Synthesis of a Novel Kind of Amphiphilic Graft Copolymer with Miktoarm Star-Shaped Side Chains

Xiaolan Luo, Guowei Wang, Xinchang Pang, and Junlian Huang*

The Key Laboratory of Molecular Engineering of Polymer, State Education Ministry of China, Department of Macromolecular Science, Fudan University, Shanghai 200433, China

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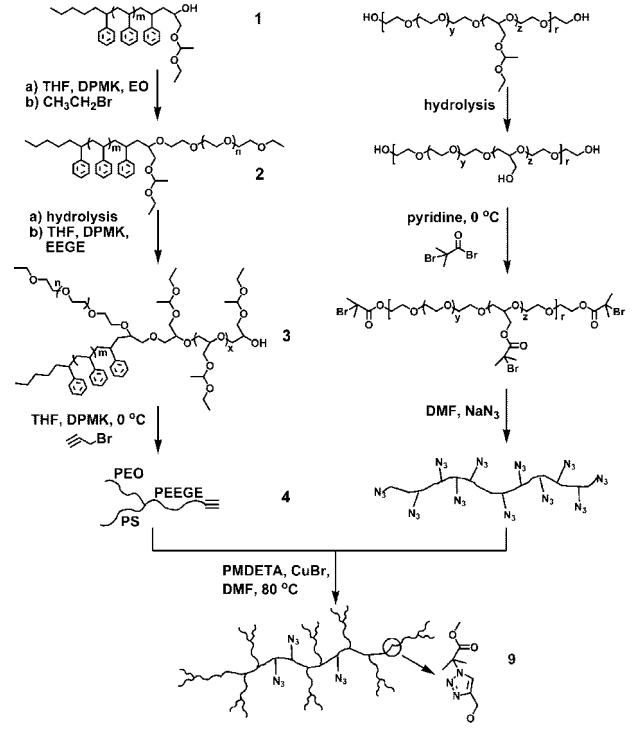
Introduction. In recent years, much attention is paid to the synthesis of copolymers with different compositions and chain architectures, such as linear, grafted, comb-shaped, star-shaped, hyperbranched, and dendrimeric chains with the purpose to establish architecture−property relationships in bulk and in solution.[1,2] Of these various architectures, the graft copolymers, especially the amphiphilic graft copolymers, are attractive materials because of their unique chemical and physical properties as well as their potential applications in drugs,[3] bimomaterials,[4] nanotechnology,[5] polymer−hybrid nanocomposites,[6] and supermolecular science.[7] Generally, three strategies were used for the preparation of amphiphilic graft copolymers:[8] (i) grafting onto,[9,10] in which side chains are preformed and then attached to the main chain; (ii) grafting from,[11,12] in which the monomer is grafted from the main chain; and (iii) grafting through,[13,14] in which the macromonomers are copolymerized.

It is well-known that controlled polymerizations such as anionic, ATRP, and RAFT are powerful tools for the synthesis of linear polymers with well-controlled molecular weight and polydispersity, and it is possible to make topological tailoring on polymer by the reactions of anion with some functional compounds or modification of the end groups.[1,2,15] And "click" reactions, as termed by Sharpless et al.,[16] are widely used in polymer chemistry[17,18] during the past few years due to their high specificity, quantitative yields, and near-perfect fidelity in the presence of most functional groups. Therefore, it is promising to combine the click reaction with controlled polymerization methods to synthesize the graft copolymers with complex structure.

Miktoarm star polymer is a kind of copolymer in which the arms with same or different chemical structure were connected at one junction point. They showed quite different microdomain morphologies in bulk[19–21] and self-assembly behavior in solution[22,23] compared with the comb-shaped,[24] block-grafted,[25,26] cyclic,[27,28] arborescent,[29] and hyperbranched[30] copolymers. In the investigation of ABC 3-miktoarm star-shaped terpolymers polystyrene−poly(ethylene oxide)−poly(ethoxyethyl glycidyl ether) (PS−PEO−PEEGE),[31] it was found that the hydroxyl end group of PEEGE block could be modified further, and then the miktoarm star copolymers with functional group as alkyne group were obtained. If these star copolymers could be fastened onto a polymer chain by reaction of functional groups between graft and main chains, then these graft copolymers with complex structure may provide new models for the investigation of morphologies and self-assembly of copolymers. Up to now, few publications are reported about the synthesis of the amphiphilic graft copolymer with miktoarm star side chains; only Yu et al.[32] reported recently the synthesis of hydrophobic graft polymers with Y-shaped branches.

Scheme 1. Synthesis of the Amphiphilc Graft Copolymer with Miktoarm Star-Shaped Side Chain by Click Reaction



In this paper, a novel kind of graft copolymers composed of the copolymers of EO and EEGE[33,34] as main chains and star-shaped functionalized ABC copolymers of PS−PEO−PEEGE as side chains were described. The copolymers main chains with pending functional groups were modified to azide groups first by a series of reactions, and then the coupling reaction of the azide groups on main chain with alkyne group at PEEGE chain end of miktoarm star copolymers could be easily carried out.

Results and Discussion. The whole preparation process is outlined in Scheme 1. First, the poly(styryl)lithium (PS^-Li^+) was capped by EEGE to form the functionalized polymer **1**, which had an active and a protected hydroxyl group at ω-end. Then the polymer **1** was used as macro-initiator for ring-opening polymerization (ROP) of EO in THF using diphenylmethylpotassium (DPMK) as protonation agent and bromoethane as cap molecule, and the PS-*b*-PEO **2** with ethoxyethyl group at the junction point was obtained. After hydrolysis, PS-*b*-PEO with an active hydroxyl group was used as macro-initiator again for ROP of EEGE under similar conditions as polymerization of EO to produce star (PS−PEO−PEEGE) copolymer **3**. The transformations of functional polymer **1** to copolymers **2** and **3** were well defined (Supporting Information). Subsequently, the propargyl group was introduced into PEEGE chain end of star copolymer **3** by the nucleophilic substitution reaction between the active hydroxyl group and propargyl bromide in the DPMK/THF system; alkyne-terminated star copolymer **4** was obtained. The structure of copolymer **4** was confirmed by analysis of the ^1H NMR spectrum (Figure 1), which presented signals at 2.43 ppm and 4.35 ppm due to the resonance of the methine proton and methylene protons of the propargyl end group in addition

* Corresponding author. E-mail: jlhuang@fudan.edu.cn.

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Table 1. Polymerization Data of the Graft Copolymers and the Precursors

	side chains		main chains			graft copolymers **9**				
entry	$M_{n,NMR}$(**3**) (g/mol)	EF[a](**4**) (%)	$M_{n,SEC}$(**5**) (g/mol)	PDI (**5**)	EF[d](**8**) (%)	$M_{n,SEC}$[c] (g/mol)	PDI[c]	$M_{n,th}$[e] (g/mol)	$M_{n,NMR}$[f] (g/mol)	Y_{gra}[g] (%)
A	5900	>99	9300[b]	1.10[b]	100	3300	1.04	57000	39000	62.5
B	5900	>99	10000[c]	1.09[c]	100	3900	1.10	93000	63000	63.9
C	13100	>99	9300[b]	1.10[b]	100	5900	1.14	114000		
D	13100	>99	10000[c]	1.09[c]	100	6700	1.09	193000		

[a] EF is the efficiency of alkyne group functionality, which was determined by ^{1}H NMR analysis (Figure 1, bottom). [b] Determined by SEC, calibrated against PEO standard using 0.1 M $NaNO_3$ as eluent. [c] Determined by SEC using PS as standard and THF as solvent. [d] EF is the azidation efficiency of the bromide atoms of copolymer **7**, which was determined by ^{1}H NMR analysis (Supporting Information). [e] Calculated using the known M_n of the backbone and the side chain. [f] Calculated by ^{1}H NMR using the formula $M_{n,NMR}(\mathbf{9}) = M_{n,SEC}(\mathbf{5}) + N_{N3} \times M_{n,NMR}(\mathbf{3}) \times Y_{grafting}$, in which N_{N3} was the number of azide groups on the main chain (Supporting Information). [g] The graft efficiency was calculated according to the ^{1}H NMR spectrum (Figure 1, top).

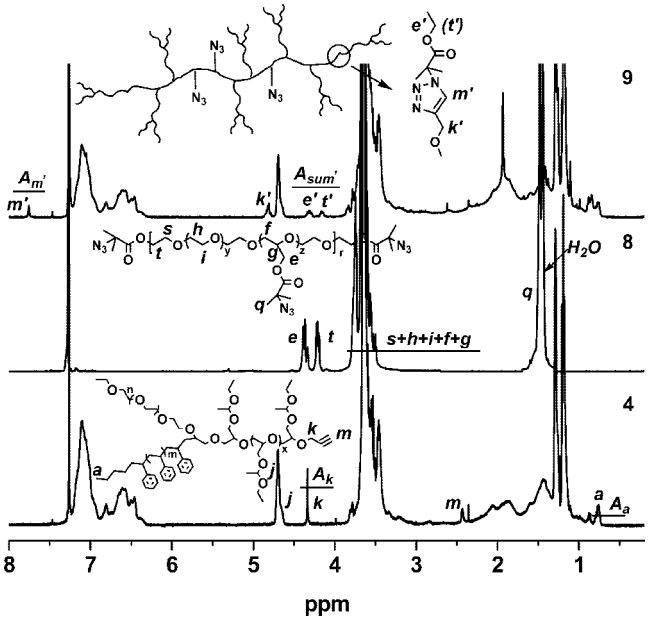

Figure 1. ^{1}H NMR spectra ($CDCl_3$) of copolymers **4**, **8**, and **9**.

to the signals characteristic of PS, PEO, and PEEGE components. The efficiency of end-group functionality of copolymer **3** was as high as 99%, which was ascertained from the ^{1}H NMR spectrum according to the following formula:

$$E_a = \frac{A_k/2}{A_a/3} \times 100\% \quad (1)$$

in which E_a is the efficiency of alkyne end group functionality; A_k and A_a are the integral areas of methylene protons of the propargyl end group at 4.35 ppm and methyl protons of *n*-butyl end group at 0.8 ppm, respectively. The FT-IR spectrum also showed a new absorption at 3252 cm^{-1} characteristic of the alkyne group (Supporting Information).

A well-defined copolymer main chain **5** was successfully prepared through the anionic copolymerization of EO and EEGE using DPMK and triethylene glycol as co-initiator, and then ethoxyethyl groups of EEGE units of the copolymer **5** were removed by hydrolysis. The formed poly(ethylene oxide-*co*-glycidol) poly(EO-*co*-Gly) **6** was esterified by the reaction between the pending hydroxyl groups of glycidol units of copolymers and 2-bromoisobutyryl bromide to produce the copolymer **7**. The pending bromide atoms of the latter were converted quantitatively into azides by reaction with sodium azide in DMF at room temperature for 24 h. Then the copolymer **8** with multiple azide groups was obtained. For each step aforementioned, the efficiency of functionality was very high, and the intermediates and object product were determined by ^{1}H NMR, SEC, and FT-IR in detail (Supporting Information). Among them, the molecular weight of copolymers **5A** and **5B** was determined by SEC using different calibrations, respectively. For copolymer **5A** with low EEGE content, its component and structure were similar as those of PEO, so the molecular weight of copolymer **5A** could be determined by SEC using PEO as standard.[35] As for copolymer **5B** with high EEGE content, its solubility was relatively poor in the water because of the hydrophobic property of PEEGE, then its molecular weight was determined by SEC using PS as standard and THF as solvent, and it was reasonable according to the previous work.[33,34,36] In the preliminary step for the anionic copolymerization, the parent copolymers with different contents of EEGE and different molecular weights could be prepared by the variation of the monomer feed ratio and the amount of the initiator. Thus, the EEGE density of the main chain could be well controlled, and the number of azide groups on the PEO chain could be ascertained.

Finally, the click reaction between the main chain with azide groups and alkyne-terminated star-shaped side chains was carried out in the presence of CuBr/PMDETA in DMF.[37] In the ^{1}H NMR spectrum of the graft copolymer **9** (Figure 1), the resonance of methylene protons of the propargyl end group was shifted from 4.35 to 4.81 ppm, and a signal at 7.76 ppm attributed to the resonance of methine proton of the triazole ring provided direct evidence for the successful coupling.[38] Moreover, in the FT-IR spectrum, a significant decrease and disappearance of the typical stretching frequency of the azide (2108 cm^{-1}) and the alkyne group (3252 cm^{-1}) and the appearance of a typical absorption of the triazole ring (1633 cm^{-1}) gave the further support to the occurrence of the coupling reaction. According to ^{1}H NMR analysis of the graft copolymer, the graft efficiency was calculated by the following formula:

$$E_g = \frac{A_{m'}}{A_{sum'}/2} \times 100\% \quad (2)$$

in which E_g is the graft efficiency; $A_{m'}$ and $A_{sum'}$ are the integral area of methine proton at 7.76 ppm for the triazole ring and at 4.15–4.35 ppm for the methylene protons linked to the esters, respectively. An efficiency of about 63% was obtained, which was in accordance with recent reports,[39–42] demonstrating the moderate efficiency in grafting-onto-type preparations of graft copolymer by click reaction. However, the signals at 7.76 ppm for methine proton of the triazole ring and at 4.81 ppm for the methylene protons linked to the triazole ring were not observed for the graft copolymer containing miktoarm star side chains with greater molecular weight of each arm, so did the signals at 4.15–4.35 ppm for the methylene protons linked to the esters. These may be attributed to the wrap of the corresponding signals for the larger bulk of the miktoarm star side chains with greater molecular weight. Nevertheless, in their FT-IR spectrum, a significant decrease and disappearance of the typical stretching frequency of the azide at 2108 cm^{-1} and the alkyne group at 3252 cm^{-1} and the appearance of a typical absorption of the

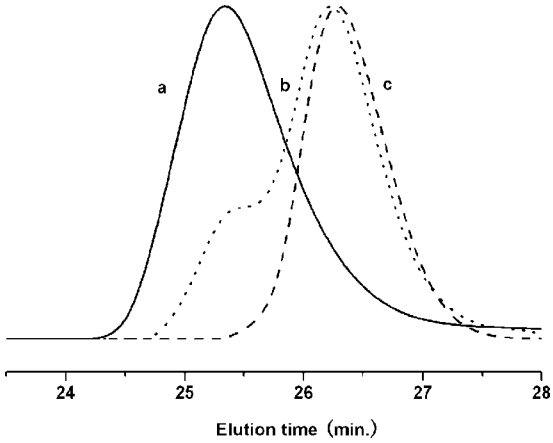

Figure 2. Typical SEC traces: (a) star (PS−PEO−PEEGE) copolymer **3** (solid line); (b) crude product **9** after click reaction (dotted line); (c) purified product **9** after separation (dashed line).

triazole ring at 1633 cm^{-1} could also be detected (Supporting Information). The characterization data of these copolymers are summarized in Table 1, from which it could be observed that in the same conditions the graft efficiency did not increase remarkably with the more contents of azide groups of the mains chains, and the efficiencies for the graft copolymers **9A** and **9B** were almost the same. It meant that not all azide groups of the main chain were taken part in the copper-catalyzed cycloaddition reaction. The result could be attributed to the large steric hindrance of the miktoarm star side chain. The highest graft efficiency was 63.9% in this system.

The SEC trace for the graft copolymer **9** showed that an apparent shift of the chromatogram toward higher elution time was unexpectedly and repeatedly observed (Figure 2). The result presented here was in agreement with a recent literature. Li et al.[41] synthesized an amphiphilic tadpole-shaped poly(ϵ-caprolactone) grafted by PEO, and the SEC trace for the tadpole-shaped copolymer after grafting of PEO by click reaction shifted to higher elution time than that for the precursor. This behavior could be attributed to the smaller hydrodynamic volume of the graft copolymer with the high branched structure than the linear polymer with same molecular weight. In order to further verify this complex structure, attempts were made to hydrolyze the ester of the graft copolymer **9** using KOH in THF/CH_3OH system, but it failed, and a similar result was reported by Laurent et al.[43]

In summary, an amphiphilic graft copolymer with well-defined star-shaped side chains was synthesized by the "grafting onto" method via combination of anionic polymerization and click reactions. The azide group functionality of the main chain and the alkyne group functionality at PEEGE chain end of the miktoarm star side chains were very high. The moderate graft efficiency in click coupling reaction was obtained due to the large steric hindrance of the miktoarm star side chain. The structure of target copolymers and intermediates were well characterized by ^1H NMR, SEC, and FT-IR. This work provided a new way to prepare the graft copolymer with complex structure.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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