Synthesis of Amphiphilic Macrocyclic Graft Copolymer Consisting of a Poly(ethylene oxide) Ring and Multi-Polystyrene Lateral Chains

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Introduction. Driven by the challenges and interests, design and synthesis of cyclic molecules have always attracted attention. The fascinating properties and applications of such cyclic molecules include the formation of organic nanotubes, ion complexes, and ion transport across membranes.[1] In this field, the representative small cyclic molecules are crown ethers and substituted crown ethers. Since the pioneering work of Pedersen revealed the complexing potential of the crown ethers,[2] cyclic molecules with complicated structures derived from crown ethers were synthesized and their properties were investigated. For example, cyclic polyamines bearing long chains grafted on nitrogen sites displayed a liquid crystal phase in which the macrocyclic units are stacked, forming a tubular mesophase.[3] Afterward, polymer chains were also introduced on the dibenzo-18-crown-6, and the resulting copolymers showed self-assembling properties in the presence of potassium cations.[4] Medium-sized cyclic molecules, commonly containing 10−20 units, such as cyclic polypeptide and cyclic phenylene−acetylene were also studied by some groups in detail. When the cyclic polypeptide was considered, nanotubes with specified internal diameters were constructed because of the stacking of cyclic polypeptides driven by the hydrogen bonds between them.[5] With respect to the cycles consisting of phenylene−acetylene units, the rigid framework and $\pi-\pi$ interaction of phenylene units between the cycles led to the molecular stacking regularly, forming hollow cylindrical brushes and supramolecular layered structures which show the ability of molecular recognition. Such cycles have been prepared, and their relative properties were investigated extensively;[6] their self-assembling properties have been reviewed by Ghadiri.[7]

Macrocyclic polymers with long and endless chains are different from the shape-persistent cycles mentioned above and show shape-flexible and other special properties.[8] Previous studies about cyclic polymers only focused on preparation of a single polymer ring including some hydrophobic homo- and copolymers such as cyclic PS, PE, PS-*b*-PI, and PS-*b*-PI-*b*-PMMA[9] and hydrophilic macrocyclic poly(ethylene oxide).[10] Studies about these polymeric macrocycles are concentrated on the synthesis and solution or crystallization properties.[11]

Up to now, except for macrocyclic poly(chloroethyl vinyl ether)-*g*-polystyrene reported by Deffieux et al.,[12] in the family of these macrocycles, limited reports are published on the preparation of amphiphilic macrocyclic grafted copolymers. In this work, we attempt to describe a novel amphiphilic macrocyclic graft copolymer with multi-side chains, which consists of a hydrophilic poly(ethylene oxide) (PEO) ring and some hydrophobic polystyrene (PS) lateral chains (*c*-PEO-*g*-PS). These copolymers were synthesized via combination of anionic ring-opening polymerization and nitroxide-mediated radical polymerization (NMRP).

Results and Discussion. To obtain the target molecules, the heterofunctional monomer 4-glycidyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl (GTEMPO) was first prepared and copolymerized with ethylene oxide (EO), and a linear α,ω-dihydroxy-poly(ethylene oxide) with pendant TEMPO groups (*l*-$\mathrm{PEO_T}$) (*l*: linear copolymer) was obtained. Then the ring closure of *l*-$\mathrm{PEO_T}$ was completed in a pseudo-high-dilute $\mathrm{CH_2Cl_2}$ solution [$C^* < 10^{-5}$ mol/L] in alkaline conditions by formation of an acetal linkage, in which $\mathrm{CH_2Cl_2}$ was also used as cyclizing agent. The whole process is outlined in Figure 1.

Figure 2 shows the gel permeation chromatography (GPC) curves of linear precursor *l*-$\mathrm{PEO_T}$ (A), crude cyclic poly(ethylene oxide) with pendant TEMPO groups (*c*-$\mathrm{PEO_T}$) (*c*: cyclic copolymer) (B), and purified *c*-$\mathrm{PEO_T}$ (C). It was found that a small shoulder peak appeared at the high elution volume for (A). It may be attributed to the termination of propagating chains by the tiny water in polymerization; its contents were about 3%. Comparing the *c*-$\mathrm{PEO_T}$ with *l*-$\mathrm{PEO_T}$, the major elution peak shifted to larger volume and the peak molecular weight of $M_{\mathrm{pl}} = 10.4$ kDa for *l*-$\mathrm{PEO_T}$ changed to $M_{\mathrm{pc}} = 8.9$ kDa for *c*-$\mathrm{PEO_T}$ owing to the smaller hydrodynamic volume of the latter, indicating that the macrocyclic compounds were formed. The cyclization efficiency of *l*-$\mathrm{PEO_T}$ derived from the GPC trace of Figure 2B was about 80%. The uncyclized *l*-$\mathrm{PEO_T}$ and chain-extended product were easily removed from the *c*-$\mathrm{PEO_T}$ by an ultrafiltration membrane, and Figure 2C shows the results. To check the purity of separated *c*-$\mathrm{PEO_T}$, it was recyclized at the high concentration of 2×10^{-2} mol/L, which favors chain-extended reaction, but no chain-extended product with high molecular weight was detected (Figure 2D). Therefore, the separation of *c*-$\mathrm{PEO_T}$ by the ultrafiltration membrane was successful, and the separated *c*-$\mathrm{PEO_T}$ was pure enough for the next application.

MALDI-TOF is the best technique to demonstrate the cyclic character of the cyclic homopolymers;[13] however, it was difficult to characterize the copolymers directly.[14] Therefore, the model copolymer was synthesized for the determination of MALDI-TOF. Figure 3 shows the MALDI-TOF spectra of linear precursor *l*-P(GTEMPO-*co*-$\mathrm{EO_{0.1}}$) (A) and cyclized product *c*-P(GTEMPO-*co*-$\mathrm{EO_{0.1}}$) (B); the spacing 44 or 228.2 amu between the peaks is ascribed to the molar mass of the EO and GTEMPO unit, and the difference of 12 amu before and after cyclization reaction supports the formation of acetal linkage which was obtained by acetalation of two hydroxyl end groups with dichloromethane. The MALDI spectra of the linear precursor and cyclization product were coincident with their proposed chemical structure (HO−(GTEMPO-*co*-EO)−OH) and (−O−(GTEMPO-*co*-EO)−$\mathrm{OCH_2}$−), respectively.

The cyclization of *l*-$\mathrm{PEO_T}$ was also confirmed by ^{1}H NMR spectroscopy. Comparing the spectrum of *l*-$\mathrm{PEO_T}$ with *c*-$\mathrm{PEO_T}$, the new significant peak at 4.6 ppm corresponding to the methylene protons of acetal linkage (−$\mathrm{OCH_2O}$−) in *c*-$\mathrm{PEO_T}$ was observed, indicating that the cyclization of *l*-$\mathrm{PEO_T}$ was successful.

The radical polymerization of styrene (St) was performed in the presence of *c*-$\mathrm{PEO_T}$ using benzoyl peroxide (BPO) as initiator, and the object products of *c*-PEO-*g*-PS with molecular weight of 16 kDa (Figure 2E) and 21 kDa were obtained by variation of the polymerization time. The samples can be figured

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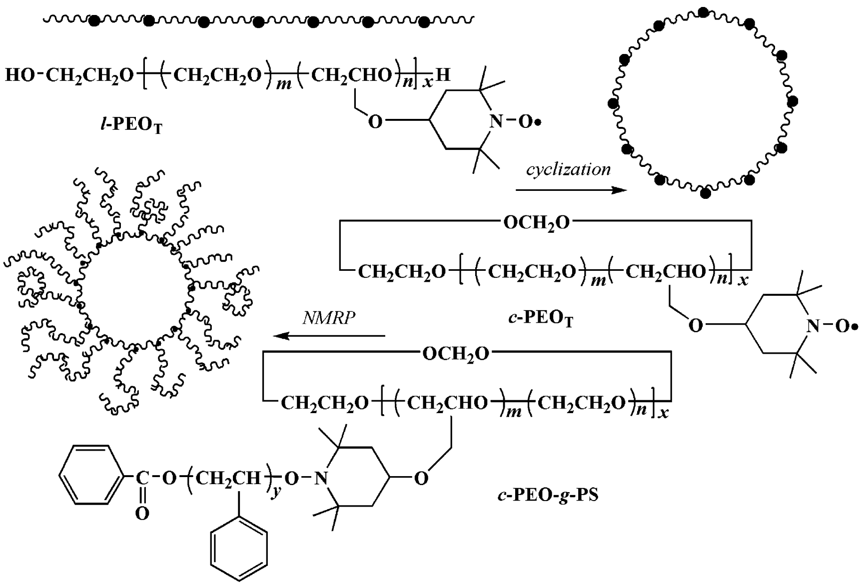

Figure 1. Schematic representation of the synthetic route of the *c*-PEO-*g*-PS.

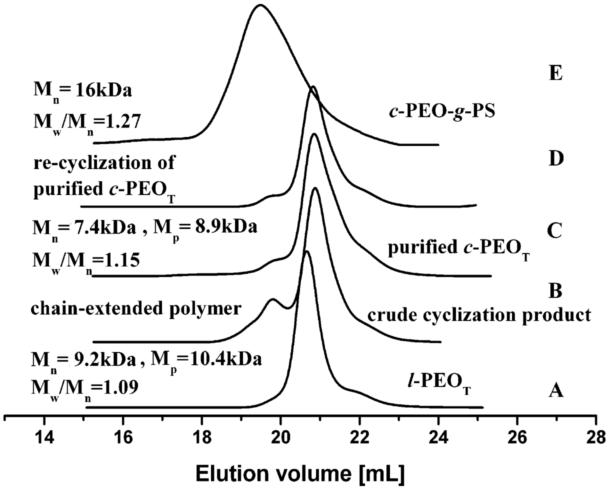

Figure 2. Typical gel permeation chromatography traces: (A) linear poly(ethylene oxide) with pendant TEMPO groups (*l*-PEO$_T$); (B) crude product of *l*-PEO$_T$ after cyclization; (C) cyclic poly(ethylene oxide) with pendant TEMPO groups (*c*-PEO$_T$) after separation; (D) recyclization of purified *c*-PEO$_T$; (E) final product *c*-poly(ethylene oxide)-*g*-polystyrene (*c*-PEO-*g*-PS) (THF as eluent and flow rate is 1 mL/mim).

as *c*-P(GTEMPO-*co*-EO$_5$)$_{20}$-*g*-PS$_6$ (A) and *c*-P(GTEMPO-*co*-EO$_5$)$_{20}$-*g*-PS$_6$ (B). For sample A, it meant that the ratio of GTEMPO to EO in *l*-PEO$_T$ was 1:5, which was estimated by the integral area of methyl protons of TEMPO at 1.2 ppm to the area of methylene protons of PEO at 3.5−3.8 ppm in the main chain; the number of TEMPO radicals (N_T) on the PEO chain could be evaluated by the combination of the molecular weight determined by GPC and ^{1}H NMR (shown in Figure 4) data according to eq 1:

$$N_T = \frac{M_n}{M_G + xM_E} \tag{1}$$

in which M_n is the molecular weight of *l*-PEO$_T$, M_G and M_E are the molar masses of GTEMPO and EO, and x is the molar ratio of EO units to GTEMPO units in *l*-PEO$_T$; the calculated N_T was about 20. A residual phenyl group from the initiator BPO was attached on the end of every side chain; the chemical shift of phenyl protons a, b, and c shown in Figure 4C was at 7.4, 7.5, and 8.0 ppm, respectively,[15] which was quite different from chemical shift of phenyl rings on PS main chains, which appeared at 6.3−7.2 ppm. Thus, the average polymerization degree (DP) of PS side chains was also easily calculated on the basis of the phenyl integral area of benzoyl end group of PS side chains and phenyl integral area of PS. For samples A and B, the average DP$_n$ of PS was 6 and 8, and the number-average molecular weight of every side chain (M_{ns}) was about 800 and 1000, respectively. Thus, the M_n of *c*-PEO-*g*-PS was the sum of molecular weight of PS plus the molecular weight of *c*-PEO$_T$, and the values were 28.9 and 34.4 kDa, respectively, which were much higher than that derived from GPC (M_n = 16 kDa). It may be caused by the relatively smaller hydrodynamic volume of the object copolymer with a special architecture. How many TEMPO groups on the *c*-PEO$_T$ participated in the radical polymerization of St was another interesting and important question, and it could be obtained by eq 2:

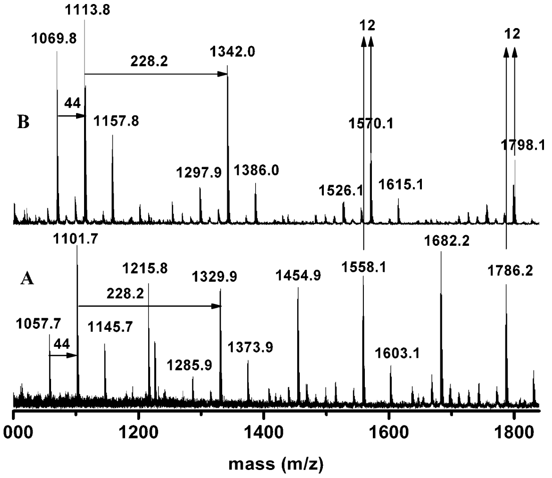

Figure 3. Matrix-assisted laser desorption/ionization time-of-flight mass spectra of model copolymer for (A) linear precursor *l*-P(GTEMPO-*co*-EO$_{0.1}$) and (B) cyclization product *c*-P(GTEMPO-*co*-EO$_{0.1}$) (see the Supporting Information).

$$E_T = \frac{16A_A}{5\left(A_C - \frac{3}{5}A_B\right)} \times 100\% \tag{2}$$

in which E_T was the reaction efficiency of TEMPO groups, A_A

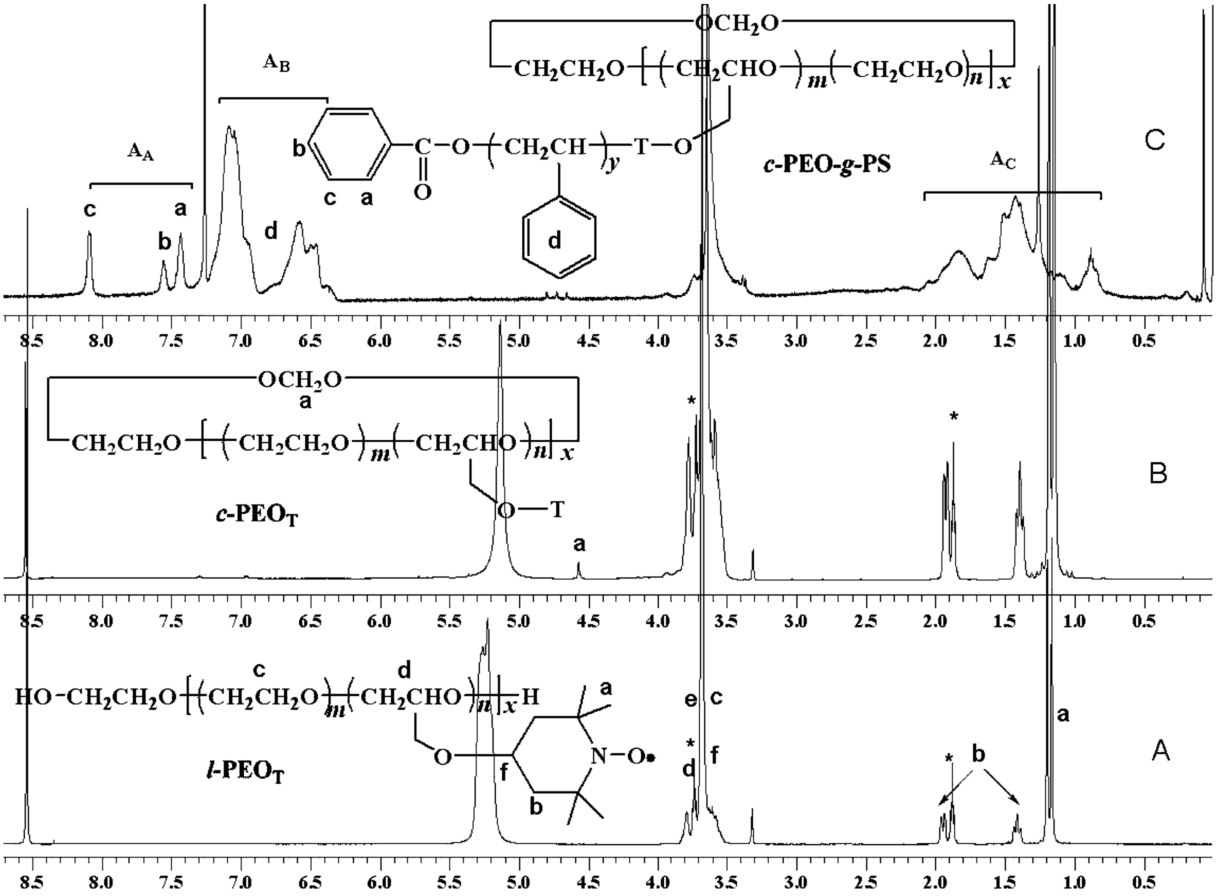

Figure 4. ^{1}H NMR spectra for (A) linear precursor *l*-PEO$_T$ in CD_3OD, (B) purified cyclic product *c*-PEO$_T$ in CD_3OD, and (C) final product *c*-PEO-*g*-PS in $CDCl_3$ ("T" refers to the TEMPO group and "*" the signals of THF).

and A_B represented the integral area of the residual phenyl protons of benzoyl end groups on every PS chains and the integral area of phenyl protons on the PS main chains, respectively, and A_C represented the integral area sum of CH_2 and CH_3 of TEMPO groups and CH and CH_2 of PS backbone; the E_T values were about 95% and 100% respectively for samples A and B. This suggested that nearly all the TEMPO groups took part in the radical polymerization.

The critical micelle concentration (cmc) of *c*-PEO-*g*-PS was measured by the common fluorescence probe technique[16] in water using pyrene as the fluorescence probe. On the basis of dependence of fluorescence intensity ratios (I_1/I_3) on the concentration of the cyclic graft copolymers, the derived cmc values are 5.75×10^{-7} and 4.46×10^{-7} g/mL for *c*-P(GTEMPO-*co*-EO$_5$)$_{20}$-*g*-PS$_6$ and *c*-P(GTEMPO-*co*-EO$_5$)$_{20}$-*g*-PS$_8$, respectively. Cyclic graft copolymer with longer side chains shows the lower cmc value.

In summary, a novel amphiphilic macrocyclic graft copolymer composed of PEO ring and multi-PS lateral chains was successfully synthesized by combination of anionic ring-opening polymerization and NMRP. The heterofunctional monomer GTEMPO was copolymerized with EO by the anionic mechanism first, and then the cyclization reaction of *l*-PEO$_T$ was successfully carried out using pseudo-high-dilute CH_2Cl_2 as cyclizing agent in alkaline conditions. The cyclized copolymer with many pendant TEMPO radicals was used as co-initiator to control the polymerization of St. The intermediates and object copolymers were characterized by GPC, MALDI-TOF, and ^{1}H NMR. The cmc values of these copolymers were also determined by the fluorescence probe technique.

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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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