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Synthesis of (ABCB)_n type ternary amphiphilic multiblock copolymer via poly(ethylene oxide) macro-chain transfer agent

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Abstract

A novel (ABCB)_n type ternary amphiphilic multiblock copolymer was synthesized by stepwise insertion of monomers into the trithiocarbonate-embedded poly(ethylene oxide) (PEO) macro-chain transfer agent (PEO-CTA)_n. (PEO-CTA)_n was synthesized first by coupling of α,ω-dihydroxyl PEO with dicarboxylic trithiocarbonate, then styrene (St) and t-butyl acrylate (tBA) were inserted into the (PEO-CTA)_n successively to yield (PEO-b-PS)_n and (PEO-b-PS-b-PBA-b-PS)_n, respectively. After hydrolysis of the (PEO-b-PS-b-PBA-b-PS)_n, the final product (PEO-b-PS-b-PAA-b-PS)_n was obtained.

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Keywords: Multiblock copolymer; Controlled radical polymerization; Poly(ethylene oxide) (PEO)

1. Introduction

Synthesis of structure-tailored copolymers is always pursued by polymer chemists for their synthetic challenges and their interesting physical properties in bulk and in solution [1,2]. Among them, linear multiblock copolymers, especially triblock copolymers have attracted considerable attention due to their synthetic convenience. By means of the sequential polymerization of three different monomers, linear triblock copolymer can be easily synthesized via conventional controlled radical polymerization or living anionic polymerization. For example, poly(t-butyl acrylate)-b-polystyrene-b-poly(4-vinylpyridine) and polystyrene-b-poly(2-vinyl pyridine)-b-poly(t-butyl methacrylate) can be prepared by living anionic polymerization [3,4], and polystyrene-b-polyacrylate-b-polystyrene-4-vinylpyridine can be prepared by atom transfer radical polymerization (ATRP) [5–7] or reversible addition–fragmentation chain transfer (RAFT) polymerization [8,9].

When the hydrophilic, pH-responsive or thermo-responsive blocks, especially the PEO block, are introduced in ABC type copolymers, abundant self-assembled aggregates with environmental multiple responsive could be observed in selective solvents [10,11], and the primary applications in metal nanoparticle fabrication [12–14] and pH-responsive particulate emulsifiers are exploited [15,16]. Moreover, latest researches indicate that multiblock copolymers such as [poly(t-lactic acid)-b-poly(ε-caprolactone)]_n and [poly(ethylene oxide)-b-poly(methylphenylsilane)]_n have shown some special crystallized and self-assembled behavior, respectively [17,18], and some of them such as [poly(ε-lysine)-b-poly(ethylene oxide)]_n are used as a non-viral gene carrier [19]. However, the construction of linear amphiphilic multiblock copolymers containing hydrophilic PEO segment is mostly confined to coupling reaction of different α,ω-bifunctional prepolymers. Generally, prepolymers with functional end groups are synthesized first and then coupled with another α,ω-bifunctional prepolymers [18–20]. Later, the multifunctional chain transfer agent (CTA) [21,22] and poly(alkoxyamine) [23,24] are synthesized and successfully used to prepare the binary multiblock copolymers as [poly(n-butyl acrylate)-b-poly(isoctyl...
acrylate)]_n and [poly(styrene)-b-poly(p-tert-butoxystyrene)]_n via control/“living” radical polymerization. The synthesis of amphiphilic multiblock copolymers as (PEO-b-PS-b-P°BA-b-PS)_n and further product (PEO-b-PS-b-PA°A-b-PS)_n, however, are still scarcely reported up to now. This kind of copolymer may show some special self-assembly morphologies which can also be used as templates for the preparation of metal nanoparticles due to the presence of PA°A blocks [25,26].

Herein, we describe a universal method to synthesize the linear (ABCB)_n type amphiphilic ternary multiblock copolymer (PEO-b-PS-b-PA°A-b-PS)_n by using trithiocarbonate-embedded PEO as macro-chain transfer agent.

2. Experimental part

2.1. Materials

Pyridine and dioxane are distilled in the presence of sodium and dichloromethane is dried with CaH₂ and distilled before use. AIBN is recrystallized from the ethanol twice. Styrene (St) and t-butyl acrylate (tBA) are dried with CaH₂ and distilled under reduced pressure before use. 2,2-Dimethyl-1,3-propanediol (99%), diphenylmethane (99%), thionyl chloride (SOCl₂) and other common agents and solvents are purchased from Sinopharm Chemical Reagent Co., Ltd (SRC) and purified by standard procedure. Trifluoroacetic acid (99%) (SRC) was used as received. CTA, S,S’-bis(α,α’-dimethyl-α’’-acetic acid)-trithiocarbonate (BDATC) 1 (see Scheme 1) is synthesized according to the previous report [27]. IR (KBr): 1700 (s, C=O), 1062 (s, C=S), 804 cm⁻¹ (s, C=S). ¹H NMR (DMSO-d₆): δ = 1.59 (s, 12H, -(CH₃)₂C=COOH)₂), 12.92 (s, 2H (-COOH)₂). C₉H₁₄O₄S₂ (228.01): Calcd. C, 38.28; H, 5.00; S, 34.06. Found C, 38.17; H, 4.92; S, 34.21. α,ω-Dihydroxyl poly(ethylene oxide) 3 (see Scheme 1) is synthesized by using 2,2-dimethyl-1,3-propanediol and diphenylmethyl potassium in THF as co-initiator according to the Gnanou’s method [28]. ¹H NMR (CDCl₃): δ = 3.2 (s, 6H, (CH₂)₃C(CH₂)₂O−), 3.6 (b, 4H, (CH₂)₂C(CH₃)₂O−), the number average molecular weight Mₓ of the obtained α,ω-dihydroxyl PEO is 2.3 × 10³ and the polydispersity index Mₓ/Mₘ is 1.12.

2.2. Measurements

The number average molecular weight Mₓ and polydispersity index Mₓ/Mₘ are measured by gel permeation chromatography (GPC). For the α,ω-dihydroxyl PEO precursor and PEO macro-CTA, GPC is performed in 0.1 M NaNO₃ aqueous solution at 40°C with an elution rate of 0.5 mL/min on an Agilent 1100 with a G1310A pump, a G1362A refractive index detector, and a G1315A diode-array detector. PEO standard samples are used for calibration. GPC traces of the binary and ternary multiblock copolymers are performed in tetrahydrofuran (THF) at 35°C with an elution rate of 1.0 mL/min on an Agilent1100 with a G1310A pump, a G1362A refractive index detector, and a G1315A diode-array detector. Polystyrene standard samples are used for calibration. ¹H NMR spectra are obtained by a DMX 500 MHz spectrometer.

Scheme 1. Schematic synthesis route of ternary multiblock copolymer (i) SOCl₂, 60°C, 1 h; (ii) pyridine, 0°C, 24 h; (iii) dioxane, AIBN (10 mol% eq. vs the trithiocarbonate groups in 4); (iv) dioxane, AIBN (10 mol% eq. vs the trithiocarbonate groups in 5); (v) CH₂Cl₂, trifluoroacetic acid (5 eq. vs the tBA units in 6) 25°C, 24 h.
with tetramethylsilane (TMS) as the internal standard and CDCl₃ as the solvent except in some specified cases. Infrared spectra (IR) are recorded on Magna 550 FT-IR instrument (KBr pellets). The Ultra Filtration Membrane Separator is purchased from Shanghai Institute of Applied Physics, Chinese Academy of Science, the cut-off molecular weight of used poly(ether sulfone) film: \( M_w \) cut-off = 20,000 (calibrated by globin).

2.3. Synthesis and purification of trithiocarbonate-embedded \( \text{PEO macro-CTA} \) [(PEO-CTA)<sub>n</sub>]

In a round-bottom flask, 7.2 g (3.1 \times 10^{-3} \text{ mol}) 3 (see Scheme 1) is dissolved in 100 mL toluene, after azetotropic distillation to remove the water, the 60 mL dry pyridine is added to dissolve the PEO and the flask is sealed with septum, and the solution is cooled in ice-water bath. To another one-neck flask, 1.0 g (3.5 \times 10^{-3} \text{ mol}) 1 (see Scheme 1) and 50 mL SOCl₂ are introduced. After stirring at 60 °C for 1 h, the excessive SOCl₂ is distilled, the remains are dissolved in 20 mL dry CH₂Cl₂ and added dropwise to the PEO solution with vigorous stirring. After continuously stirring for 24 h at 0 °C, the product is filtered to remove the pyridine chloride and precipitated twice in excess diethyl ether, the filtered solid is dried in vacuo. The purified product is obtained by dissolution of the product in water and then separating by ultra filtration membrane separator. The separated aqueous solution is extracted by chloroform thrice and the organic phase is collected and dried over anhydrous MgSO₄. Then the filtrate is concentrated to about 10 mL and precipitated in about 50 mL diethyl ether, the solid filtered is dried in vacuo for 24 h to give 1.9 g purified product. \(^1\text{H} \text{NMR} (\text{CDCl}_3): \delta = 3.2 \text{ (s, 6H, CH}_3\text{C(CH}_2\text{O)~}), 3.6 \text{ (b, 4H, (CH}_2\text{CH}_3\text{O)}_n \text{PEO backbone), 0.88 (s, 4H, (CH}_3\text{)}_2\text{C(CH}_2\text{O)~}, 1.66 (s, 12H, }-S-(\text{CH}_3\text{)}_2\text{C}=\text{COO})-\).

3. Results and discussion

3.1. Synthesis of trithiocarbonate-embedded PEO macro-CTA [(PEO-CTA)<sub>n</sub>]

In early reports, PEO is often chosen as one of the blocks in triblock copolymer due to its recognized biocompatibility and solubility in both aqueous and organic media [29,30]. The macro-CTA based PEO with monofunctional end group and bis-functional end groups are synthesized and used to control the polymerization of different monomers to yield linear triblock copolymers [31,32]. In this presentation, the dicarboxylic trithiocarbonate \( S,S'\text{-bis(azimuthellal-acidic acid)-trithiocarbonate} \ (\text{BDATC}) \) was converted to BDATC-acety chloride 2 (see Scheme 1) first, then the \( \alpha,\omega\text{-dihydroxy PEO} \) 3 is reacted with 2, the obtained trithiocarbonate-embedded multifunctional PEO macro-CTA 4 is used to synthesize the amphiphilic binary multiblock copolymer (PEO-b-PS), 5, and further to mediate the polymerization of third monomer \( \text{BA} \) to obtain the ternary multiblock copolymer (PEO-b-PS-b-PAA-b-PS)<sub>n</sub>, 6. The whole procedure is outlined in Scheme 1. The molecular weight and chemical composition are listed in Table 1.

![GPC trace](7617)

Fig. 1A shows the GPC trace of the \( \alpha,\omega\text{-dihydroxy PEO} \) precursor 3 used in this work, its \( M_u \) (GPC) < sub > 3 </ sub > is 2300 g/mol and \( M_w/M_d < 1.12 \). After coupling with 2 and separation to remove the byproduct of lower molecular weight formed by the partial acidolysis of PEO, the PEO macro-CTA 4 (named as (PEO-CTA)<sub>n</sub>) is obtained as Fig. 1B shows. Its \( M_u \) (GPC) < sub > 4 </ sub > is 14,200 g/mol and \( M_w/M_d < 1.60 </ sub > (Table 1). Thus the average block number of PEO can be calculated by comparing the molecular weight of (PEO-CTA)<sub>n</sub> with that of \( \alpha,\omega\text{-dihydroxy PEO} \) precursor, it is 6.2.

Typical \(^1\text{H} \text{NMR spectra} \) of the macro-CTA (PEO-CTA)<sub>n</sub> and binary multiblock copolymer (PEO-b-PS)<sub>n</sub> are given in Fig. 2A and B, respectively. It was observed that all the data of the characteristic peaks as the signals at 3.6 ppm for the PEO units, at 0.88 and 3.20 ppm for the methyl and methylene groups respectively in the middle of the PEO chains, at
ternary amphiphilic multiblock copolymer (PEO-CTA) was about 6.5 for (PEO-CTA)

<table>
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<th>Sample</th>
<th>Time* (h)</th>
<th>Conv% (%)</th>
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<th>1H NMR c</th>
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<td></td>
<td>2300</td>
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<td>76</td>
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<td>7</td>
<td></td>
<td></td>
<td>71.00</td>
<td>20.0</td>
</tr>
</tbody>
</table>

a Polymization time of St and BA.
b The conversion was calculated based on the gravimetrical method.
c Calculated based on Eqs. (1)–(3).

\[
\begin{align*}
M_n(\text{NMR}) &= (4I_{6.22-7.22}/I_{5.65}) \times (104/44) \times M_n(\text{GPC})_1 + M_n(\text{GPC})_2 \\
M_n(\text{NMR}) &= (4I_{7.22}/I_{5.65}) \times (128/44) \times M_n(\text{GPC})_3 + M_n(\text{NMR})_4 \\
M_n(\text{NMR}) &= [4(I_{1.20-2.40} - 3I_{0.90}/5)I_{5.65}] \times (72/44) \times M_n(\text{GPC})_4 + M_n(\text{NMR})_5
\end{align*}
\]

Here \(I_{5.65}\) is the integral value of peak at 3.65 ppm, \(I_{6.22-7.22}\), \(I_{7.22}\), and \(I_{1.20-2.40}\) are the integral values of peaks at 6.22–7.22, 7.22, and 1.20–2.40 ppm in Figs. 2B, 4A and B, respectively. \(M_n(\text{GPC})_4\) is the molecular weights of (PEO-CTA)_n. While 44, 104, 128 and 72 are the molecular weights of EO, St, BA and AA monomers, respectively.
d The third block is PBA or PAA.

1.66 ppm for methyl group of BDTAC and the triplet at 4.25 for the protons of methylene of PEO adjacent to the oxygen atom of the ester bond demonstrated the successful coupling of PEO with BDTAC. Indeed, in its IR spectrum as shown in Fig. 3A, the appearance of typical C=O, C=S and C–O–C– stretching bands at 1731, 1046 and 1100 cm⁻¹, respectively, also implies the formation of macro-CTA agent. Additionally, the number of trithiocarbonates (\(N_T\)) in macro-CTA could be calculated by the comparison of the peak integral area of methyl groups at 0.88 ppm (\(I_{0.88}\)) located in the middle of PEO with that of methyl groups at 1.66 ppm (\(I_{1.66}\)) for the methyl group of BDTAC as Eq. (4) showed; it was about 6.5 for (PEO-CTA)_n.

\[
N_T = \frac{6.2I_{1.66}}{I_{0.88}}
\]

Actually, as Fig. 1 shows that the polydispersity index of (PEO-CTA)_n is wide (\(M_w/M_n = 1.60\)), the number of trithiocarbonates in (PEO-CTA)_n is in the range of 3–25, and 6.5 is only an average number of trithiocarbonates derived from the number average molecular weight of (PEO-CTA)_n.

3.2. Synthesis of binary multiblock copolymer (PEO-b-PS)_n

The macro-CTA (PEO-CTA)_n is used to mediate the polymerization of styrene to yield the (PEO-b-PS)_n as Fig. 1C shows, its \(M_n\) (GPC) equals to 19,000 g/mol and \(M_w/M_n\) is 1.43 (Table 1). The low polydispersity index relative to the macro-CTA and the unimodal GPC traces indicate that the...
polymerization of St mediated by the macro-CTA is under control. It was observed that an obvious tailing with low molecular weight was detected from Fig. 1C, it may be caused by the coupling of some propagating chain radicals with AIBN end groups each other to form some dead polymer. In Fig. 2B, a new peak at 4.50–4.70 ppm corresponding to the methine protons in the St unit adjacent to trithiocarbonate groups appeared besides the characteristic signals at 1.27–2.25 and 6.27–7.22 ppm. It is found that the distinct peak of methyl protons of BDATC shifts from 1.66 ppm for (PEO-CTA)_n to 1.25 ppm for (PEO-b-PS)_n because of the change of carbon—sulfur bond to carbon—carbon bond of the tertiary carbon. The initiating efficiency of trithiocarbonates in (PEO-CTA)_n (E_{T1}) can be calculated by comparison of integral values of signal at 4.50–4.70 ppm (I_{4.50–4.70}) with the signal at 4.25 ppm (I_{4.25}) ascribed to the methylene protons of PEO adjacent to the oxygen atom of ester linkages in Fig. 2B (Eq. (5)), the value

$$E_{T1} = \frac{2I_{4.50–4.70}}{I_{4.25}}$$

was about 90%. Thus it was confirmed that most trithiocarbonates in macro-CTA participated in the RAFT polymerization of St.

The IR spectrum of (PEO-b-PS)_n is shown in Fig. 3B, the characteristic bands of PS blocks (C=C aromat stretching at 1450–1600 cm⁻¹, C–H aromat stretching at 3020–3080 cm⁻¹, C–H aromat bending at 690–754 cm⁻¹) indicate the successful polymerization of St monomer.

### 3.3. Synthesis of ternary multiblock copolymer (PEO-b-PS-b-PAA-b-PS)_n

The (PEO-b-PS-b-P'BA-b-PS)_n 6 is prepared by using (PEO-b-PS)_n as RAFT agent to mediate the polymerization of t'BA. It should be noted that the trithiocarbonate selected in this work is symmetrical, when the third monomer t'BA is polymerized, the resulted P'BA block is inserted into the PS block, and (PEO-b-PS)_n is changed to (PEO-b-PS-b-P'BA-b-PS)_n (Scheme 1). Fig. 1D shows the GPC curve of the copolymer 6, the molecular weight M_n (GPC)_6 is 43,000 g/mol and the polydispersity is about 1.45, the latter does not change much when compared to the value of (PEO-b-PS)_n (PDI: 1.43), which means that the polymerization of the third monomer t'BA is still under control. Fig. 4A is the 1H NMR spectra of the ternary multiblock copolymer 6, the new peak at 2.22 ppm corresponding to the methine proton on the main chain of t'BA units appears besides the characteristic signals of EO at 3.65 ppm and St units at 6.22–7.22 ppm. Additionally, in Fig. 4A, beside the appearance of methylene protons (c) of PEO adjacent to the oxygen atom of ester linkages at 4.25 ppm, signal at 4.60–4.70 ppm ascribed to the methine protons (h) of t'BA units adjacent to trithiocarbonate groups could be also be observed. Based on the comparison of the
integral values of signal \( I_{4.60-4.70} \) with that of \( e \left( I_{4.25} \right) \), the initiating efficient \( E_{T2} \) of trithiocarbonates in \((\text{PEO-b-PS})_n\) can also be calculated by Eq. (6):

\[
E_{T2} = \frac{2I_{4.60-4.70}}{I_{4.25}}
\]

(6)

the value of \( E_{T2} \) was about 72\%, which was lower than that of the \((\text{PEO-CTA})_n\) because of the space hindrance in the case of \((\text{PEO-b-PS})_n\). The IR spectrum of \((\text{PEO-b-PS-b-P}^\beta\text{BA-b-PS})_n\) is shown in Fig. 3C, except the typical absorption peaks of PS blocks (C–C\(_{\text{aromat}}\) stretching at 1450–1600 cm\(^{-1}\), C–H\(_{\text{aromat}}\) stretching at 3020–3080 cm\(^{-1}\), C–H\(_{\text{aromat}}\) bending at 690–754 cm\(^{-1}\)) and PEO blocks (stretching band at 1100 cm\(^{-1}\)), a strong peak at 1727 cm\(^{-1}\) for \( P^\beta\text{BA} \) block (C=O stretching band) is observed. It is confirmed that the chemical components of desired ternary multiblock copolymer are synthesized successfully. After hydrolysis of \( P^\beta\text{BA} \) blocks of \((\text{PEO-b-PS-b-P}^\beta\text{BA-b-PS})_n\), the amphiphilic multiblock copolymer \((\text{PEO-b-PS-b-AA-b-P}^\beta\text{PS})_n\) was obtained. Fig. 4B shows the \(^1\text{H} \) NMR spectrum of 7 (DMSO-\(d_6 \) as solvent), the appearance of a new broad peak at 12.23 ppm belonging to the protons of carboxyl groups and the decrease of the peak strength at 1.44 ppm overlapped with methylene protons of \( \text{St} \) units assigned to the methyl protons of \( \text{BA} \) units confirmed the successful hydrolysis of the ester groups of \( \text{BA} \) units. Meanwhile, the weight percentage (wt\%) of every blocks in \((\text{PEO-b-PS-b-AA-b-P}^\beta\text{PS})_n\) and its precursors can be calculated from \(^1\text{H} \) NMR spectra and the results are listed in Table 1. In the final product, 20 wt\% PEO blocks, 25.1 wt\% PS blocks and 54.9 wt\% PAA blocks were achieved.

4. Conclusion

In conclusion, a novel strategy for synthesis of \((\text{ABCB})_n\) ternary amphiphilic multiblock copolymer is described. Trithiocarbonate-embedded PEO macro-CTA is synthesized first via coupling reaction procedure and is employed to control the polymerization of \( \text{St} \) and \( \text{BA} \) successively. The resulting ternary amphiphilic multiblock copolymer \((\text{PEO-b-PS-b-AA-b-P}^\beta\text{PS})_n\) and its corresponding precursors is well characterized by the IR, GPC and \(^1\text{H} \) NMR. The unimodal GPC traces and narrow polydispersity indicated that the synthesis of this type of copolymer is under controlled.

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References