Core-Crosslinked Nanoparticles from Amphiphilic Poly (Ethylene Oxide) Macro-RAFT Agent and Styrene: Preparation and Characterization

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Abstract. An unseeded surfactant-free styrene emulsion polymerization is employed to prepare core-crosslinked particles with poly (ethylene oxide) monomethyl ether (mPEO) macro-reversible addition fragmentation chain transfer (RAFT) agent as both the stabilizer and the control agent. The pegylated amphiphilic macro-RAFT agent (mPEO5000-TTC) was synthesized via coupling poly(ethylene oxide) monomethyl ether with a hydrophobic dodecyl trithiocarbonate chain and utilized to form the micelles and control the polymerization and crosslinking of styrene in aqueous solution. The FTIR, 1H NMR, TEM (transmission electron microscopy), dynamic light scattering (DLS) were used to clarify the structure and morphology of nanoparticle. The thermal performance of nanoparticles was measured by TGA (thermogravimetric analysis). The results showed that with the increasing of concentration monomer, the produced size of particles enlarged and then tended to be maximum, while the thermal stability was decreased comparative to the mPEO precursor. The thermal stability of crosslinked particles reflected lower than that of uncrosslinked, which is elucidated with formation and collapse of micelles and micro-phase separation.

1. Introduction
Nanostructure polymers, including nanoparticles [1], micelles and nanogel [2], hollow nanoparticles [3] and other structures such as Janus particles [4] formed by the regioselective crosslinking of the core of amphiphilic block copolymer micelles have been extensively studied in recent years, which were used as pH-[3] and/or photo-responsive particles [5], tunable optical device, agent for molecule encapsulation [2], drug delivery carriers [6], release systems [7] and so forth. The block copolymer precursors are constructed from molecular block assembly into complex nano-structures based on their composition and structures, which are controlled by synthesis using living polymerization techniques and/or by post-polymerization modifications. Emulsion polymerization is the major method of choice to synthesize large quantities of polymer and latex in industrial scale. To stabilizing the latexes in emulsion, ionic surfactant is usually introduced resulting decreased the properties such as adhesive, mechanical strength and compatibility with other components. Surfactant-free emulsion polymerization was adopted to eliminate the said drawbacks and enhance the operationability and processability. Using amphiphilic molecules or macromolecules as initiator or chain transfer agent,
amount of nanostructure latexes and particles were designed and prepared by living/controllable polymerization techniques [8].

Among the available controlled free-radical polymerization (CRP) methods, the RAFT (reversible addition fragmentation chain transfer) polymerization imparts the controlled polymerization to a wide variety of monomers at convenient temperatures, as well as developing in homogeneous phase, inhomogeneous phase in water or even variable systems [9]. Poly(ethylene oxide) (PEO) as hydrophilic block is utilized to install the macromolecular amphiphilic RAFT agents, and synthesized with the monomer of styrene (St), acrylic acid (AA), butyl acrylate (BA), N-2-hydroxypropyl methacrylamide (HPMA) and others [6]. The main aspects investigated were covered with the polymerization mechanism in formation and stability of micelles, the controlling of molecular weight and distribution, as well as the theories of polymerization kinetics and thermal dynamic et al. Furthermore, the PEO block molecular weight of PEO-RAFT used was almost lower than 2000 g mol⁻¹. Molecular weight of PEO or mPEO which larger than 3000 g/mol was not be used hitherto. In this paper, the weight of mPEO 5000 g mol⁻¹ was chosen as hydrophilic block coupled with s-1-dodecyl-s′-(α, α′-dimethyl-α″-acetic acid) trithiocarbonate (DMAT) and styrene as monomer, divinyl benzene as core-crosslinker in aqueous emulsion system, the nanoparticles size and morphology and the thermal properties were observed and the explanation of polymerization process derivation was proposed.

2. Experimental Sections

2.1. Materials

Acetone, 1-dodecanethiol, carbon disulfide, isopropanol, triocytethylmethyl ammonium chloride (Aliquot 336), sodium hydroxide, dichloromethane, chloroform, hexane, and diethyl ether were purchased from Sinopharm Chemical Reagent Company, China. N, N’-dicyclohexyl carbodiimide (DCC, >99%), 4-(dimethyl aminopyridine) (DMAP, >99%) were commercial products and used as received. 2.2’-Azo (bis (2-amidino propane) dihydrochloride (Va 044, 99.5%) was supplied from Sigma-Aldrich and used directly. Poly (ethylene oxide) monomethyl ether (mPEO) (Mn=5000 g mol⁻¹, Sigma-Aldrich) was dried by successive azeotropic distillations with dry toluene before use. Styrene was distilled under vacuum prior to polymerization. Divinylbenzene (DVB, 97%) was received from Beijing Da Tian Feng Tuo Chemical Technique Co. Ltd and used directly. Dichloromethane was dried with 4Å molecular sieve before use. Deionized water was used for all polymerizations. The s-1-dodecyl-s′-(α, α′-dimethyl-α″-acetic acid) trithiocarbonate (DMAT) was synthesized according to the method and characterized detailly in our previous paper [10].

2.2. Synthesis of the poly (ethylene oxide) macro-RAFT agent (mPEO-DMAT)

DCC (1.03 g, 5×10⁻³ mol) and 0.06 g DMAP (4×10⁻³ mol) were added successively to a solution of mPEO (12.5 g, 2.5×10⁻³ mol) and DMAT (1.82 g, 5×10⁻³ mol) in 100 mL dried dichloromethane. The mixture was stirred at room temperature for 5 days. After filtered to remove the precipitated salt, the filtrate was concentrated under rotary evaporation. The product was dissolved in CH₂Cl₂ and precipitated in diethyl ether for three times. The product was obtained after vacuumized at 40 °C and stored at 5-8 °C. Yield: 82%. FTIR (KBr pellet, cm⁻¹): 2940(s, -CH₃), 2885(s, -CH₂CH₂-), 1735(s, -CO-), 1465(,-CH₂-), 1110(, C-O-C), 840(s, -C-S-). 1H NMR (CDCl₃, ppm): 0.86(t, 3H, -CH₂CH₃), 1.23(m,16H, -CH₂(CH₂)₉CH₃), 1.67(s, 6H, -C(CH₃)₂SC(S)S-), 3.24(t, 2H, =SC(S)CH₂CH₃-), 3.36(s, 3H, CH₃OCH₂-), 3.6(m, -O-CH₂CH₂-), 4.25 (t, 2H, -CH₂CH₂O-).

2.3. Preparation of crosslinked nanoparticles via surfactant-free emulsion polymerization of Styrene

In a typical experiment (Table 1, sample B₂), 0.7405 g mPEO-DMAT (0.138 mmol) were dissolved in deionized water (15.26 g). Then, 2.08 g of styrene (20.0 mmol) were added to the solution in a 50 mL septum-sealed flask. An aqueous stock solution of Va 044 was prepared (10 mg/mL) and neutralized by NaHCO₃ (3.0 molar equivalents with respect to DMAT). Consequently, 0.011 g of this solution (V
a 044: 0.037 mmol) and 0.104 g DVB (0.80 mmol) were added to the mixture, degassed with nitrogen for 30 min at 5 °C and then the reaction was allowed to continue at 80 °C in an oil bath under stirring. For comparison, the sample without crosslinker was prepared in the same conditions (Table 1, A2). The reaction was performed at regular time and the polymerization was stopped by immersion of the flask in iced water. The crude products were dialyzed and cut off the average molecular weight 8000 Dolton for a week. The detailed information was listed in Table 1.

Table 1. RAFT-mediated polymerization of styrene (St) and divinylbenzene (DVB) in water with mPEO-DMAT trithicarbonate chain transfer agent at 80°C

| Entry | St (mmol) | mPEO-DMAT (mmol) | [St]₀/Va044 | DVB (mmol) | reaction time (h) | conversion (%) | Dz (nm) | PDI | diameter (nm) |
|-------|-----------|------------------|-------------|------------|------------------|---------------|---------|-----|---------------|
| A1    | 13.8      | 0.138            | 100         | 0.037      | 0                | 15            | 72      | 181.7 | 0.218         | 58.1   |
| A2    | 20        | 0.138            | 145         | 0.037      | 0                | 15            | 68      | 220.2 | 0.326         | 89.2   |
| A3    | 30        | 0.138            | 200         | 0.037      | 0                | 15            | 64      | 295.1 | 0.457         | 98.3   |
| B1    | 13.8      | 0.138            | 100         | 0.037      | 0.052           | 15            | 63      | 190.1 | 0.247         | 74.6   |
| B2    | 20        | 0.138            | 145         | 0.037      | 0.800           | 15            | 62      | 297.3 | 0.328         | 91.4   |
| B3    | 27.6      | 0.138            | 200         | 0.037      | 1.104           | 15            | 36      | 242.6 | 0.349         | 50.3   |

*a monomer conversion determined by gravimetry vs time; *b Dz is the average particle diameter from dynamic light scattering analysis (the lower the dispersity factor, the narrower the particle size distribution). *c observed from TEM.

2.4. Characterizations
The chemical structures of the synthesized chemicals were characterized by ¹H NMR spectroscopy on a Bruker ARX 400MHz spectrometer, using CDCl₃ as the solvent and tetramethylsilane (TMS) as the internal standard. Fourier transform infrared (FTIR) spectra were obtained from a Nicolet iS50 spectrometer (thermosisher Instruments Co.). The sample was dispersed in a KBr pellet. The z-average particle diameter (Dz) and polydispersity of the diluted aqueous dispersions were measured by dynamic light scattering (DLS) at 25 °C, with a Nano ZS from Malvern (173° angle, 5 mW He-Ne laser at 633 nm). Transmission electron microscopy (TEM) observation was conducted on a Hith T-600 electron microscope instrument operating at an acceleration voltage 75 kV. Negative staining technique with phosphotungstic acid (PTA, 3% solution) as staining agent was used for TEM sample preparation. A drop of polymer emulsion was placed on formvar-coated copper grids and stained with PTA about 15 minutes and then allowed to dry prior to observation. Thermogravimetric analysis (TGA) was made using a TA instruments TGAQ500. Samples were heated at 10°C/min from room temperature to 650 °C in a dynamic nitrogen atmosphere at a flow rate of 50 mL/min.

3. Results and Discussion
The synthesis of mPEO-DMAT macro-RAFT agent was carried out by esterification using mPEO and DMAT under the assistant of DMAP and DCC in dichloromethane. Scheme 1 shows the synthesis routes of mPEO-DMAT and the core-crosslinked nanoparticles. The structure of mPEO-DMAT was confirmed through FTIR and ¹H NMR. The FTIR spectra of DMAT, mPEG5000 and mPEG-DMAT are illustrated in Fig.1 (A). As shown in Fig.1, the bands at 1064 cm⁻¹ and 825 cm⁻¹ are attributed to the stretching vibration of the -C=S and -C-S- of the DMAT respectively; the band at 1113 cm⁻¹ to the stretching vibration of the C-O-C ether linkage, 1468 cm⁻¹ to the vibration of the –CH₂-CH₂ to the mPEG5000 as well as the emergence of peak at 1735 cm⁻¹ are attributed to the vibration of the –C=O- of mPEG-DMAT. For the core-crosslinked nanoparticles, the DVB as crosslinker and styrene as monomer, mPEO-DMAT-St nanoparticles were prepared.
Fig. 1 (B) shows the $^1$H NMR of mPEO-DMAT and mPEO. Some new peaks are apparent compared with the mPEO: the peak at 4.26 ppm corresponding to the proton -CH$_2$-O(C=O) and the signal at 3.65 ppm which is assigned to the proton in the methylene of the PEG chain. By integrating the peak areas of the signals at 3.65 ppm and 0.87 ppm (the CH$_3$CH$_2$- of the C$_{12}$H$_{25}$ chain moiety), the degree of terminal functionalization can be calculated about 97% [2]. The crosslinked nanoparticles chemical structure was confirmed by FTIR and $^1$H NMR. The 1736 cm$^{-1}$ and 1631 cm$^{-1}$ vibration absorption in Fig. 1 (A) of mPEG-DMAT crosslinked nanoparticles are assigned to the -C=O stretching and styrene core respectively. Additionally, the 6.30-6.83 ppm chemical shift is characteristic absorption of -CH$_2$-CH- of polystyrene and 6.87-7.24 ppm is assigned the benzene ring absorption. These results indicate the polystyrene particles were obtained.
Figure 1. FTIR spectrum of DMAT(a), mPEG5000(b), mPEG-DMAT(c) and mPEG-DMAT-St (d) and 1H NMR spect, rum of mPEO5000 and mPEG-DMAT.
Figure 2. $^1$H NMR spectrum of mPEG-DMAT-St core-crosslinked nanoparticles (A) and the hydrodynamic diameter of corresponding crosslinked and without crosslinked nanoparticles (B).

The core-crosslinked nanoparticles were formed using mPEG-DMAT as micelles in water and St as monomer droplets which encapsulated into micelles accompanied with DVB. Fig.2 (B) illustrate the hydrodynamic diameters of particles with or without DVB. During the polymerization in micelles self-assembled from mPEG-DMAT amphiphilic macromolecules, with the increasing of concentration of St, the diameter of latex is increased gradually from 182 nm to 296 nm and the ratio of St to macromolecular RAFT agent is enhanced to 200 (in table 1 and Fig.3). Added the crosslinker DVB, the micelles were enlarged and polymerization was occurred directly located in hydrophobic segment of RAFT quite similarly to a bulk system [9]. With the concentration increased to 1.104 mmol of DVB,
the micelles expanded and collapsed and the size of particles were decreased dramatically. It is showed in the table 1 and the Fig.2 (B). Furthermore, the TEM observation was also testified the above transformation.

![Figure 3](image)

**Figure 3.** TEM photographs of cross-linked nanoparticles. mPEG-DMAT-St100; (a) mPEG-DMAT-St100+DVB; (b) mPEG-DMAT-St145; (c) mPEG-DMAT-St145+DVB (d); mPEG-DMAT-St 200(e) and mPEG-DMAT-St 200+DVB(f).

The thermal property of nanoparticles was measured by TGA. Fig.4. shows the decomposition of nano-particles with and without crosslinked latexes. Increasing the St Concentration, the particle stability decreased; increased the DVB content, the onset temperature of degradation is lower than that of without DVB. The core-crosslinked density is higher with the addition of St and DVB, while the thermal stability is lower which is attributed to microphase separation of the PEO block and the PS segment in domain of nanoparticles. During the heating the outside PEO block firstly melted and then PS domain began to melt and degrade, the compatibility of PEO and PS is poor and microphase separation is underwent. As a resulting, the two-step thermal degradation is occurred.
Figure 4. TG and DTG curves of mPEG5000 (a), mPEG-TTCA-St100 (b), mPEG-TTCA-St100+DVB (c), mPEG-TTCA-St145 (d) and mPEG-TTCA-St145+DVB (e).

4. Conclusion
Core-crosslinked nanoparticles were prepared using mPEO-DMAT as macromolecular RAFT agent and surfactant, St as monomer and DVB as crosslinker. The size evolution and morphology of nanoparticles were investigated with the increasing of monomer and crosslinker. The microphase separation was used to elaborate the nanoparticles thermal stability. The core-crosslinked nanoparticles were potential to be used as compatilizer or additive for the plastics.
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