, **39**, 4873.
15 Y. H. Bae, K. M. Huh, Y. Kim and K. H. Park, *J. Controlled Release*, 2000, **64**, 3.
16 J. H. Kim and Y. H. Bae, *Eur. J. Pharm. Sci.*, 2004, **23**, 245.
17 T. M. Hyun, Y. K. Lee, J. K. Han and Y. R. Byun, *J. Biomater. Sci., Polym. Ed.*, 2002, **13**, 817.
18 M. Pechar, K. Ulbrich, V. Subr, L. W. Seymour and E. H. Schacht, *Bioconjugate Chem.*, 2000, **11**, 131.
19 M. Bikram, C. H. Ahn, S. Y. Chae, M. H. Lee, J. W. Yockman and S. W. Kim, *Macromolecules*, 2004, **37**, 1903.
20 X. J. Loh, K. B. Colin and J. Li, *Biomaterials*, 2008, **29**, 3185.
21 O. Jeon, S. H. Lee, S. H. Kim, Y. M. Lee and Y. H. Kim, *Macromolecules*, 2003, **36**, 5585.
22 Q. Zhang, J. Ye, Y. Lu, T. Nie, D. Xie, Q. Song, H. Chen, G. Zhang, Y. Tang, C. Wu and Z. Xie, *Macromolecules*, 2008, **41**, 2228.
23 K. H. Sun, Y. S. Sohn and B. Jeong, *Biomacromolecules*, 2006, **7**, 2871.
24 D. Pavlovic, J. G. Linhardt, J. F. Kunzler and D. A. Shipp, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 7033.
25 Z. Jia, C. Liu and J. Huang, *Polymer*, 2006, **47**, 7615.
26 Y. Zhou, K. Jiang, Q. Song and S. Liu, *Langmuir*, 2007, **23**, 13076.
27 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004; L. Zhao, X. Pang, R. Adhikary, J. W. Petrich and Z. Q. Lin, *Angew. Chem., Int. Ed.*, 2011, **50**, 3958; X. Pang, L. Zhao, C. W. Feng and Z. Q. Lin, *Macromolecules*, 2011, **44**, 7176; P. L. Golas and K. Matyjaszewski, *Chem. Soc. Rev.*, 2010, **39**, 1338; C. J. Hawker and K. L. Wooley, *Science*, 2005, **309**, 1200; H. He and C. Gao, *Curr. Org. Chem.*, 2011, **15**, 3667; J. Han, B. Zhao, Y. Gao, A. Tang and C. Gao, *Polym. Chem.*, 2011, **2**, 2175; J. Han and C. Gao, *Nano-Micro Lett.*, 2010, **2**, 213; A. J. Qin, J. W. Y. Lam and B. Z. Tang, *Chem. Soc. Rev.*, 2010, **39**, 2522.
28 P. L. Golas, N. V. Tsarevsky, B. S. Sumerlin, L. M. Walker and K. Matyjaszewski, *Aust. J. Chem.*, 2007, **60**, 400.
29 W. Wang, T. Li, T. Yu and F. Zhu, *Macromolecules*, 2008, **41**, 9750.
30 Y. Zhang, H. He and C. Gao, *Macromolecules*, 2008, **41**, 9581.
31 J. Wu and C. Gao, *Macromol. Chem. Phys.*, 2009, **210**, 1697.
32 H. L. Cohen, *J. Polym. Sci., Polym. Chem. Ed.*, 1981, **19**, 3269; A. Scarpaci, C. Cabanetos, E. Blart, Y. Pellegrin, V. Montembault, L. Fontaine, V. Rodriguez and F. Odobel, *Polym. Chem.*, 2011, **2**, 157.
33 D. Konkolewicz, M. J. Monteiro and S. Perrier, *Macromolecules*, 2011, **44**, 7067; C. A. Bell, Z. Jia, J. Kulis and M. J. Monteiro, *Macromolecules*, 2011, **44**, 4814; C. N. Urbani, C. A. Bell, M. R. Whittaker and M. J. Monteiro, *Macromolecules*, 2008, **41**, 1057; C. N. Urbani, C. A. Bell, D. Lonsdale, M. R. Whittaker and M. J. Monteiro, *Macromolecules*, 2008, **41**, 76; L. R. Hutchings, *Soft Matter*, 2008, **4**, 2150; L. R. Hutchings, J. M. Dodds and S. J. Roberts-Bleming, *Macromolecules*, 2005, **38**, 5970.
34 C. Gao and D. Yan, *Prog. Polym. Sci.*, 2004, **29**, 183; D. Y. Yan, C. Gao and H. Frey, in *Hyperbranched Polymers*, John Wiley & Sons, Inc., Hoboken, 2011, ch. 4, p. 107; A. Qin, J. W. Y. Lam, C. K. W. Jim, L. Z. Yan, M. Haussler, J. Liu, Y. Dong, D. Liang, E. Chen, G. Jia and B. Z. Tang, *Macromolecules*, 2008, **41**, 3808; Y. Tang, C. K. W. Jim, Y. Liu, L. Ye, A. Qin, J. W. Y. Lam, C. Zhao and B. Z. Tang, *ACS Appl. Mater. Interfaces*, 2010, **2**, 566; W. Liu and C. M. Dong, *Macromolecules*, 2010, **43**, 8447.
35 Z. P. Zhou and D. Y. Yan, *Macromolecules*, 2008, **41**, 4429; D. Y. Yan, A. H. E. Müller and K. Matyjaszewski, *Macromolecules*, 1997, **30**, 7024.
36 B. Wunderlich, *Macromolecular Physics*, Academic, London, 1973, vol. 1–3.