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SHORT COMMUNICATION

Synthesis of polyaspartate macromonomer having a vinyl end group and application to dispersion copolymerization of styrene

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Abstract Sodium polyaspartate (PAspNa) macromonomer with an acryloyl end group was synthesized for dispersion polymerization. At first, a poly(succinimide) (PSI) derivative with a hydroxyphthalimide end group was synthesized by polycondensation of L-aspartic acid and 4-hydroxyphthalic acid. Then, the PSI derivative was end-capped with an acryloyl group by a reaction with acrlyloyl chloride. Finally, a PAspNa derivative with a vinyl end group was synthesized by a hydrolysis of succinimide units by sodium hydroxide. The synthesized macromonomer was applied as a polymerizable stabilizer in dispersion copolymerization of styrene in a mixture of ethanol and water. The PAspNa macromonomer acted as an effective stabilizer and gave sub-micron-sized polymeric particles in dispersion polymerization in polar medium.

Keywords Macromonomer · Polyaspartate · Particle · Dispersion polymerization

Introduction

Particles having a hydrophobic core and a hydrophilic layer are called hairy particles. A layer of concentrated polymer chains is formed on these particle surfaces and provides high stability and functionality. Hairy particles with well-designed functionality are promising for the applications such as affinity particles, drug delivery carriers, and catalyst. Therefore, the design of functionality of the hairy chains is a key factor for the particle usage in these applications.

Generally, there are two methods to prepare hairy particles from existing core particles: (1) "grafting onto" method [1–3], where end-functionalized polymer chains are coupled with core particles, and (2) "grafting from" method [4–11], where hairy chains are grown from the surface of core particles modified with initiators. Especially, surface-initiated living radical polymerization has been used in recent years by a lot of researchers to prepare hairy particles because this method produces hairy chains with controlled chain length on the particle surface. However, multistep reactions are required to produce the core particles modified with initiators.

Heterogeneous polymerization with macromonomer is an alternative for preparing hairy particles. Heterogeneous polymerization, such as emulsion polymerization and dispersion polymerization, is a one-pot polymerization method to obtain polymeric particles in nano- to micro-scale, and the particle diameter can be controlled by changing the reaction parameters. Polymeric particles prepared by dispersion copolymerization [12–27] or emulsion copolymerization [26–34] with macromonomer have high stability and functionality derived from anchoring of hydrophilic polymer chains on the particle surface. Almost all studies used the macromonomer based on poly(ethylene oxide) (PEO) in the heterogeneous polymerization [13, 17, 20–22, 24–26, 29, 31–34] because of the high solubility in various solvents. However, the functionalization of PEO chains is difficult owing to chemical stability of the ethylene oxide units. Thus, the heterogeneous polymerization with PEO macromonomer is not suitable to design the functionality of hairy chains.

Sodium polyaspartate (PAspNa), a hydrophilic biodegradable polymer, can easily accept the introduction of

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functional groups into the side chains. PAspNa is derived from poly(succinimide) (PSI), product from the polycondensation of L-aspartic acid, by hydrolysis with sodium hydroxide [35]. PSI reacts with various amine compounds without any coupling agent. Therefore, PAspNa derivatives with various functional pendant groups are easily designed [35–38].

In this study, we synthesized PAspNa macromonomer with an acryloyl end group and applied to prepare functionalized hairy particles. The outline of the synthesis route is shown in Scheme 1. At first, a PSI derivative with a hydroxyphthalimide end group (**1**) was synthesized by polycondensation of L-aspartic acid and 4-hydroxyphthalic acid. Then, **1** was end-capped with an acryloyl group to obtain a PSI derivative with a vinyl end group (**2**). Finally, PAspNa macromonomer (**3**) was synthesized by a hydrolysis of **2**. The synthesized PAspNa macromonomer was used as a polymerizable stabilizer in dispersion copolymerization of styrene to prepare the polymeric particles. A PAspNa derivative without vinyl end group was also synthesized in order to compare the results obtained between macromonomer and nonpolymerizable stabilizer.

Experimental

Materials

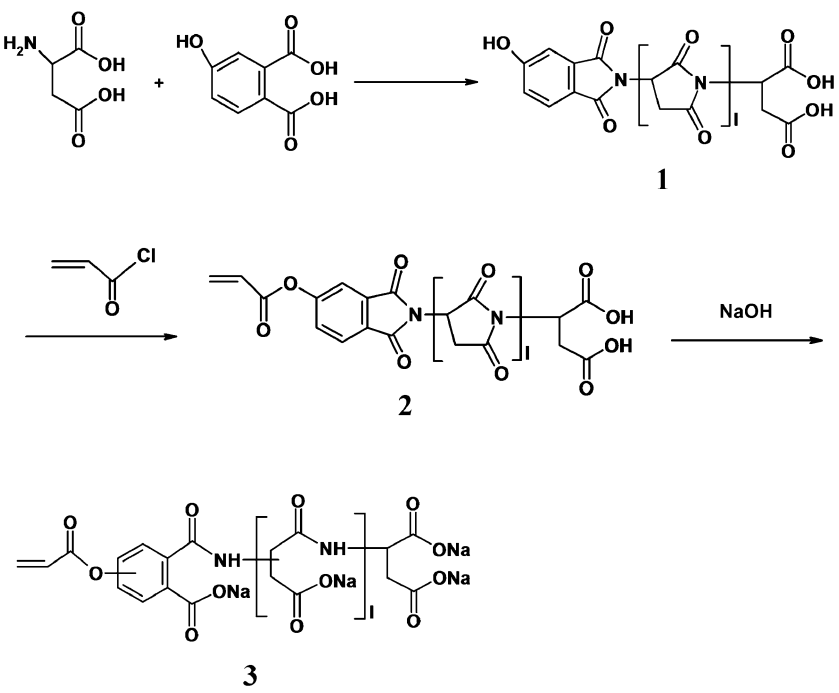
All materials were obtained from Wako Pure Chemical Industries. *N*,*N*-Dimethylformamide (DMF) was dehydrated by adding dried molecular sieves. Styrene was purified by distillation under reduced pressure. 2,2′-Azobisisobutyronitrile (AIBN) was purified by recrystallization from ethanol. Other materials were used without further purification. Water was purified by a Millipore Milli-Q purification system.

Synthesis of PSI derivative with a hydroxyphthalimide end group (**1**)

A typical procedure for the synthesis of **1** is as follows: 23.4 g of L-aspartic acid (Asp), 1.19 g of 4-hydroxyphthalic acid (HPA), 9.94 g of phosphoric acid, and 1.81 g of water were mixed in a flask. The flask was placed in a rotary evaporator and heated at 453 K for 7 h under reduced pressure. The product was dissolved in 300 ml of DMF, and the solution was poured into 2 l of methanol. The precipitate was washed three times with methanol and three times with water. The resultant polymer was dried in a vacuum at 313 K to obtain the **1** (15.0 g, 83%).

Synthesis of PSI derivative with a vinyl end group (**2**)

1 (3.0 g) was dissolved in 30 ml of dry DMF, and more than ten excess of acryloyl chloride (AC) and more than ten excess of triethylamine (TEA) were added to the solution. The mixture was stirred at room temperature for 24 h and then poured into 300 ml of methanol. The precipitate was washed six times with methanol and three times with water. The resultant polymer was dried in a vacuum at room temperature to obtain the **2** (2.68 g, 88%).



Scheme 1 Synthesis of PAspNa derivative with a vinyl end group

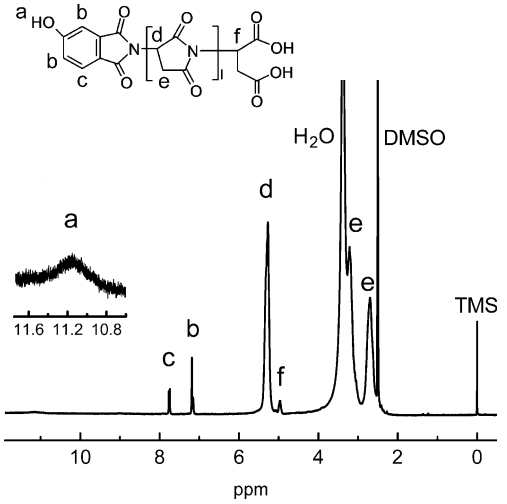


Fig. 1 ^{1}H NMR spectrum of **1** in DMSO-d_6

Synthesis of PAspNa derivative with a vinyl end group (**3**)

2 (2.5 g) was dispersed in 100 ml of water, and 1 N sodium hydroxide (NaOH) solution was added dropwise so as not to exceed pH 10 in the solution. The solution was then neutralized by 1 N hydrochloric acid solution and concentrated under reduced pressure. The solution was recrystallized from methanol. The precipitate was dried in a vacuum to obtain the **3** (3.48 g, 99%).

Synthesis of a PAspNa derivative without a vinyl end group (**3′**)

3′ was synthesized from **1** and 1 N NaOH solution using the same method for **3** (3.53 g, 99%).

Dispersion copolymerization

Dispersion copolymerization was carried out in a reactor equipped with a reflux condenser and a magnetic stirrer and placed in an oil bath equipped with a temperature control. A typical procedure for dispersion copolymerization of styrene with **3** is presented below: 0.107 g of AIBN and 1.34 g of styrene were dissolved in ethanol 27 ml, and it was added into 18 ml of aqueous solution containing of 0.10 g of **3**. The mixture was polymerized in the reactor at 343 K for 6 h under nitrogen atmosphere. The resultant particles were refined by centrifugating washes with water three times.

Measurements and characterization

^{1}H NMR spectra were measured using a NMR spectrometer (JEOL AL300 SC-NMR). Weight-average molecular weight (M_w) and molecular weight distribution (M_w/M_n) of a PSI derivative were determined by a gel permeation chromatography (TOSOH HLC-8120 GPC system) using polystyrene standards with DMF as an eluant. The flow rate and the column temperature were 0.6 ml/min and 313 K, respectively. The particle diameter and the diameter distribution were determined by scanning electron microscopy (SEM, Hitachi S-4700). The number-average particle diameter was obtained by counting 200 particles in SEM photographs. Coefficient of variation of the particle diameter was calculated using the following equation:

$$\mathrm{CV}(\%) = \frac{\text{Standard derivation } (\mu\text{m})}{\text{Number} - \text{average particle diameter } (\mu\text{m})} \times 100$$

Styrene monomer conversion was calculated from the unreacted styrene monomer concentration, which is measured by high-performance liquid chromatography. Small amount of resultant latex was added to methanol with 4-*t*-butylpyrocatechol to terminate polymerization. These solutions were centrifuged at 30,000 rpm for 15 min to remove the particles. Unreacted styrene concentration in the supernatant was measured by high-performance liquid

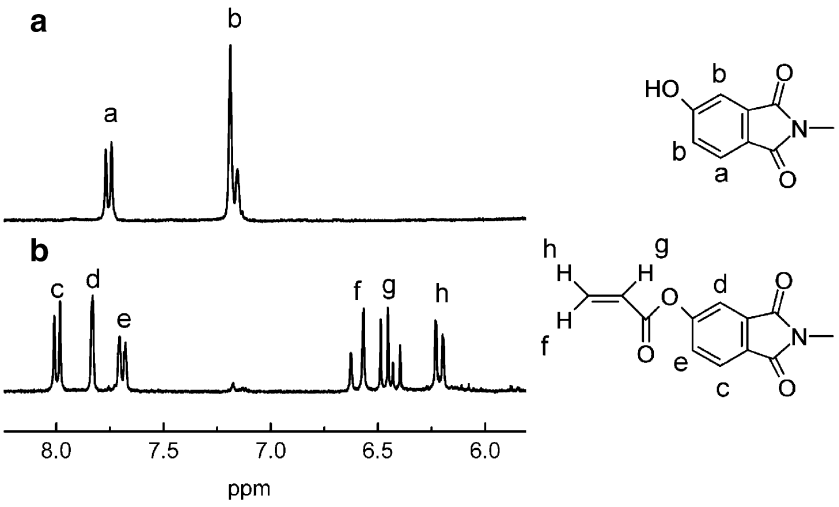
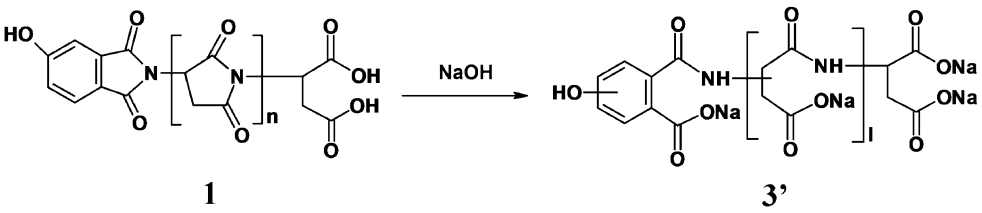


Fig. 2 ^{1}H NMR spectra **1** (**a**) and **2** (**b**) in DMSO-d_6

Scheme 2 Synthesis of PaspNa derivative without a vinyl end group



1 **3'**

chromatography (SHIMADZU Prominence HPLC system) with a UV–VIS detector (SPD-M20A, λ=254 nm) with the mixture of methanol/water=7:3 (vol/vol) as an eluant. The column was a TSK-Gel ODS-80Ts QA (150×4.6 mm, TOSOH). The flow rate and the column temperature were 0.8 ml/min and 313 K, respectively.

Results and discussion

A PSI derivative with a hydroxyphthalimide end group (**1**) was synthesized by the bulk polycondensation of Asp and HPA in the presence of phosphoric acid. The polymer with M_w of 7,700 was obtained, and the distribution was broad (M_w/M_n=4.2). Figure 1 shows the ^{1}H NMR spectrum of **1** in deuterated dimethyl sulfoxide (DMSO-d_6). The peak at 4.9 ppm is assigned to a methine proton of the succinic acid end group, and the peaks at 7.2 and 7.8 ppm are assigned to aromatic protons of the phthalimide end group. The end functionality of **1** was estimated from the integration value ratio at 4.9 and 7.8 ppm. The number-average molecular weight (M_n) was calculated by the integration values of a peak at 4.9 and 5.3 ppm for a methine proton of the succinimide unit. The hydroxyphthalimide end functionality (f_{OH}) and M_n estimated by ^{1}H NMR spectrum were 98% and 3,400, respectively. A PSI derivative with a vinyl end group (**2**) was synthesized by the reaction of hydroxyphthalimide end group of **1** and AC in the presence of TEA. Expanded region of the ^{1}H NMR spectra of **1** and **2** are shown in Fig. 2. This figure shows that the peaks at 7.2 ppm disappeared as well as three peaks at 6.2~6.7 ppm and three peaks at 7.7~8.0 ppm in ^{1}H NMR spectrum of **2**. These peaks were assigned to the vinyl and aromatic protons of the acryloxyphthalimide group, respectively. Vinyl end functionality (f_{vinyl}) of **2** was calculated by follow equation:

$$f_{vinyl} = \frac{I_{6.3}/3}{I_{6.3}/3 + I_{7.2}/2} \times f_{OH}$$

where I_i is the integration value of the peak at i ppm in ^{1}H NMR spectrum of **2**. **2** with 91% of f_{vinyl} was obtained by the reaction with a large excess of AC. Hydrolysis of succinimide units in **2** by NaOH solution produced PAspNa macromonomer with a vinyl end group (**3**). The hydrolysis of succinimide units was confirmed by disappearance of the peak at 5.3 ppm and appearance of the peaks at 4.5 and 4.7 ppm for methine protons of an aspartic acid unit in ^{1}H NMR spectrum in deuterium oxide (data not shown). A PAspNa derivative without a vinyl end group (**3′**) was synthesized by the hydrolysis of **1** (Scheme 2).

Dispersion (co)polymerization using **3** or **3′** as a dispersion stabilizer in a mixture of ethanol and water were carried out. By dispersion polymerization using **3′**, polymer colloid was obtained in 78% conversion; however, much coagulum was also formed. On the other hand, polymer colloid with no coagulum was obtained in 88% conversion by dispersion copolymerization with **3**. Figure 3 shows the SEM images of the particles prepared using macromonomer **3** and nonpolymerizable stabilizer **3′**. Particle diameter of the particles prepared using **3′** and **3** were 2.33 and 0.407 μm, respectively. Macromonomers are chemically anchored on the particle surface during dispersion poly-

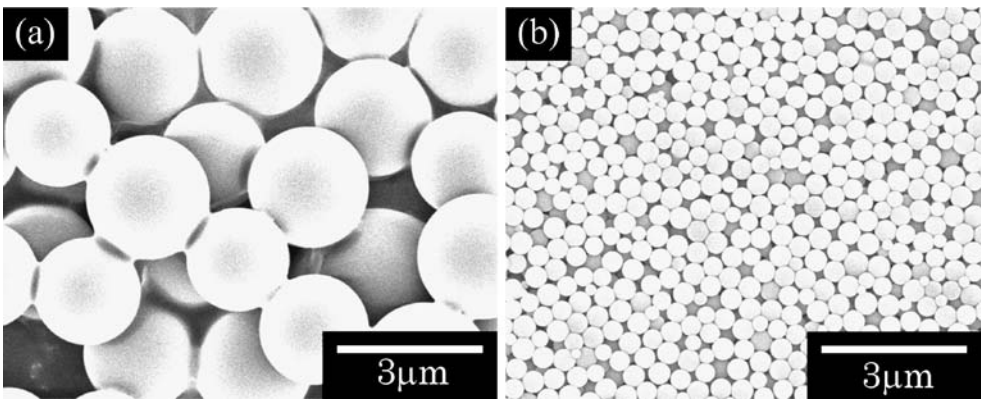


Fig. 3 SEM images of the particles prepared by dispersion (co)polymerization of styrene with PAspNa derivatives: **a** nonpolymerizable stabilizer (**3′**); **b** macromonomer (**3**). [**3** or **3′**]=2.22 g/l

merization and provide high dispersion stability [14]. Thus, the particles prepared using **3** were much smaller than those prepared using **3′**. The comparison results indicated that the PAspNa macromonomer is an effective stabilizer in dispersion polymerization in polar medium.

Conclusion

A PSI derivative with a hydroxyphthalimide end group was synthesized by bulk polycondensation of Asp and HPA in the presence of phosphoric acid. This polymer was reacted with AC in the presence of TEA and hydrolyzed by NaOH solution to obtain PAspNa macromonomer with an acryloyl end group. Sub-micron-sized polymeric particles were obtained by dispersion copolymerization of styrene and PAspNa macromonomer in a mixture of ethanol and water. These particles obtained were smaller than those prepared using a PAspNa derivative without polymerizable group as a dispersion stabilizer.

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