Article

# Synthesis and Phase Behavior of a Linear Amphiphilic Multiblock Copolymer

Xin Chen and Fengqi Liu*

Read Online

ACCESS | Metrics & More | Article Recommendations

**ABSTRACT:** Linear amphiphilic multiblock copolymer PPMPEs, obtained through a stepwise method, and linear amphiphilic random copolymer PPMPEs-1, obtained through a one-pot method, were synthesized using poly(propylene glycol) diglycidyl ether (PPGDGE), poly(ethylene glycol) diglycidyl ether (PEGDGE), and monoethanolamine (MEA) as the main raw materials. The structures of PPMPEs and PPMPEs-1 were characterized by FT-IR, $^1$H NMR, and gel permeation chromatography, which proved that the copolymers were synthesized with different components. Transmittance of the copolymer was tested by UV−vis. By changing the ratio of PEGDGE content and the concentration of the copolymer aqueous solution, the phase behaviors of PPMPEs and PPMPEs-1 were compared and studied in depth. It mainly highlighted the advantages of the stepwise method compared to the one-pot method. The transmittance of the polymer solutions could be improved by lowering the pH value in the acidic solution or increasing the pH value in the alkaline solution. Moreover, as the reaction degree of the PPMPEs hydrophobic chain segment increased, the transmittance decreased.
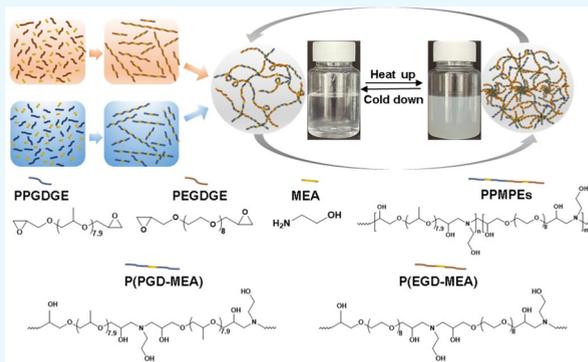


## 1. INTRODUCTION

The amphiphilic copolymer, one of the most explored copolymers, has attracted a great amount of interest in terms of its design diversity for intelligent materials and its application in various fields in recent years.[1,2] Intelligent materials that spring up like mushrooms have been gaining much interest owing to their controllable polymerization and flexible synthetic methods. This kind of intelligent material, including temperature-sensitive, pH-sensitive, and biosensitive polymers, has been extensively explored for its application in a large number of fields, such as temperature-sensitive hydrogels,[3−11] controllable drug loading and release,[12−16] material separation,[17] functional nanomaterial preparation,[18−20] and biological simulation.[21−23] Meanwhile, other fields have initially shown the broad application prospects of this polymer.[24−26]

The amphiphilic copolymer with an external stimuli shows a corresponding response behavior in different physical states. Due to the Brownian motion of solvent molecules, which is required for the process of replacing solvent molecules by a macromolecular segment, and the lowest energy of the polymer, the temperature[27] and acid−base responsive behavior of macromolecules[28] are most easily observed in polymer solutions. Physical or chemical external stimuli mainly affect secondary forces, including electrostatic interactions, hydrophobic interactions, and hydrogen bond simple chemical reactions such as acid−base reactions in polymer reaction solutions. Macromolecules show changes in molecular size, secondary structure, solubility, or degree of intramolecular cross-linking.

Based on the unique linear structure and hydrophilic or hydrophobic properties, researchers have paid great attention to the research and application of the linear amphiphilic copolymer.[29,30] However, the research on the relationship among synthesis, structure, and properties remains largely unexplored. In particular, the effect of electrostatic interaction and hydrogen bonding on the phase behavior of the linear amphiphilic copolymer in aqueous solution has hardly been paid attention to. There is also very little applied research on the phase transition and adjustment conditions of the subsequent gelation. Shi's research group developed a synthesis route for amphiphilic network (APCN) gels, which were first synthesized by ring-opening polymerization of the macromolecular monomer and then formed APCN gels by a macromolecular monomer and a single chain. The gel has the characteristics of temperature sensitivity and amphiphilicity.[31]

Our research group prepared an amphiphilic random copolymer by a one-pot method, which could undergo phase-transition behavior in an aqueous solution.[32] However, the phase-transition temperature of the random copolymer solution was too high, which was not conducive to the gelation research in subsequent experiments. On the basis of the above discussion, we synthesized hydrophilic and hydrophobic prepolymers by a stepwise method and prepared amphiphilic multiblock copolymers with a more regular block arrangement. The effects of hydrogen bonds and electrostatic interactions under alkaline and acidic conditions were emphatically discussed to prove the amphiphilic multiblock polymer properties. The mechanism of phase-transition regulation, the critical transparent-opaque phase transition behavior in polymer aqueous solution, and the effect of the state of the polymer segment on its aqueous solution phase transition behavior also have been further explored and given detailed elaboration. The amphiphilic polymers have a certain impact on the acid−base response amphiphilic system, which is expected to be used in drug delivery systems[33,34] and catalyst carriers[35] and modify photovoltaic devices[36] in the future.

## 2. RESULTS AND DISCUSSION

**2.1. Characterization of PPMPEs.** The infrared spectra characteristics for the raw materials PPGDGE, PEGDGE, MEA, prepolymer P(PGD-MEA), P(EGD-MEA), and polymer PPMPEs in the range of 500−4000 cm$^{-1}$ are shown in Figure 1. In the FT-IR spectrum of ethanolamine, with a typical peak
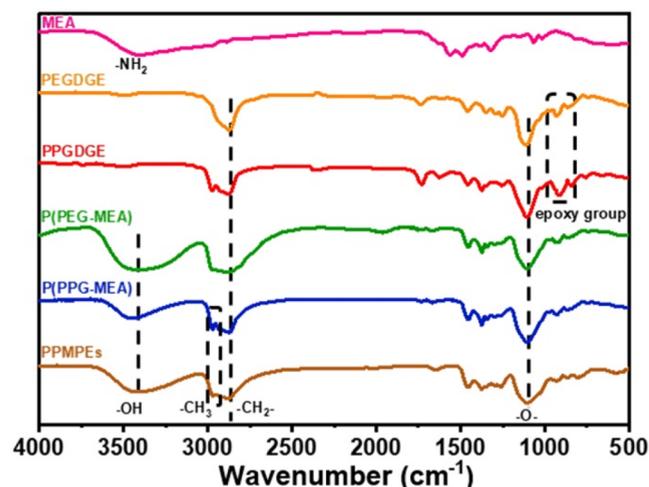


**Figure 1.** FTIR spectra of PPGDGE, PEGDGE, MEA, P(PGD-MEA), P(EGD-MEA), and PPMPEs.

of 3400 cm$^{-1}$ for the primary amino group, was observed. The peaks at ∼2874 cm$^{-1}$ could be ascribed to the stretching vibration of the methylene group of PEGDGE. The peaks at ∼2973 cm$^{-1}$ results from the methyl group of PPGDGE. In addition, the characteristic absorption peaks of the epoxy groups appeared at about ∼930 cm$^{-1}$. Prepolymers P(EGD-MEA) and P(PGD-MEA) and polymer PPMPEs showed a characteristic peak of OH$^-$ around ∼3420 cm$^{-1}$. The absorption peak of the epoxy groups for PPGDGE and PEGDGE disappeared. P(PGD-MEA) and PPMPEs showed the same methyl characteristic peaks as the PPGDGE at ∼2975 cm$^{-1}$. At the same time, an obvious absorption peak for −O− at 1109 cm$^{-1}$ still existed. Based on the infrared spectroscopy

analysis, the PPMPEs had been proven to be prepared successfully.

As shown in Figure 2, the signal peak of the tertiary carbon proton H$_a$ connecting with a hydroxyl group appeared at 3.81
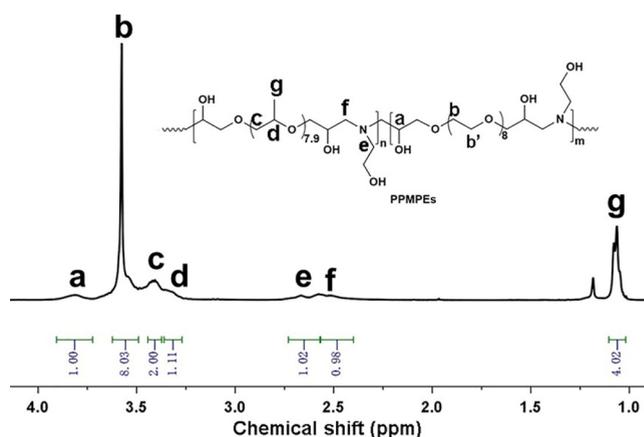


**Figure 2.** $^1$H NMR spectrum of PPMPEs in CDCl$_3$.

ppm, and that of the secondary carbon proton H$_b$ connecting with an ether bond appeared at 3.58 ppm. The signal peak of the secondary carbon proton and the tertiary carbon proton, which could form an ether bond, appeared at 3.42 and 3.38 ppm, respectively. The positions of the signal peaks for H$_b$, H$_c$, and H$_d$ involving the formation of ether bonds were different due to the different surrounding environments. The signals at 2.57 and 2.67 ppm consisted of the protons of two types of secondary carbons close to tertiary amino groups, respectively, and the methyl proton signal peak of PPGDGE was observed at 1.14 ppm.

The chemical environments at H$_b$ and H$_{b'}$ were similar, and the touch positions were close, resulting in a larger peak area for H$_b$. Its peak area ratio to H$_c$ was 2:1, which was consistent with the H$_b$/H$_d$ area ratio of 4:1. These results indicated that this method could be used to calculate the ratio of the two. At the same time, the calculated ratio was the same as the feeding ratio. The feeding molar ratio of hydrophobic groups and hydrophilic groups in this sample was 2:1, revealing that the monomer possessed a high reactivity. The molecular weight of PPMPEs132 measured by GPC was 20245 g/mol, and the "m" and "n" values can be calculated to be 26.08 and 13.04.

Table 1 lists the average molecular weight of the PPMPEs samples with different proportions of PPGDGE, PEGDGE,

**Table 1. $M_n$, $M_w$, and PDI of PPMPEs**

| samples | $M_n$ (g/mol) | $M_w$ (g/mol) | PDI |
|---|---|---|---|
| PPMPEs110 | 16228 | 22346 | 1.44 |
| PPMPEs231 | 18176 | 23189 | 1.32 |
| PPMPEs121 | 19776 | 24255 | 1.18 |
| PPMPEs132 | 20245 | 22562 | 1.32 |
| PPMPEs011 | 16462 | 24256 | 1.53 |

and MEA. It can be seen that the molecular weight of PPMPEs with different ratios is about 2.3 × 10$^4$ g/mol.

The graphic data based on molecular weight displacement and different proportions of polymer are shown in Figure 3. These results prove the successful synthesis of PPMPEs.

**2.2. Phase Behavior of PPMPEs Solution.** To express the degree of transmission, the rate of the projected luminous
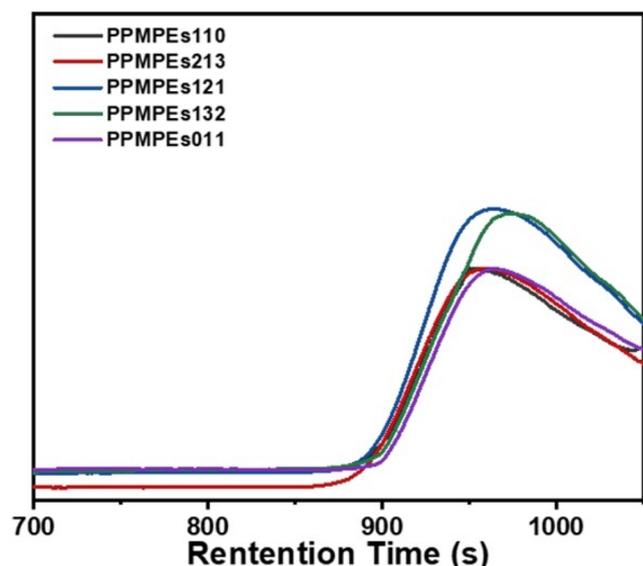
**Figure 3.** The GPC curves for PPMPEs.

flux to the incident luminous flux was defined as the transmittance. The transmittance of the deionized water was defined as 100%, and then the transmittance of the other solution was measured. The PPMPEs produced by the stepwise method showed a uniform distribution of the chain segment in the low-temperature solution to make the solution transparent. After heating up, the chain segment in the solution was entangled and solution became opaque, resulting in phase-transition behavior.

### 2.2.1. Effect of PPMPEs Concentration on Phase Behavior.

The samples of PMPPEs132 and PMPPEs132-1 were tested at pH = 7 and with a temperature at 50% transmittance that acted as the phase-transition temperature. The effect of the concentrations of PPMPEs and PPMPEs-1 on the phase-transition behavior is organized in Figure 4 with the stepwise and one-pot methods.

Figure 4a,b shows the effect of the concentration of the copolymers, PPMPEs132 and PPMPEs132-1, on transmittance under the stepwise method and the one-pot method. The transmittance rises with the concentration of PPMPEs132 or with PPMPEs132-1 decreasing from 25 wt % to 5 wt %. The transmittance of the stepwise method was much lower than that of the one-pot method. The molecular chains would be reduced due to the lower concentrations of PPMPEs132 and PPMPEs132-1. Therefore, molecular association force was weakened, leading to the increase of transmittance. The relative uniform chain segment was produced by the stepwise method, which leads to a lower transmittance. The chain segment of PPMPEs132-1 was disorganized through the one-pot method.

Figure 4c shows the effect of the concentration of PPMPEs132 on the transition temperature under the stepwise method. When the concentration increased from 5 wt % to 25 wt %, the transition temperature gradually decreased from 34 to 22 °C. Figure 4d expresses the difference between the transition temperature and the concentration of the stepwise method and the one-pot method. As the concentration of PPMPEs132 and PPMPEs132-1 increases, the number of macromolecules in the solution increases and the intermolecular association force increases, which increases the possibility of intermolecular polymerization[37] and leads to
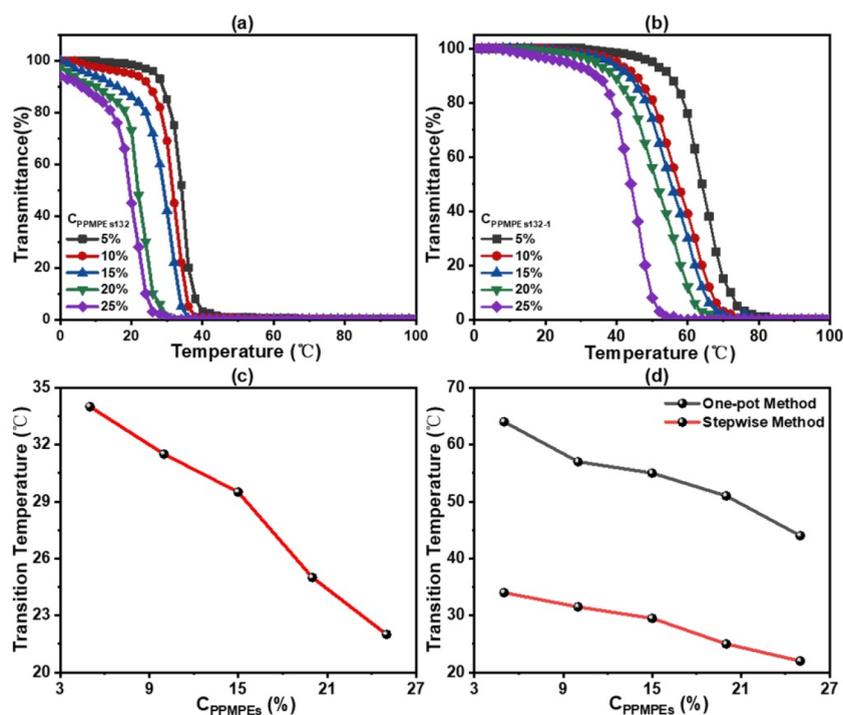


**Figure 4.** Phase transition behavior of different concentrations of PPMPEs: (a) effect of PMPPEs132 concentration on transmittance under the stepwise method; (b) effect of PMPPEs132-1 concentration on transmittance under the one-pot method; (c) effect of PMPPEs132 concentration on the phase-transition temperature under the stepwise method; (d) effect of the concentration on the phase-transition temperature under one-pot and stepwise methods.
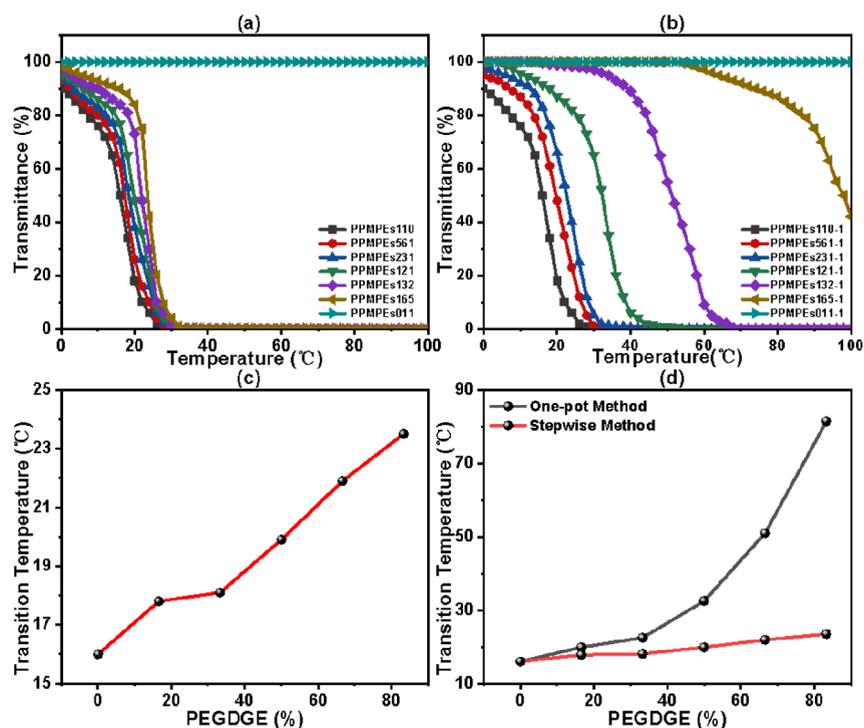
**Figure 5.** Phase transition behavior with different PEGDGE content: (a) dependence of transmittance on the PEGDGE content under the stepwise method; (b) dependence of transmittance on PEGDGE content under the one-pot method; (c) dependence of the transition temperature on PEGDGE content under the stepwise method; (d) effect of PEGDGE content on the phase-transition temperature under the stepwise and one-pot methods.
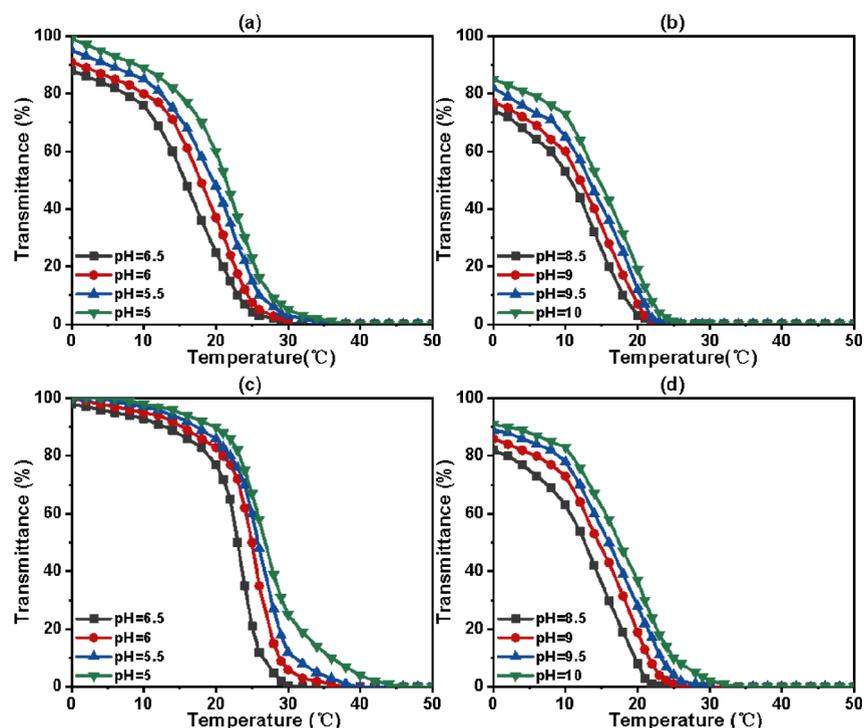


**Figure 6.** Phase transition behavior of 20 wt % aqueous solution of PPMPEs with different PEGDGE content at different pHs: (a, b) the transmittance of PPMPEs231 under different pH aqueous solutions; (c, d) the transmittance of PPMPEs132 under different pH aqueous solutions.

the reduction of the phase-transition temperature. It was also observed that the transition temperature of PPMPEs132 was about 50 °C lower than that of PPMPEs132-1. It confirmed that the copolymer with a uniform chain segment was more prone to phase transition at a low temperature.

### 2.2.2. Effect of PEGDGE Content on Phase Behavior.
The molecular chains of PPMPEs, including a hydrophilic PEGDGE segment and a hydrophobic PPGDGE segment, could make the polymer amphiphilic and affect the phase-transition behavior of the polymer. Therefore, the content of
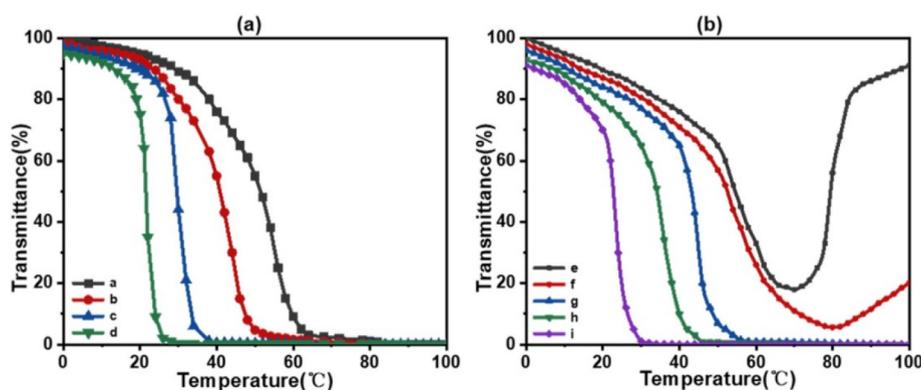
**Figure 7.** (a) The effect of the degree of hydrophobic segment reaction on transmittance when the molar ratio was PPGDGE/PEGDGE/MEA = 1:2:3. (b) The effect of the degree of hydrophobic segment reaction on transmittance when the molar ratio was PPGDGE/PEGDGE/MEA = 1:2.5:3.5.

PEGDGE affected the phase-transition behavior. The phase-transition behavior of the polymer with different PEGDGE content is worth discussing. The phase-transition temperature is at 50% transmittance, pH = 7, and 20 wt % concentration of PPMPEs aqueous solution.

We investigated the effect of PEGDGE% on transmittance under the stepwise and one-pot methods through regulating the PEGDGE% = $n(\text{PEGDGE})/[n(\text{PEGDGE}) + n(\text{PPGDGE})] \times 100\%$ ratios that were 0%, 16.7%, 33.3%, 50%, 66.7%, 83.3%, and 100%. The transmittance for PPMPEs made by the stepwise method and PPMPEs-1 made by the one-pot method would gradually increase with the PEGDGE content addition in Figure 5a,b. In addition, the PPMPEs and PPMPEs-1 had the same transmittance when only two raw materials (PEGDGE and MEA or PPGDGE and MEA) participated in the synthesis and the PEGDGE content was 0% or 100%. Both the transmittance of Figure 5a and b increased with the increase of PEGDGE content. It was because intramolecular and intermolecular associations were more difficult with increasing PEGDGE content, resulting in a higher transmittance. Interestingly, the transmittance for the stepwise method was lower than that of the one-pot method. It was because the one-pot method of the chain segment was chaotic and less prone to phase-transition behavior.

The relationship between transition temperature and PEGDGE content is shown in Figure 5c. With the addition of PEGDGE content, the transition temperature of PPMPEs increased. When the PEGDGE content was 0%, the lowest transition temperature was 15.9 °C. When the PEGDGE content was 83.3%, the highest transition temperature was 23.6 °C. These results showed the content of PEGDGE had an important effect on the phase-transition behavior, proving the hydrophilicity of PPMPEs and the transition temperature increased with increasing PEGDGE content. Figure 5d shows the corresponding relationship between PEGDGE% and transition temperature under the stepwise method and the one-pot method. With the increasing content of PEGDGE, the transition temperature of PPMPEs and PPMPEs-1 increased, but the transition temperature of the stepwise method was lower than that of the one-pot method. This was also because the reaction was more complete under the stepwise system and the lengths of the hydrophilic and hydrophobic segments were more uniform.

### 2.2.3. Effect of the pH Value of PPMPEs Aqueous Solution on Phase Behavior.
HCl and NaOH were added into the PPMPEs aqueous solution to adjust the pH. As the PPMPEs synthesized by the stepwise method were long blocks, the corresponding chain segment was relatively regular. The transmittance change of PPMPEs231 in the acidic solution is displayed in Figure 6a. The transmittance was lowest at pH = 6.5. The transmittance was increased with more $H^+$. HCl protonated the primary amino group on the PPMPEs molecular chains, which increased the positive charge and repelled each other, inhibited association, and raised the transmittance. Figure 6b showed the transmittance change of PPMPEs231 in the alkaline solution. The transmittance was lowest at pH = 8.5. It could be seen that the more $OH^-$ in the solution, the higher the transmittance. It was because the nonprotonated primary amino group itself was negatively charged, it would electrostatically repel the $OH^-$ in the sodium hydroxide, which also inhibited the association and increased the transmittance.

The transmittance changes of PPMPEs132 in the acidic solution (Figure 6c) or in the alkaline solution (Figure 6d). The transmittance would be also increased with the more $H^+$ or $OH^-$, which was the same as the transmittance change trend of PPMPEs231. It was further proved that the transmittance of PPMPEs increased with the more $H^+$ or $OH^-$. Meanwhile, it was also confirmed that with the increase of PEGDGE content, the transmittance also increased by 10 °C, which was also consistent with the test results in Figure 5.

### 2.2.4. Effect of the Degree of Reaction of the Hydrophobic Segment on the Phase Behavior.
The concentration of the aqueous solution was set to 20 wt % and the pH = 7 under the stepwise method. Different contents of MEA reacted with different contents of PPGDGE and PEGDGE, which synthesized hydrophilic and hydrophobic segments of different lengths. The transmittance decreased to 0% with increasing temperature, shown in Figure 7a. The transmittance decreased before 68 °C in Figure 7b, where samples "g", "h", and "i" decreased to 0%. However, sample "e" increased after 68 °C. Sample "f" increased after 80 °C. As can be seen from Tables 2 and 3, MEA-a has more than PPGDGE in the synthetic hydrophobic segment, which caused the epoxy ring opening at both ends of the hydrophobic prepolymer to produce the product shown in Scheme 1.

According to the eq 1, the relation between the degree of polymerization, $\overline{x_n}$, and the degree of reaction, $p$, follows:[38]

**Table 2. PPMPEs of Different Proportions by the Stepwise Method (PPGDGE/PEGDGE/MEA = 1:2:3)**

| samples | molar ratio | | | |
|---|---|---|---|---|
| | PPGDGE | MEA-a | PEGDGE | MEA-b |
| a | 1 | 2.5 | 2 | 0.5 |
| b | 1 | 2 | 2 | 1 |
| c | 1 | 1.5 | 2 | 1.5 |
| d | 1 | 1 | 2 | 2 |

**Table 3. PPMPEs of Different Proportions by the Stepwise Method (PPGDGE/PEGDGE/MEA = 1:2.5:3.5)**

| samples | molar ratio | | | |
|---|---|---|---|---|
| | PPGDGE | MEA-a | PEGDGE | MEA-b |
| e | 1 | 3 | 2.5 | 0.5 |
| f | 1 | 2.5 | 2.5 | 1 |
| g | 1 | 2 | 2.5 | 1.5 |
| h | 1 | 1.5 | 2.5 | 2 |
| i | 1 | 1 | 2.5 | 2.5 |

**Scheme 1. Hydrophobic Segment Structure**
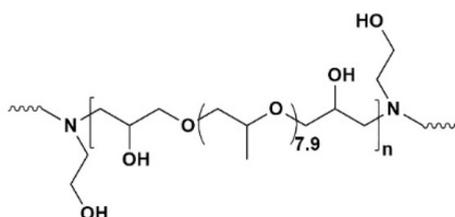


$$\overline{x_n} = n = \frac{1}{1 - p} \tag{1}$$

where $n$ is the number of structural units of the hydrophobic segment and $p$ is the fraction of the number of functional groups involved in the reaction of ethanolamine to the number of initial functional groups.

The ethanolamine involved in the reaction depends on the content of PPGDGE. According to the formula, the reaction degree $p$ of the hydrophobic chain segment can be calculated, and then the number of structural units $n$ of the hydrophobic chain segment can be calculated, and these are listed in Tables 4 and 5.

**Table 4. Degree of Reaction and the Number of Structural Units in the Hydrophobic Segment (PPGDGE/PEGDGE/MEA = 1:2:3)**

| samples | a | b | c | d |
|---|---|---|---|---|
| $p$ | 1/2.5 | 1/2 | 1/1.5 | 1/1 |
| $n$ | 1.67 | 2 | 3 | ∞ |

**Table 5. Degree of Reaction and the Number of Structural Units in the Hydrophobic Segment (PPGDGE/PEGDGE/MEA = 1:2.5:3.5)**

| samples | e | f | g | h | i |
|---|---|---|---|---|---|
| $p$ | 1/3 | 1/2.5 | 1/2 | 1/1.5 | 1/1 |
| $n$ | 1.49 | 1.67 | 2 | 3 | ∞ |

It can be seen that samples "a"–"d" or "e"–"i", $n$, and $p$ were getting bigger and bigger. When the reaction system was used

to synthesize the prepolymer, since PPGDGE in the synthetic hydrophobic segment was less than MEA-a, there were no epoxy groups in the system. When the content of PEGDGE was more than that of MEA-b, there were unreacted epoxy groups. As MEA-a decreased, its reaction degree $p$ gradually increased, and $\overline{x_n}$ also gradually increased. As the degree of the hydrophobic segment reaction increased, the transmittance of the copolymer was decreased. The hydrophilic chain segment of samples "e" and "f" were relatively short, and the chain flexibility was poor. When a certain temperature was reached, the chain segment broke, causing the transmittance to rise again.

At the same time, comparing the data between Figure 7a and b horizontally, the transmittance of Figure 7b was higher than that of Figure 7a. It was because the PPGDGE was inputted as the same, the PEGDGE content was increased, which made the transmittance higher. It was also consistent with the test results in Figure 5.

## 3. CONCLUSIONS

In this study, linear amphiphilic multiblock copolymer PMPPEs and random copolymer PPMPEs-1 were synthesized through the stepwise method and the one-pot method, respectively, which were sensitive to changes in the environment. Increasing the concentration of the copolymer aqueous solution could advance the phase-transition behavior, and the phase-transition temperature of PPMPEs was 50 °C lower than that of PPMPEs-1. Improving the PEGDGE content could increase the phase-transition temperature with the increase of PEGDGE content, and the phase-transition temperature of PPMPEs was obviously lower than that of PPMPEs-1. It proved that the stepwise method was more sufficient and the length of the hydrophilic and hydrophobic segments were more uniform. The transmittance was increased with the increasing $H^+$ content in acidic solutions or increasing $OH^-$ content in alkaline solutions. At the same time, the transmittance of the hydrophobic segments decreased with the increase of the reaction degree. The short hydrophilic segments led to poor flexibility of their segments, and the transmittance increased when it reached a certain temperature.

## 4. EXPERIMENTAL SECTION

**4.1. Materials and Characterization Instrument.** Poly-(propylene glycol) diglycidyl ether (PPGDGE) (the epoxide value was 0.1701, provided by a hydrochloric acid–acetone solution), poly(ethylene glycol) diglycidyl ether (PEGDGE) (the epoxide value was 0.2075, provided by a hydrochloric acid–acetone solution), and monoethanolamine (MEA) were

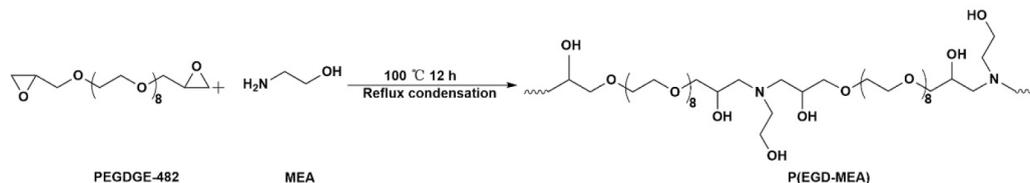**Table 6. Raw Material Compositions of PPMPEs by the Stepwise Method**

| samples | molar ratio | | | | |
|---|---|---|---|---|---|
| | PPGDGE | MEA-a | PEGDGE | MEA-b | PEGDGE%[a] |
| PPMPEs110 | 1 | 1 | 0 | 0 | 0 |
| PPMPEs561 | 5 | 5 | 1 | 1 | 16.7 |
| PPMPEs231 | 2 | 2 | 1 | 1 | 33.3 |
| PPMPEs121 | 1 | 1 | 1 | 1 | 50 |
| PPMPEs132 | 1 | 1 | 2 | 2 | 66.7 |
| PPMPEs165 | 1 | 1 | 5 | 5 | 83.3 |
| PPMPEs011 | 0 | 0 | 1 | 1 | 100 |

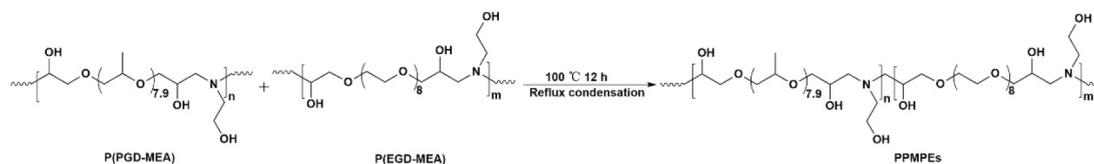[a]PEGDGE% = $n_{PEGDGE}/(n_{PEGDGE} + n_{PPGDGE})$ × 100%.

**Scheme 2. Reaction Scheme of Prepolymer P(PGD-MEA)**
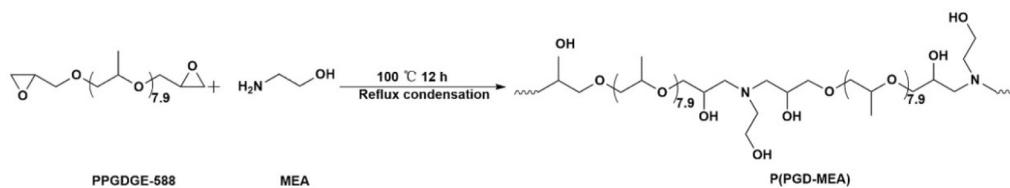


**Scheme 3. Reaction Scheme of Prepolymer P(EGD-MEA)**



**Scheme 4. Reaction Scheme of Polymer PMPPEs**
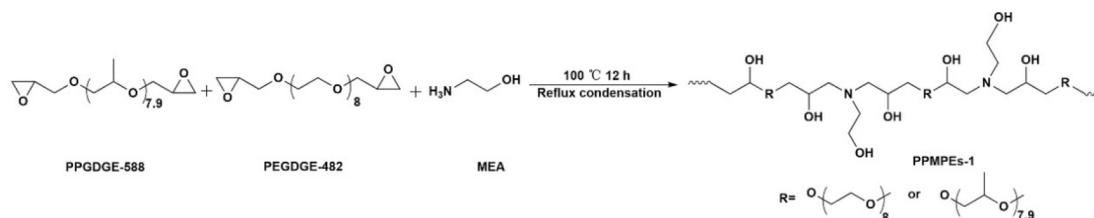


**Scheme 5. Reaction Scheme of Polymer PMPPEs-1**



**Table 7. Raw Material Compositions of PPMPEs-1 by the One-Pot Method**

| | molar ratio | | | |
| --- | --- | --- | --- | --- |
| samples | PPGDGE | MEA | PEGDGE | PEGDGE%[a] |
| PPMPEs110 | 1 | 1 | 0 | 0 |
| PPMPEs561-1 | 5 | 6 | 1 | 16.7 |
| PPMPEs231-1 | 2 | 3 | 1 | 33.3 |
| PPMPEs121-1 | 1 | 2 | 1 | 50 |
| PPMPEs132-1 | 1 | 3 | 2 | 66.7 |
| PPMPEs165-1 | 1 | 6 | 5 | 83.3 |
| PPMPEs011 | 0 | 1 | 1 | 100 |

[a]PEGDGE% = $n_{PEGDGE}/(n_{PEGDGE} + n_{PPGDGE}) \times 100\%$.

used. The relative molecular weights of PPGDGE and PEGDGE were calculated to be 588 and 482 g/mol, respectively, by the epoxy value. Deionized water, purified by Experimental Water System (Lab-UV-20), was used in relevant experiments.

Fourier transform infrared (FT-IR) spectra were collected on a Fourier Transformation iS10 IR absorption spectrometer. ^{1}H NMR spectra were recorded on Bruker AVANCE 400 MHz Hydrogen NMR instrument at 298 K. The molecular weight and molecular weight distribution were collected on a PL-GPC-220 gel permeation chromatography (GPC).

**4.2. Synthesis of Polymer PMPPEs.** *4.2.1. Stepwise Method.* The prepolymers P(PGD-MEA) and P(EGD-MEA) were synthesized by the stepwise method. The raw materials PPGDGE and MEA-a were added into the reaction flask in different ratios based on Table 6. After the mixture was reacted under 100 °C for 12 h, the prepolymer P(PGD-MEA) was obtained (Scheme 2).

According to the reaction ratio of PEGDGE and MEA-b in Table 1, the mixture was added into a flask to react for 12 h under 100 °C. Then the prepolymer P(EGD-MEA) was obtained (Scheme 3).

The prepolymers P(PGD-MEA) and P(EGD-MEA) were reacted in a flask for 12 h at 100 °C. Then the final product was dried in a vacuum drying oven to obtain the amphiphilic multiblock polymer PMPPEs (Scheme 4).

*4.2.2. One-Pot Method.* The random copolymer PPMPEs-1 was synthesized according to a previous literature report in our research group,[27] and the preparation process is shown in Scheme 5. PPGDGE, PEGDGE, and MEA were added to the reaction flask according to reaction ratios in Table 7, and the mixture were reacted at 100 °C for 12 h. After the reaction finished, the amphiphilic random polymer PPMPEs-1 was obtained after drying in a vacuum drying oven for 12 h (Scheme 5).

**4.3. Transparency Measurements.** PPMPEs and PPMPEs-1 of different proportions were dissolved in water,
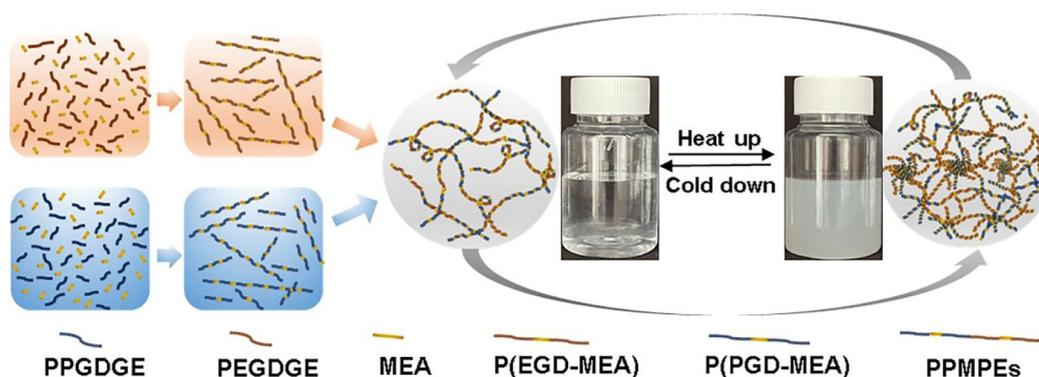
**Figure 8.** Schematic diagram for the phase transition behavior of PPMPEs aqueous solution.

and aqueous solutions of different concentrations were prepared. After being fully mixed, they were placed in cuvettes and then placed in a water bath at a preset temperature for 30 min. When measuring, a cuvette of distilled water was placed in the sample cell of the UV-2450 spectrophotometer as a reference sample, and another sample was placed in the cell to be tested. The sample cell was connected to a temperature-controlled water bath through a connecting tube to ensure that the temperature was consistent with the preset temperature. In the experiment, the transmittance with a wavelength of 600 nm was selected to characterize the phase behavior of the PMPPEs. In Figure 8, it can be observed that the multiblock copolymer solution was transparent at low temperatures, and the aggregation of the hydrophobic segments at a high temperature made the solution appear opaque.

## ■ AUTHOR INFORMATION

### Corresponding Author

**Fengqi Liu** − *College of Chemistry, Key Laboratory of High Performance Plastics, Ministry of Education, Jilin University, Changchun 130012, People's Republic of China;* ⊙ orcid.org/0000-0003-2279-2400; Email: liufq@jlu.edu.cn

### Author

**Xin Chen** − *College of Chemistry, Key Laboratory of High Performance Plastics, Ministry of Education, Jilin University, Changchun 130012, People's Republic of China*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acsomega.2c00734

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

## ■ REFERENCES

(1) Onaca, O.; Enea, R.; Hughes, D. W.; Meier, W. Stimuli-responsive polymersomes as nanocarriers for drug and gene delivery. *Macromol. Biosci.* **2009**, *9*, 129−139.

(2) Chiessi, E.; Lonardi, A.; Paradossi, G. Toward Modeling Thermoresponsive Polymer Networks: A Molecular Dynamics Simulation Study of N-Isopropyl Acrylamide Co-oligomers. *J. Phys. Chem. B* **2010**, *114*, 8301−12.

(3) Adrus, N.; Ulbricht, M. Novel hydrogel pore-filled composite membranes with tunable and temperature-responsive size-selectivity. *J. Mate. Chem.* **2012**, *22*, 3088−0.

(4) Chuang, W. J.; Chiu, W. Y.; Tai, H. J. Thermally crosslinkable poly(N-isopropylacrylamide) copolymers: Synthesis and character-ization of temperature-responsive hydrogel. *Mater. Chem. Phys.* **2012**, *134*, 1208−1213.

(5) Ishida, K.; Uno, T.; Itoh, T.; Kubo, M. Synthesis and Property of Temperature-Responsive Hydrogel with Movable Cross-Linking Points. *Macromolecules.* **2012**, *45*, 6136−6142.

(6) Kajjari, P. B.; Manjeshwar, L. S.; Aminabhavi, T. M. Novel pH- and Temperature-Responsive Blend Hydrogel Microspheres of Sodium Alginate and PNIPAAm-g-GG for Controlled Release of Isoniazid. *AAPS PharmSciTechnol.* **2012**, *13*, 1147−1157.

(7) Liang, X.; Kozlovskaya, V.; Chen, Y.; Zavgorodnya, O.; Kharlampieva, E. Thermosensitive multilayer hydrogels of poly(N-vinylcaprolactam) as nanothin films and shaped capsules. *Chem. Mater.* **2012**, *24*, 3707−3719.

(8) Park, J. K.; Kim, K. S.; Yeom, J.; Jung, H. S.; Hahn, S. K. Facile Surface Modification and Application of Temperature Responsive Poly(N-isopropylacrylamide-co-dopamine methacrylamide). *Macromol. Chem. Phys.* **2012**, *213*, 2130−2135.

(9) Pester, C. W.; Konradi, A.; Varnholt, B.; van Rijn, P.; Boker, A. Responsive Macroscopic Materials From Self-Assembled Cross-Linked SiO₂-PNIPAAm Core/Shell Structures. *Adv. Funct. Mater.* **2012**, *22*, 1724−1731.

(10) Sun, L.; Zhang, X.; Zheng, C.; Wu, Z.; Xia, X.; Li, C. Glucose- and temperature-responsive core−shell microgels for controlled insulin release. *Rsc Adv.* **2012**, *2*, 9904−9913.

(11) Trongsatitkul, T.; Budhlall, B. M. Microgels or microcapsules? Role of morphology on the release kinetics of thermoresponsive PNIPAm-co-PEGMa hydrogels. *Polym. Chem.* **2013**, *4*, 1502.

(12) Cunningham, A.; Oh, J. K. New design of thiol-responsive degradable polylactide-based block copolymer micelles. *Macromol. Rapid Commun.* **2013**, *34*, 163−168.

(13) Hocine, S.; Cui, D.; Rager, M.-N.; Di Cicco, A.; Liu, J.-M.; Wdzieczak-Bakala, J.; Brulet, A.; Li, M.-H. Polymersomes with PEG corona: structural changes and controlled release induced by temperature variation. *Langmuir* **2013**, *29*, 1356−1369.

(14) Deok Kong, S.; Sartor, M.; Jack Hu, C.-M.; Zhang, W.; Zhang, L.; Jin, S. Magnetic Field Activated Lipid-Polymer Hybrid Nano-particles for Stimuli-Responsive Drug Release. *Acta Biomater.* **2013**, *9*, 5447−5452.

(15) Madhusudana Rao, K.; Mallikarjuna, B.; Krishna Rao, K.S.V.; Siraj, S.; Chowdoji Rao, K.; Subha, M.C.S. Novel thermo/pH sensitive nanogels composed from poly(N-vinylcaprolactam) for controlled release of an anticancer drug. *Colloids Surf. B* **2013**, *102*, 891−897.

(16) Sedghi, R.; Oskooie, H. A.; Heravi, M. M.; Nabid, M. R.; Zarnani, A. H. Divergent synthesis of dendrimer-like pH-responsive macromolecules through a combination of ATRP and ROP for

controlled release of anti-cancer drug. *J. Mater. Chem.* **2013**, *1*, 773−786.

(17) Balof, S. L.; P'Pool, S. J.; Berger, N. J.; Valente, E. J.; Shiller, A. M.; Schanz, H. Olefin metathesis catalysts bearing a pH-responsive NHC ligand: a feasible approach to catalyst separation from RCM products. *Dalton Trans.* **2008**, 5791−5799.

(18) Karimi, M.; Zangabad, P. S.; Ghasemi, A.; Amiri, M.; Bahrami, M.; Malekzad, H.; Asl, H. G.; Mahdieh, Z.; Bozorgomid, M.; Ghasemi, A.; Boyuk, M. R. R. T.; Hamblin, M. R. Temperature-Responsive Smart Nanocarriers for Delivery of Therapeutic Agents: Applications and Recent Advances. *ACS Appl. Mater. Interfaces* **2016**, *8*, 21107−21133.

(19) Song, L.; Zhang, B.; Jin, E.; Xiao, C.; Li, G.; Chen, X. A Reduction-sensitive Thermo-responsive Polymer: Synthesis, Characterization, and Application in Controlled Drug Release. *Eur. Polym. J.* **2018**, *101*, 183−189.

(20) Xue, X.; Thiagarajan, L.; Braim, S.; Saunders, B. R.; Shakesheff, K. M.; Alexander, C. Upper critical solution temperature thermo-responsive polymer brushes and a mechanism for controlled cell attachment. *J. Mater. Chem. B* **2017**, *5*, 4926−4933.

(21) Gros, D.; Ringsdorf, H.; Schupp, D. Polymeric Antitumor Agents on a Molecular and on a Cellular Level? *Angew. Chem., Int. Ed.* **1981**, *20*, 305−325.

(22) Lavasanifar, A.; Samuel, J.; Sattari, S.; Kwon, G. S. Block copolymer micelles for the encapsulation and delivery of amphotericin B. *Pharm. Res.* **2002**, *19*, 418−422.

(23) Rzaev, Z.; DincEr, S.; PisKin, E. Functional copolymers of N-isopropylacrylamide for bioengineering applications. *Pro. Polym. Sci.* **2007**, *32*, 534−595.

(24) Sundaram, H. S.; Cho, Y.; Dimitriou, M. D.; Finlay, J. A.; Cone, G.; Williams, S.; Handlin, D.; Gatto, J.; Callow, M. E.; Callow, J. A.; Kramer, E. J.; Ober, C. K. Fluorinated Amphiphilic Polymers and Their Blends for Fouling-Release Applications: The Benefits of a Triblock Copolymer Surface. *ACS Appl. Mater. Interfaces* **2011**, *3*, 3366−3374.

(25) Gu, L.; Faig, A.; Abdelhamid, D.; Uhrich, K. Sugar-based amphiphilic polymers for biomedical applications: from nanocarriers to therapeutics. *Acc. Chem. Res.* **2014**, *47*, 2867−2877.

(26) Wang, S. pH-Responsive Amphiphilic Carboxylate Polymers: Design and Potential for Endosomal Escape. *Front. Chem.* **2021**, *9*, 645297.

(27) NykaNen, A.; Nuopponen, M.; Laukkanen, A.; Hirvonen, S.; Rytela, M.; Turunen, O.; Tenhu, H.; Mezzenga, R.; Ikkala, O.; Ruokolainen, J. Phase behavior and temperature-responsive molecular filters based on self-assembly of polystyrene-block-poly(N-isopropylacrylamide)-block-polystyrene. *Macromolecules.* **2007**, *40*, 5827−5834.

(28) Qiao, B.; Liu, Y.; Lee, S.; Pink, M.; Flood, A. H. A high-yield synthesis and acid−base response of phosphate-templated [3] rotaxanes. *Chem. Commun.* **2016**, *52*, 13675−13678.

(29) Heo, K.; Kim, Y. Y.; Kitazawa, Y.; Kim, M.; Jin, K. S.; Yamamoto, T.; Ree, M. Structural Characteristics of Amphiphilic Cyclic and Linear Block Copolymer Micelles in Aqueous Solutions. *Acs Macro Lett.* **2014**, *3*, 233−239.

(30) Yi, Z.; Xi, F.; Chen, Y. M. Synthesis and self-assembly of dendronized-linear amphiphilic block copolymer. *Acta Polym. Sin.* **2011**, *11*, 494−501.

(31) Shi, X.; Wu, J.; Wang, Z.; Song, F.; Gao, W.; Liu, S. Synthesis and properties of a temperature-sensitive hydrogel based on physical crosslinking via stereocomplexation of PLLA-PDLA. *RSC Adv.* **2020**, *10*, 19759−19769.

(32) Liu, F.; Liu, F. Synthesis and phase behavior of double sensitive linear amphiphilic prepolymers before gelation. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **2020**, *57*, 310−318.

(33) Huang, J.; Deng, Y.; Ren, J.; Chen, G.; Wang, G.; Wang, F.; Wu, X. Novel in situ forming hydrogel based on xanthan and chitosan re-gelifying in liquids for local drug delivery. *Carbohydr. Polym.* **2018**, *186*, 54−63.

(34) Kiene, K.; Porta, F.; Topacogullari, B.; Detampel, P.; Huwyler, J. Self-assembling chitosan hydrogel: A drug-delivery device enabling the sustained release of proteins. *J. Appl. Polym. Sci.* **2018**, *135*, 45638.

(35) Ghorbanloo, M.; Heydari, A.; Yahiro, H. Ag-nanoparticle embedded p(AA) hydrogel as an efficient green heterogeneous Nano-catalyst for oxidation and reduction of organic compounds. *Appl. Organomet. Chem.* **2018**, *32*, No. e3917.

(36) Lee, M. M.; Teuscher, J.; Miyasaka, T.; Murakami, T. N.; Snaith, H. J. Efficient hybrid solar cells based on meso-structured organometal halide perovskites. *Sci.* **2012**, *338*, 643−647.

(37) Gooch, J. W. *Intermolecular Polymerization*; Springer: New York, 2011; p 321.

(38) Chang, H. B. Derivation of the Formula between Number Average Degree of Polymerization and the Systemic Extent of Reaction in the Polycondensation. *Chin. J. Chem. Educ.* **2015**, *14*, 13−15.