Synthesis of Eight-shaped Poly(ethylene oxide) by the Combination of Glaser Coupling with Ring-opening Polymerization

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The eight-shaped poly(ethylene oxide) (PEO) is synthesized by a combination of Glaser coupling with ring-opening polymerization (ROP). Firstly, the star-shaped (PEO-OH)$_4$ is synthesized by ROP of ethylene oxide (EO) using pentaerythritol as an initiator and diphenylmethyl potassium (DPMK) as a deprotonated agent, and then the alkyne group is introduced onto the PEO arm-end to give (PEO-Alkyne)$_4$ in a NaH/tetrahydrofuran (THF) system. The intramolecular cyclization is carried out by a Glaser coupling reaction in a pyridine/CuBr/N$_3$N$_3$,N$^\text{0},$N$^\text{0},$N$^\text{00},$N$^\text{00}$-penta-methyldiethylenetriamine (PMDETA) system at room temperature in an air atmosphere, and eight-shaped PEO was formed with high efficiency (almost 100%). The target polymers and intermediates were well characterized by SEC, MALDI-TOF MS, $^1$H NMR and FT-IR in detail.

Introduction

Cyclic polymers with endless polymer main chains show distinctively unique characteristics and physical properties due to their closed ring topology compared to linear analogs.[1] Several strategies[2] have been adopted for the cyclization based on various polymerization mechanisms[3–6] and coupling techniques,[7–9] cycle-based polymers including single cycle, eight-shaped, tadpole-shaped and theta-shaped have been reported.[10] Unlike the widely researched copolymers formed by linking several linear sub-chains together, copolymers consisting of cyclic sub-chains have rarely been studied. Among them, eight-shaped copolymers are the simplest, composed of two cyclic sub-chains, which might be used as a model (co)polymer for theoretical research, as well as be endowed with some special properties and applications.

The eight-shaped (co)polymers may be constructed by several methods, for example, an electrostatic self-assembly and covalent fixation process was used to give eight-shaped poly(tetrahydrofuran) (PTHF)[11,12] and poly(styrene) (PS),[13] the intramolecular photo-cross-linking of pendant unsaturations was used to give eight-shaped poly(ε-caprolactone) (PCL),[14] the reaction between acetal and styrenyl functions was used to give eight-shaped poly(chloroethyl vinyl ether) (PCEVE),[15] the coupling reaction between living dicarbanions with tetrachlorosi-lane was used to give eight-shaped PS[16] and polyisoprene (PI),[17] the “click” reaction between alkyne and azide groups[18] and the reaction between amine and glutaric acid was used to give eight-shaped PS.[19] In addition, the atom...
Synthesis of Eight-shaped Poly(ethylene oxide) by the Combination of Glaser Coupling and CuAAC Chemistry

Transfer radical polymerization ring-closing metathesis (ATRP-RCM) method was used to give eight-shaped poly(methyl acrylate) (PMA) from 4-armed star telechelics. However, all of the above methods had limitations in terms of the selection of polymer precursors and the operation conditions, and could not be used to synthesize eight-shaped poly(ethylene oxide) (PEO) due to the synthesis difficulties. On the other hand, the simplest single ring of PEO has been synthesized using several strategies (such as ring closure between –OH groups using p-toluenesulfonyl chloride or CH2Cl2 as cyclizing agents and the electrostatic self-assembly and covalent fixation method) and investigated. The results showed that the cyclic PEO had lower parameters of Tg, Tm, and Xc than its linear counterpart. Thus, looking for an efficient method to prepare eight-shaped PEO would be an interesting work, which might promote the further study of the relationship between structures and properties of PEOs.

Usually, an efficient cyclization method should meet the following requirements: (a) the modification procedure of functionalities should be easily realized; (b) the cyclization should show high efficiency (i.e., no linear by-product and no further purification procedure involved); (c) the cyclization should be able to be conducted under mild conditions (the use of a solvent with a low boiling point, under room temperature should be able to be conducted under mild conditions); (d) the cyclization should show high efficiency (i.e., no linear by-product and no further purification procedure involved); and (e) the cyclization should be able to be conducted under mild conditions (the use of a solvent with a low boiling point, under room temperature, without serious deoxygenization procedure and so on). For example, the widely used Cu-catalyzed azide/alkyne cycloaddition (CuAAC) “click” chemistry shows the high efficiency. Boyd et al. first synthesized macrocyclic PS by CuAAC “click” chemistry in N,N-dimethylformamide (DMF) at 120 °C and later Monteiro et al. synthesized various topologies tailored from cyclic PS by an improved rapid CuAAC “click” chemistry in toluene at 25 °C. However, the introduction of alkyno and azide groups into polymer chains needs multi-step reactions, and separation and purification are necessary. Recently, the Glaser coupling reaction between alkyno and azide groups has been widely used in organic and polymer chemistry. It not only showed high efficiency but also provided the mild reaction conditions and simple operation. Using this method, we had previously successfully synthesized A2B2 star-shaped copolymers and cyclic homo-PS or PEO polymers. Herein, a combination of ring opening polymerization (ROP) of ethylene oxide (EO) with Glaser coupling, a novel eight-shaped PEO with high efficiency was obtained.

Experimental Section

Materials

The ethylene oxide (EO) monomer and propargyl bromide (>99%) were dried with CaH2 and then distilled and stored at −20 °C before use. Tetrahydrofuran (THF, SCR, 99%) was refluxed over sodium wire, then distilled from sodium naphthalenide solution. Dimethyl sulfoxide (DMSO) (SCR, 98%) was distilled over CaH2 under reduced pressure just before use. Copper (I) bromide (CuBr, 95%) was stirred overnight in acetic acid, filtered, washed with ethanol and diethyl ether successively, and then dried in vacuo. The ligand NN,N,N,N,N-penta-methyl diethylenetriamine (PMDETA, Aldrich) was used as received. Pentaaerythritol (Aldrich, 98%) was dried at 50 °C under a vacuum. All other reagents and solvents were purchased from Sinopharm Chemical Reagent Co., Ltd. (SCR) and used as received except for declaration. Diphenylmethylpotassium (DPMK) solution was prepared according to a literature method and the concentration was 0.75 mol·L−1.

Measurements

Size-exclusion chromatography (SEC) was performed in 0.1 M NaNO3 aqueous solution at 40 °C with an elution rate of 0.5 mL·min−1 on an Agilent 1100 equipped with a G1310A pump, a G1362A refractive index detector and a G1315A diode-array detector. Three TSKgel PW columns in series (molecular weight ranges of 0 to 5 × 105, 5 × 104 to 8 × 106 and (5–8) × 105 g·mol−1, respectively) were calibrated with PEO standard samples. 1H NMR spectra were obtained using a DMX500 MHz spectrometer with tetramethylsilane (TMS) as the internal standard and CDCl3 as the solvent. Fourier Transform infrared (FT-IR) spectra were recorded on a NEXUS 470 FT-IR instrument, the polymer samples were dissolved in dry THF and then cast onto a NaCl disk to form the film by evaporation of the solvent under an infrared lamp. The MALDI-TOF MS measurements were performed using a Perspective Biosystem Voyager-DE STR MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight) mass spectrometer (PE Applied Biosystems, Framingham, MA). The matrix solution of dithanol (20 mg·mL−1), polymer (10 mg·mL−1) and cationizing salt of sodium trifluoroacetate (10 mg·mL−1) in THF were mixed in the ratio of matrix:cationizing salt:polymer = 10:1:2, and 0.8 μL of mixed solution was deposited on the sample holder.

Synthesis of Star-shaped Poly(ethylene oxide) with a Hydroxyl Group at the PEO Arm-end ([PEO-OH]n) by ROP

Typically, the dried pentaerythritol (4.10 g, 30.15 × 10−3 mol) was dissolved in a co-solvent of 80 mL of THF and 60 mL of DMSO, and charged into a 300 mL dried kettle, then the DPMK solution needed was added into magnetic stirring. The kettle was then placed into an ice bath and the cold EO (120 mL, 104.33 g) was added quickly. The solution was heated to 55 °C and stirred for 72.0 h, and then the solution was terminated by acid methanol and the solvent was evaporated. Subsequently, star-shaped [PEO-OH]n were precipitated into anhydrous and cold ethyl ether slowly three times and dried under a vacuum at 45 °C for 12.0 h until a constant weight of 103.18 g was reached (98.9% yield).

1H NMR (CDCl3, δ): 3.46 (m, −C(CH2O)−), 3.52 (m, −C(CH2O)−); $M_{n\,SEC}$ = 3300 g·mol−1, PDI = 1.06, $M_{n\,NMR}$ = 3900 g·mol−1.
Synthesis of Star-shaped Poly(ethylene oxide) with an Alkyne Group at each PEO Arm-end [(PEO-Alkyne)] by Modification

Dried (PEO-OH)$_4$ (10.00 g, 10.26 x $10^{-3}$ mol hydroxyl groups, $M_n$ NMR = 3900 g·mol$^{-1}$) was added to a 250 mL round bottomed flask. The polymer was dissolved in THF (150 mL) and NaH (0.7387 g, 30.78 x $10^{-3}$ mol) was added. After the solution was allowed to stir at 40 °C for 1.0 h, propargyl bromide (2.39 mL, 30.78 x $10^{-3}$ mol) was added dropwise at 0 – 5 °C. The solution was stirred at 0 – 5 °C for another 24.0 h and the pH of the solution was adjusted to 7.0 by the addition of 0.1 mol·L$^{-1}$ hydrochloride solution. After the THF was removed by rotary evaporation, the crude products were extracted with CH$_2$Cl$_2$ (150 mL) and then the organic layer was dried over MgSO$_4$ before purification and then precipitated into anhydrous and cold ethyl ether slowly three times. (PEO-Alkyne)$_4$ was obtained and dried under a vacuum at 45 °C for 12.0 h until a constant weight was reached (yield: 8.92 g, 89.2%).

$^1$H NMR (CDCl$_3$, δ): 2.47 (–CH$_2$C=C), 3.46 (m, –C(H$_2$O)$-$_4), 3.52 – 3.92 (m, –CH$_2$CH$_2$O$-$_), 4.25 (–CH$_2$C=C); FTIR: ν = 3248 cm$^{-1}$ (–C=C–).

Synthesis of Eight-shaped Poly(ethylene oxide) by Glaser Coupling

Typically, into a 1000 mL round bottomed flask were added pyridine (300 mL), CuBr (0.4376 g, 3.06 x $10^{-3}$ mol), and PMDETA (0.57 mL, 3.06 x $10^{-3}$ mol), then the solution was stirred for 2.0 h. To a separate flask, (PEO-Alkyne)$_4$ (0.5000 g, 0.51 x $10^{-3}$ mol alkyne groups) was dissolved in pyridine (500 mL), and this solution was then added to the CuBr/PMDETA solution via a peristaltic pump at a rate of 4.17 mL·h$^{-1}$. After another 12.0 h, pyridine was removed by reduced pressure distillation. The crude products were extracted with CH$_2$Cl$_2$ (150 mL x 2), and then the organic layer was dried over MgSO$_4$ before purification by precipitation into anhydrous and cold ethyl ether slowly three times. The eight-shaped PEO was obtained and dried under a vacuum at 45 °C for 12.0 h until a constant weight was reached (yield: 0.4026 g, 80.5%).

$^1$H NMR (CDCl$_3$, δ): 3.46 (m, –C(H$_2$O)$-$_4), 3.52 – 3.92 (m, –CH$_2$CH$_2$O$-$_), 4.25 (–CH$_2$C=C); $M_n$ NMR SEC = 1800 g·mol$^{-1}$, PDI = 1.09.

Results and Discussion

For the target eight-shaped poly(ethylene oxide) (PEO), the star-shaped (PEO-OH)$_4$ was firstly synthesized by ROP of EO using pentaerythritol as an initiator and diphenylmethy1-potassium (DPMK) as a deprotonated agent under 55 °C, and the alkyne group was introduced onto the PEO arm-end for the Glaser coupling reaction in a pyridine/CuBr system under 0 – 5 °C. The intramolecular cyclization was then carried out by a Glaser coupling reaction in a pyridine/CuBr/N,N,N',N'',N'''-pentamethyldiethylenetriamine (PMDETA) system at room temperature in the air atmosphere. The whole preparation process is shown in Scheme 1. The target polymers and their intermediates were well characterized by SEC, MALDI-TOF MS, $^1$H NMR and FT-IR in detail.

Synthesis and Characterization of Star-shaped (PEO-OH)$_4$ and (PEO-Alkyne)$_4$

It is well known that the exchange rate of protons between hydroxyl groups and alkoxides is much faster than that of the propagation, and usually, 20 – 30 mol% of hydroxyl groups are deprotonated by DPMK when a small molecular weight initiator is used.$^{[34]}$ Herein, 28 mol% of the hydroxyl groups were deprotonated, and successful ROP was proved by the monomodal SEC curve and low PDI (Figure 1). Subsequently, the hydroxyl group at each PEO arm end was transformed into an alkyne group by the reaction with propargyl bromide. Figure 2 shows the $^1$H NMR spectra of (PEO-OH)$_4$ and (PEO-Alkyne)$_4$. In Figure 2(A), for (PEO-OH)$_4$, the signals for the methylene group protons (–C(H$_2$O)$-$_4) at the core were observed at 3.46 ppm, and the signals for the methylene group protons (–CH$_2$CH$_2$O$-$_) on each PEO arm were observed at 3.52 – 3.92 ppm. After the reaction with propargyl bromide, as indicated in Figure 2(B), the occurrence of the signals for the methylene group protons (–CH$_2$C=C–) at 4.25 ppm and the methine proton (–CH$_2$C=CCH$_2$) at 2.47 ppm confirmed the successful transformation of the hydroxyl groups into alkynyl groups at the PEO arm-end, and (PEO-Alkyne)$_4$ was obtained. Because of the branched structure, the molecular weight of the obtained (PEO-OH)$_4$ using SEC ($M_n$ SEC) was always a
departure from the actual one, and the latter could be derived using $^1$H NMR spectra according to Equation (1).

$$M_{n, \text{NMR}} = \frac{A_{bc,c}}{A_d/8} \times 44 + 136$$  

(1)

Where $A_{bc,c}$ and $A_d$ are the integral areas of the resonance signals at 3.52 – 3.92 ppm and that at 3.46 ppm, respectively. The values of 44 and 136 are the molecular weight of the EO monomer unit and pentaerythritol part at the core, respectively. The obtained results for $M_{n, \text{NMR}}$ are listed in Table 1. The transformation efficiency (E.F.) of hydroxyl groups into alkyne groups could also be obtained according to Equation (2).

$$E.F. = \frac{A_a}{A_d} \times 100\%$$  

(2)

Where $A_d$ is the integral areas of the resonance signals at 4.25 ppm. The E.F. of Entry A and Entry B were all close to 100%.

As a powerful tool for structural characterization, MALDI-TOF mass spectra were used to verify the transformation procedure from $(\text{PEO-OH})_4$ into $(\text{PEO-alkyne})_4$. From Figure 3, for Entry A, we could observe an increase of 38.02 Da from peak $[\text{C}_5\text{H}_8\text{O}_4-(\text{C}_2\text{H}_4\text{O})_{76}-\text{H}_4-\text{Na}^+ = 3506.3 \text{Da}, \text{calcd} \ m/z = 3506.06]$ of $(\text{PEO-OH})_4$ to peak $[\text{C}_5\text{H}_8\text{O}_4-(\text{C}_2\text{H}_4\text{O})_{76}-(\text{C}_3\text{H}_2)_4-\text{H}_4-\text{Na}^+ = 3658.5 \text{Da}, \text{calcd} \ m/z = 3659.12]$ of $(\text{PEO-alkyne})_4$, which corresponded to the successful introduction of an alkyne group onto each PEO arm-end.

Synthesis and Characterization of Eight-shaped PEO

In the pyridine/CuBr/PMDETA system, the Glaser coupling between alkyne and alkyne groups at PEO arm-ends proceeded under room temperature in the air atmosphere. By comparing the curves of Figure 1(A) and Figure 1(B), it was found that the SEC curves of eight-shaped PEO shifted to longer elution time, meaning that the hydrodynamic volume of the eight-shaped PEO product was noticeably smaller than that of their star-shaped precursors. The unimodal SEC curves of eight-shaped PEO with low PDIs indicated that the cyclization process was rather successful. The $R$ ratios (0.53 and 0.82) between the apparent peak molar mass ($M_p$) corresponding to the signals of eight-shaped PEO and star-shaped PEO was derived from SEC (Table 1), which reflected the difference in the solution dimensions of the two topological polymer chains. In this work, the $R$ value in Entry B (0.82) agreed with the data (0.76 – 0.95) reported in references for eight-shaped (co)polymers. However, the $R$ value in Entry A (0.53) was much lower than the above $R$ range, which might be caused by the lower $M_n$,
of PEO. A similar phenomenon was also reported in our previous work for single PEO rings and their linear counterparts (where the \( R \) value was between 0.63 – 0.78).\(^{[32]}\)

Usually, the cyclization was carried out under high dilution conditions in order to avoid the formation of by-product by intermolecular condensation. In this work, using the Glaser coupling and a continuous addition technique, it was observed that a monomodal peak appeared for the eight-shaped PEO when a precursor concentration of 0.625 g/L (it was higher than the 0.417 g/L reported in the literature\(^{[25,36]}\)) was applied, while a shoulder peak corresponding to the by-product appeared at a lower elution time when the concentration of 1.000 g/L was applied. In the latter case, some condensation product was observed from the SEC (Figure 1(C)), and the time-consuming isolation and purification procedures were unavoidable.

From the \(^1\)H NMR spectrum in Figure 2(C), the signal for the methine proton (\(-\text{CH}_2\text{C} \equiv \text{CH}\)) at 2.44 ppm disappeared and confirmed the successful synthesis of eight-shaped PEO. From MALDI-TOF mass spectra (Figure 3), for Entry A, after the Glaser coupling reaction, a clear shifting of 4.04 Da from the peak \([\text{C}_9\text{H}_8\text{O}_4-(\text{C}_2\text{H}_4\text{O})_{76}-(\text{C}_3\text{H}_2)_4-\text{Na}^+ = 3658.5 \text{ Da, calcd } m/z = 3659.12]\) of \((\text{PEO-alkyne})_4\) to \([\text{C}_10\text{C}_5\text{H}_8\text{O}_4-(\text{C}_2\text{H}_4\text{O})_{76}-(\text{C}_3\text{H}_2)_4-\text{Na}^+ = 3654.5 \text{ Da, calcd } m/z = 3655.09]\) of eight-shaped PEO also confirmed the successful cyclization of PEO arms. The \( \text{C}_1^0 \) peak \([\text{C}_5\text{H}_8\text{O}_4-(\text{C}_2\text{H}_4\text{O})_{76}-(\text{C}_3\text{H}_2)_4-K^+ = 3670.5 \text{ Da, calcd } m/z = 3671.07\) was also attributed to eight-shaped PEO, which had a difference of 16.0 Da to the \( \text{C}_1' \) peak caused by the difference between a \( \text{K}^+ \) and \( \text{Na}^+ \) ion. Similarly, the MALDI-TOF mass spectrum for Entry B was also measured and discriminated (See Figure S1 and Figure S2 in the Supporting Information). The results also showed the complete transformation of \((\text{PEO-OH})_4\) to \((\text{PEO-alkyne})_4\) as well as the successful cyclization procedure for eight-shaped PEO with an efficiency of 100%.

Furthermore, eight-shaped PEO and its precursors were also traced with FT-IR spectroscopy (see Figure S3 in the Supporting Information). In all three spectra, a strong band at 1115 cm\(^{-1}\) was attributed to the ether linkage \((-\text{C}-\text{O}-\text{C}-\text{)}\) on the PEO chains. The stretch absorption at 3255 cm\(^{-1}\) for the alkyne group \((-\text{C} \equiv \text{CH})\) was detected after the reaction of the hydroxyl group with propargyl bromide, using the Glaser coupling method.

### Table 1: The data for eight-shaped PEO and their precursors.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Star-shaped (PEO-OH)(_4)</th>
<th>Eight-shaped PEO</th>
<th>( R )(^{[c]} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( M_n ) (_{\text{SEC}})</td>
<td>( M_p ) (_{\text{SEC}})</td>
<td>( M_n ) (_{\text{NMR}})</td>
</tr>
<tr>
<td>A</td>
<td>3300</td>
<td>3650</td>
<td>1.06</td>
</tr>
<tr>
<td>B</td>
<td>12 100</td>
<td>13 920</td>
<td>1.07</td>
</tr>
</tbody>
</table>

\( a \) Determined by SEC with 0.1 M NaNO\(_3\) as the eluent using PEO standards; \( b \) The molecular weights of star-shaped (PEO-OH)\(_4\) were calculated according to \(^1\)H NMR using Equation (1); \( c \) The \( R \) was ratio of the apparent peak molar masses (\( M_p \)) derived from SEC curves of eight-shaped polymer to their star-shaped precursors.
and this characteristic signal disappeared again once the 1,3-dinyes group formed after the Glaser coupling reaction. These results were consistent with the target polymer structure.

Conclusion

The four armed PEO with alkyne end groups (PEO-alkyne)₄ was prepared by ROP of EO monomer first and the subsequent propargylation of the hydroxyl groups on each PEO. The eight-shaped PEO was then obtained by Glaser coupling in a pyridine/CuBr/PMDETA system at room temperature in the air atmosphere. The cyclization procedure was rather successful, and the pure eight-shaped PEO could be obtained by feeding 0.625 g L⁻¹ of precursors. The efficiency was nearly as high as 100%.

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