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Supramolecular control over self-assembly and double thermoresponsive behavior of an amphiphilic block copolymer

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ABSTRACT

A poly(ethylene glycol)-*b*-poly[*N*, *N*-dimethylacrylamide-*ran*-2-acrylamidoethyl nonanoate] (PEG-*b*-P(DMA-AAEN)) block copolymer has been demonstrated to show double thermoresponsive behavior in aqueous solution in the presence of hydroxypropylated cyclodextrin (HPCD). The polymer itself is insoluble in water due to the presence of hydrophobic alkyl chain, however, with the presence of HPCD, fully dissolution of the polymer could be obtained indicating the formation of host-guest interaction between HPCD and the alkyl chain. The clear solution of HPCD/polymer complex showing a first thermoresponsiveness during heating and led to the formation of small micelles stabilized by PEG chains and DMA segments. Upon further heating of the aqueous solution, the small micelles aggregated and formed multimicellar aggregates. The reported double thermoresponsive behavior may provide a new strategy of designing smart polymeric systems, which can find broad applications in the fabrication of smart materials.

1. Introduction

Thermoresponsive polymers that change solubility in aqueous solution upon heating or cooling have attracted increased attentions due to their potential applications, such as sensors, actuators, delivery materials.[1–8] The most reported thermoresponsive polymers are those that undergo a hydrophilic-to-hydrophobic phase transition upon heating, so-called lower critical solution temperature (LCST) behavior. Examples of LCST polymers include poly(*N*-isopropyl acrylamide) (PNIPAM),[9,10] poly(2-oxazoline)s and polypeptides.[11,12] In addition, polymers that show reverse phase behavior, i.e. precipitate upon cooling, are known as upper critical solution temperature (UCST) polymers,[13–15] e.g. poly(sulfobetaine methacrylate) (PSBM).[16]

Besides LCST and UCST polymers, thermoresponsive polymers that exhibit two or more phase transition temperatures are more sophisticated and interesting for the construction of smart polymeric materials, e.g. shape changing polymer assemblies and hierarchy self-assembly materials.[17,18] Most of the reported multi-thermoresponsive polymers are block copolymers comprising two or more thermoresponsive blocks, where the thermally induced phase transitions originate from different blocks,[19–22] e.g. PNIPAM-*b*-PSBM with PNIPAM showing LCST behavior and PSBM showing UCST behavior. [19] Construction of non-block copolymers, e.g. homopolymers or statistic copolymers that combine multi-thermoresponsive properties is more challenging and has much less been reported.[23–26] One of the examples is poly(*N,N*-dimethylaminoethyl methacrylate) in the presence of multi-anionic counter-ions showing a LCST and, at high temperature, a UCST type phase transition.[26,27] Statistical copolymers with double LCST or double UCST behavior have not often been reported yet. The statistical copolymer poly[2-(2-methoxyethoxy) ethyl methacrylate–*ran*-poly (ethylene glycol) methyl ether methacrylate] was reported to reveal a two-stage aggregation process upon heating by Tam et al. [28] The copolymer undergoes a LCST type of phase transition in aqueous solution and subsequently rearrangement of the assembly at a higher temperature, leading to a more compact self-assembled structure.

Recently, we have developed a new type of LCST polymers based on temperature sensitive host-guest interaction between hydroxypropylated β cyclodextrin (HPβCD) and poly[(2-ethyl-2-oxazoline)-*ran*-(2-nonyl-2-oxazoline)].[29] The hydrophobic nonyl groups could be shielded by HPCD *via* thermo-sensitive host-guest interaction to facilitate the dissolution of the polymer. Upon heating, the thermo-sensitive host-guest interaction can be broken to release the hydrophobic

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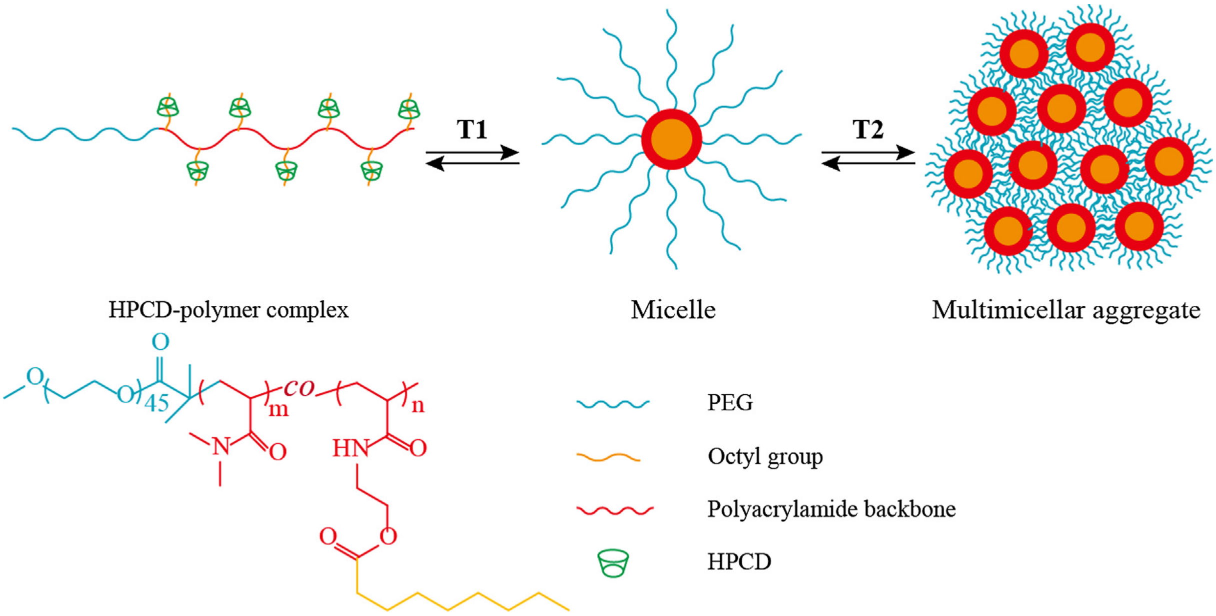

Scheme 1. Scheme of double thermoresponsive behavior of PEG-*b*-P(DMA-AAEN) in aqueous solution in the presence of HPCD.

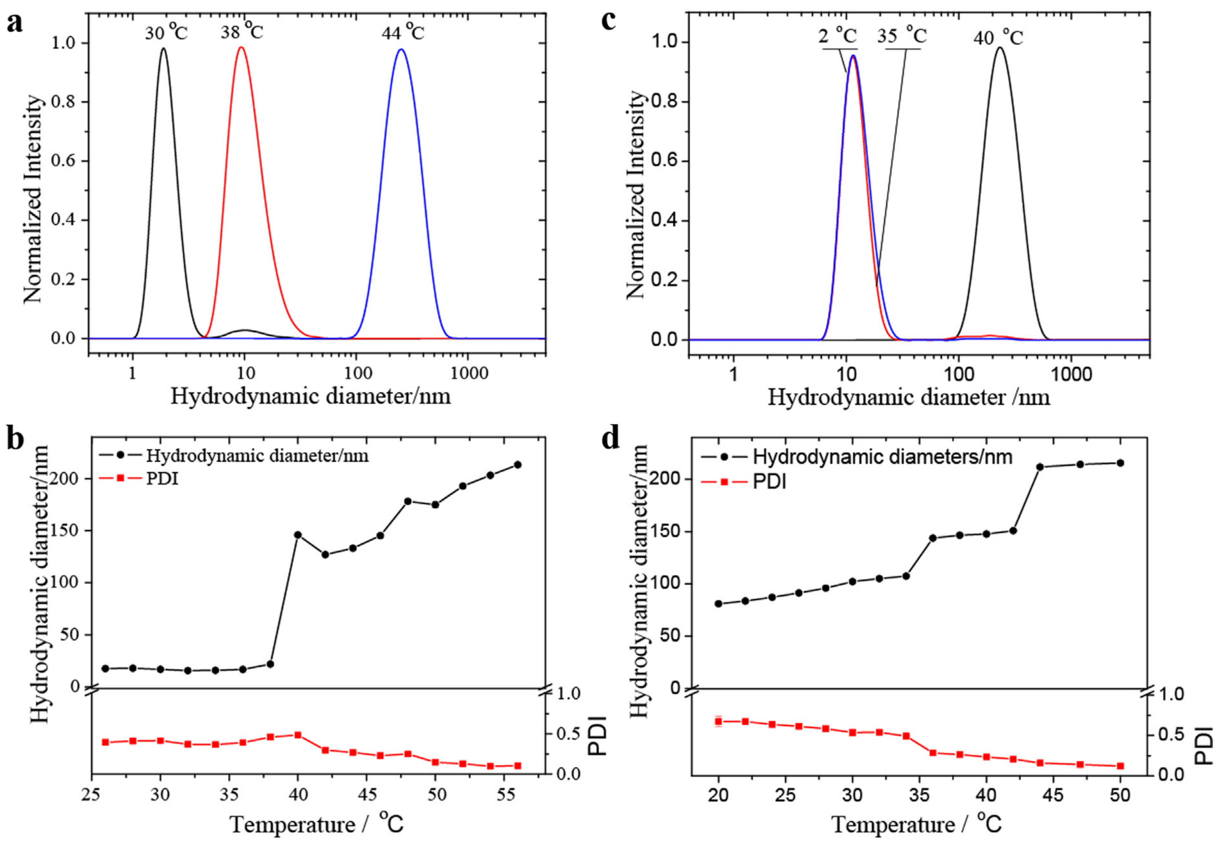

Fig. 1. Dynamic light scattering characterization for the aqueous ED7A3-HPβCD system during (a,b) heating and (c,d) cooling process. (a, c) Volume-weighted size distribution; (b,d) Hydrodynamic diameters and polydispersity (PDI) versus temperature. Polymer in solution was 1 mg/mL, with 3 equivalents HPβCD.

nonyl groups and induce the phase transition in aqueous solution. The resulting aggregates were found to have high stability upon cooling as the alkyl chains are kinetically frozen, leading to a large hysteresis between heating and cooling phase transition temperatures.

Inspired by this previous researches, we here report the formation a double thermoresponsive block copolymer system with the assistance of the reversible host-guest complexation between HPβCD and hydrophobic alkyl-chains of an amphiphilic block copolymer (Scheme 1).

2. Results and discussions

To demonstrate the principle, a series of block copolymers with a poly(*N,N*-dimethylacrylamide-*ran*-2-acrylamidoethyl nonanoate) (P

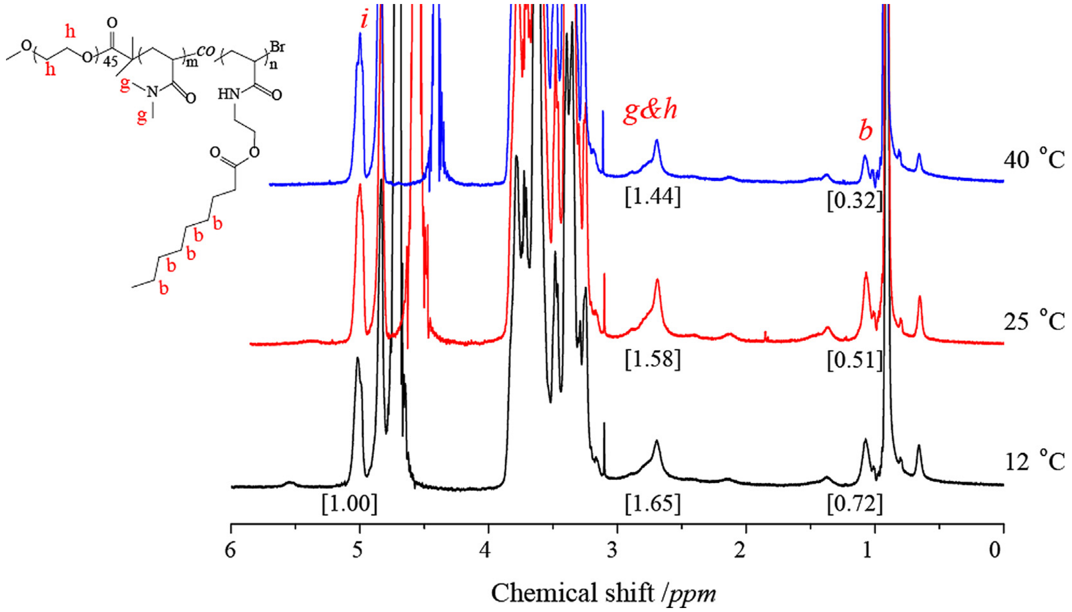

Fig. 2. ^{1}H NMR spectra of ED7E3 in D_2O (1 mg/mL) with 3 equivalents HPβCD, at 12 °C after incubation at 2 °C overnight; at 25 °C after incubation at 40 °C for 30 min; and at 40 °C. The data in brackets are integration of the peaks.

(DMA-AAEN)) block and a permanent hydrophilic poly(ethylene glycol) (PEG, Mn = 2 kg/mol) block were prepared by atom transfer radical copolymerization of *N,N*-dimethyl acrylamide (DMA) and hydroxyethyl acrylamide (HEAA) using a PEG macroinitiator[30,31] followed by post-polymerization modification with nonanoyl chloride to install the octyl alkyl side chains (Scheme 1, see ESI for detailed synthesis route and characterization data). The conversions and DPs of the resulted polymers were characterized by gas chromatography (GC), which determines the conversion of each monomer separately. Similar conversions of DMA and HEAA were always observed in different polymerization trials and different samples during polymerization, which suggested random structures of DMA-HEAA and DMA-AAEN blocks. The resulting copolymers were then named as EDxAy, with E, D and A representing EG, DMAA and AAEN respectively, while *x*/*y* represents the ratio of DMAA and AAEN.

The solubility of the copolymers was first investigated with and without the presence of hydroxypropylated β-cyclodextrin (HPβCD) (see Table S2). All the synthesized copolymers (see Table S1) were not soluble in pure water due to the relatively high content of hydrophobic octyl groups. However, with the presence of HPβCD, the copolymer ED7A3(Mn = 14.1 kDa, Đ = 1.43) with the lowest content of hydrophobic units, was found to become soluble when 2.5 equivalents of HPβCD were added relative to octyl group, which indicates that the presence of HPβCD can promote the dissolution of the polymer in water *via* host-guest complexation.[32] Note that it is not possible to determine the association constant as the system is not soluble with lower amounts of HPβCD.

The thermoresponsive behavior of ED7A3 in aqueous solution was first evaluated by dynamic light scattering (DLS) during heating and cooling of the polymer solution at a concentration of 1 mg/mL with the presence of 3 equivalents of HPβCD. Representative volume based size distributions at 30 °C, 38 °C and 44 °C are shown in Fig. 1. A double size-distribution was detected at 30 °C with a main distribution at around 2 nm in diameter (Fig. 1a). Considering the composition of the system, this small size distribution was initially assigned to the excess of HPβCD. However, DLS analysis of a HPβCD solution without polymer (HPβCD concentration was the same as the ED7A3-HPβCD system) did not show any significant scattering indicating that HPβCD could not have been detected during the characterization of the polymer-HPβCD system either. Hence, the distribution around 2 nm was assigned to individual ED7A3 chains complexed to HPβCD. The rather small size indicates that the polymer may self-collapse due to the hydrophobic interaction between parts of the alkyl chains (there are still short chains located outside of the HPβCD cavity) as confirmed by ^{1}H NMR of the system in D_2O (will be discussed later). Small aggregates were detected at ~38 °C as indicated by the size distribution at around 10 nm (diameter). Such small aggregates formed by block copolymers are usually ascribed to micelles. Further heating the sample to 40 °C induced the formation of larger nanoparticles with an average diameter of ~256 nm. To fully understand the double thermoresponsive behavior of the ED7A3-HPβCD system, the temperature dependent hydrodynamic diameter (D_h) of the solutions was determined (Fig. 1b, note that the intensity averaged diameters of the nanoparticles may be overestimated due to the presence of small portion of aggregates). With increasing temperature, the size of the nanoparticles in the system exhibited a sharp increasing from 36 °C to 38 °C due to the formation of aggregates, which indicates the first critical temperature (CT). The detected size smoothly increased upon further heating without sharp changes, hence the second CT was determined based on the comparison of the size distributions at various temperatures. It is found that at 43 °C the size distribution at ~14 nm disappears and the peak at about 300 nm became the only distribution, which indicates the second CT. In addition, the polydispersity (PDI) of the detected nanoparticles decreased upon heating and reached ~0.1 above 50 °C indicating the formation of defined aggregates.

The cooling process of ED7E3 solution (1 mg/mL) was also investigated with 3 equivalents of HPβCD, as shown in Fig. 1. Representative volume based hydrodynamic diameter (D_h) distributions at 40 °C, 35 °C and 2 °C were collected. Both large aggregates and micelles with main size distribution around 250 nm and 15 nm were detected at 40 °C and 35 °C, respectively, which is in accordance with the two types of aggregates observed upon heating. Unimers were not detected even at 2 °C, unless annealing the sample in the fridge (2 °C) for overnight. Such a big hysteresis was also observed for poly(2-oxazoline)s with nonyl side chains, where the alkyl groups were kinetically trapped in the precipitates.[29] In our case for ED7A3, the aggregation of the alkyl groups in the micelles was also believed to be the reason for the observed hysteresis. Temperature dependent DLS was also performed during cooling (Fig. 1d), revealing the morphology change from large aggregates to micelles at 35 °C, which is lower than the CT during heating indicating a slight hysteresis.

To confirm the double thermoresponsive behavior of ED7A3-HPβCD system, ^{1}H NMR spectra of the polymer solution were recorded at various temperatures in deuterated water (see Fig. 2). To quantitatively characterize the results, the resonance peak at ~2.6 ppm (protons from PEG and methyl groups of DMA, assigned as *g* and *h,* respectively, see Fig. S1 and Fig. S3–5) and ~1.1 ppm (protons from octyl group, assigned as b, see Fig. S1) were integrated using the peak at ~5.0 ppm as internal standard (protons from HPβCD, assigned as *i*). At 40 °C and 25 °C, the integrals from both *b* and $g + h$ were found to decrease in comparison with those at 12 °C, at which temperature the polymer was molecularly dissolved in D_2O and hence all signals are present in the expected integral ratios. As the PEG block is hydrophilic, the change on the integral of peak $g + h$ was ascribed to the chemical environment change of DMA residues due to the aggregation of polymer chains. Lower integrated values were found at 40 °C than at 25 °C, which can be ascribed to the less inhibited motion of DMA residues and octyl groups in micelles than large aggregates. It has been also noticed that the integration of octyl group was still underestimated at 12 °C in comparison with ^{1}H NMR of ED7A3 performed with $CDCl_3$ as solvent (the integration of peak at 1.1 ppm was about 0.44 and 0.58 with D_2O and $CDCl_3$ as solvent, respectively, if keeping the integration of $g + h$ as 1), which confirm our assumption that the polymers chains were still partially collapsed below the first critical temperature.

The morphologies of the assemblies were characterized by transmission electron microscopy (TEM), as shown in Fig. 3. The samples were first prepared by dropping ED7A3-HPβCD solution (at 50 °C, with 1 mg/mL ED7A3 and 3 equivalents of HPβCD) on carbon film coated copper grid (200 mesh) followed by evaporation of the water at 50 °C. Representative TEM images are shown in Fig. 3a and Fig. S6. Only small spherical nanoparticles with a diameter of ~6 nm were observed, which is significantly smaller than the D_h obtained by DLS of the system at the same temperature (~176 nm, see Fig. S7). It is, therefore, proposed that a morphology change from larger aggregates to micelles occurred during the evaporation of water while preparing the TEM sample. To confirm the micelle structure, *cryo*-TEM was then performed for ED7A3-HPβCD solution (at 50 °C, with 1 mg/mL ED7A3 and 3 equivalents of HPβCD, see Fig. 3b and Fig. S7) showing spherical nanoparticles with a diameter of about 50 nm, which confirmed the formation of larger aggregates. Note that the size determined by microscopy are smaller than D_h from DLS, as TEM only shows the size of the hydrophobic core of the sphere, while D_h is the size of the core and the hydrated shell.

The mechanism of the double thermoresponsive behavior and hierarchy self-assembling is not clear yet. However, we believe that the thermosensitive host-guest interaction between HPβCD and alkyl chains plays the key role. There are two possible thermoresponsive processes upon heating: the breaking of host-guest interaction between HPβCD and alkyl chains, or dehydration of the DMA segments and short PEG chains. Base on the characterization mentioned, it is still arbitrary to tell which mechanism is related to the two thermoresponsiveness of the HPCD/polymer system. Regarding the two self-assembling structures formed upon heating of the HPCD/polymer complex, it is certain that micelles stabilized by DMA segment and PEG chains was formed after the first CT. Upon further heating, the micelles start to aggregate due to the dehydration of PEG and DMA segments or the breaking of HPβCD/alkyl chains complex, leading to the aggregate of micelles forming multimicellar aggregates. Such micellar aggregation usually are coursed by the weak stabilization of the micelle shield, as have been observed by our previous research [33] and reports from other groups. [34–38] Based on the above discussion, a scheme of the two-step self-assembly behavior is proposed as shown in Scheme 1.

To show the possibility of tuning the CT's of the complex system, the thermoresponsive behavior of ED7E3 with 2.5 or 5 equivalents of HPβCD in aqueous solution has also been investigated (Figs. S9–S12). CT's were determined and are plotted in Fig. 4. With 5 equivalents of HPβCD, a similar double thermoresponsive behavior could be detected during heating of the sample, with the transition temperatures increased to 51 °C and 61 °C, respectively. During cooling of the system, the micelles to unimer transition was detected at 36 °C, which is ascribed to the high concentration of guest molecules enabling reformation of the polymer-host–guest complex. For the system with 2.5 equivalents HPβCD, the molecular dissolved state was not achieved even after incubation under ice/water bath for more than 10 h, which is due to the lower amount of host molecules. CT's for both first and second transitions increased smoothly with increasing HPβCD equivalents, which can be mainly ascribed to the high ratio of HPβCD/ octyl complex due to the high concentration of HPβCD. In addition, the high concentration of HPβCD may also change the solvent property and increases the solubility of the polymer.

Next, we investigated the influence of the type of host molecules on the double thermoresponsive behavior. Host-guest complex system with 2.5, 3 or 5 equivalents of hydroxypropyl-α-cyclodextrin (HPαCD) and ED7A3 at 1 mg/mL in water were then prepared and investigated by DLS during heating and cooling (Figs. S13–S18). CT's were determined and plotted in Fig. 4. All of the CT's based on HPαCD systems were found to be lower than ED7A3-HPβCD systems with the same concentrations of host molecules, which may be ascribed to weaker interactions between HPαCD and alkyl group compared to HPβCD.[39]

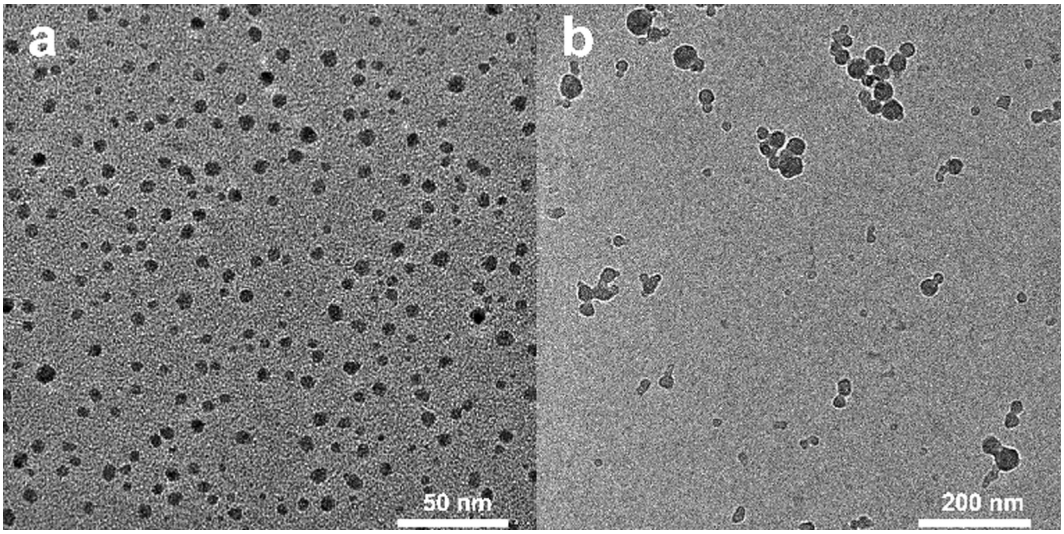

Fig. 3. Microscopy images of ED7A3 assemblies in aqueous solution (1 mg/mL) with the presence of 3 equivalents HPβCD, collected by (a) TEM and (b) *cryo*-TEM.

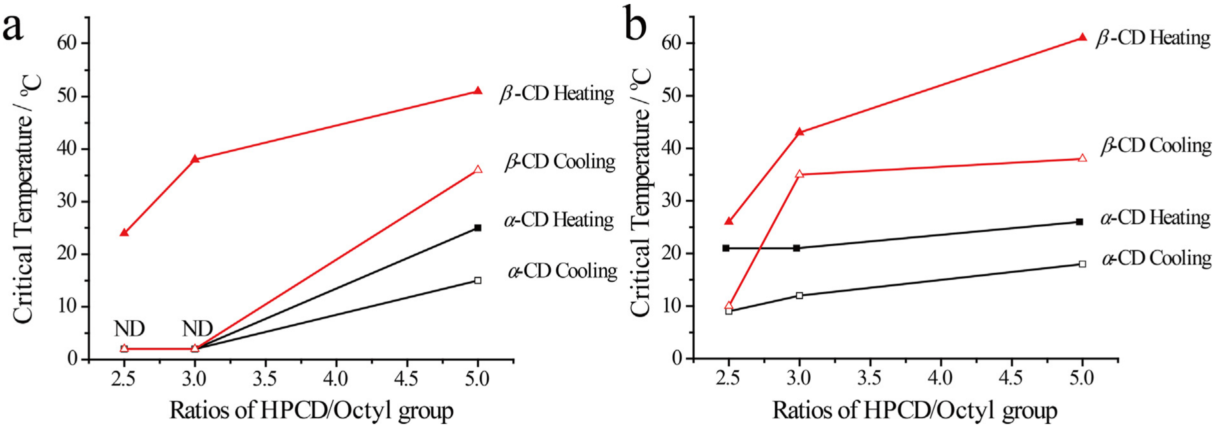

Fig. 4. Critical temperatures (CT's) of ED7A3 with HPβCD (red) and HPαCD (black) at (a) transitions between unimers and micelles; and (b) transitions between micelles and multimicellar aggregates. 'ND' represents not detected upon cooling to 2 °C. Lines are a guide for the eye.

Moreover, the complexation between HPαCD and PEG chain may also hinder the shield of alkyl chains via lowering the concentration of available host molecules. The above results indicate that the double thermoresponsive behavior of the ED7A3 can be well influenced within a wide temperature range.

3. Conclusions

In summary, we have designed and synthesized a new type of amphiphilic block copolymer PEG-*b*-P(DMA-AAEN) showing double thermoresponsive behavior and two-step hierarchical self-assembly in the presence of HPCD. The hydrophobic P(DMA-AAEN) block with octyl groups can be molecularly dissolved in water in presence of HPβCD due to the formation host–guest complexes. Upon heating of the solution, the aqueous solution of HPβCD/polymer showing a double thermoresponsive beahvior. Based on the characterization of DLS, ^{1}H NMR, TEM and *cryo*-TEM characterization, the two type of self-assembly structures were formed, i.e. micelles stabilized by PEG chains and DMA segments and multimicellar aggregates. We have also shown that such thermoresponsive behaviors can be influenced by varying the concentration and type of host molecules. The double thermoresponsive and hierarchy self-assembly behavior reported in this communication may provide a new strategy to design smart polymers, which may find broad application in the development of smart polymeric materials and devices.

CRediT authorship contribution statement

Yuchen Wei: Investigation, Writing - original draft. **Haohui Huo:** Investigation. **Chaobo Huang:** Writing - review & editing. **Qilu Zhang:** Conceptualization, Methodology, Writing - review & editing. **Richard Hoogenboom:** Writing - review & editing. **Feng Liu:** Resources, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eurpolymj.2020.109537.

References

[1] Q. Zhang, C. Weber, U.S. Schubert, R. Hoogenboom, Thermoresponsive polymers with lower critical solution temperature: from fundamental aspects and measuring techniques to recommended turbidimetry conditions, Mater. Horiz. 4 (2017) 109–116.
[2] D. Roy, W.L.A. Brooks, B.S. Sumerlin, New directions in thermoresponsive polymers, Chem. Soc. Rev. 42 (2013) 7214–7243.
[3] S. Agarwal, S. Jiang, Y. Chen, Progress in the field of water- and/or temperature-triggered polymer actuators, Macromol. Mater. Eng. 304 (2019) 1800548.
[4] L. Liu, H. Bakhshi, S. Jiang, H. Schmalz, S. Agarwal, Composite polymeric membranes with directionally embedded fibers for controlled dual actuation, Macromol. Rapid. Commun. 39 (2018) 1800082.
[5] A. Bordat, T. Boissenot, J. Nicolas, N. Tsapis, Thermoresponsive polymer nanocarriers for biomedical applications, Adv. Drug Deliver. Rev 138 (2019) 167–192.
[6] C. Zhao, Z. Ma, X.X. Zhu, Rational design of thermoresponsive polymers in aqueous solutions: a thermodynamics map, Prog. Polym. Sci. 90 (2019) 269–291.
[7] F. Lin, F. Cousin, J.-L. Putaux, B. Jean, Temperature-controlled star-shaped cellulose nanocrystal assemblies resulting from asymmetric polymer grafting, ACS Macro Lett. 8 (2019) 345–351.
[8] D. Wang, H. Huang, M. Zhou, H. Lu, J. Chen, Y.-T. Chang, J. Gao, Z. Chai, Y. Hu, A thermoresponsive nanocarrier for mitochondria-targeted drug delivery, Chem. Commun. 55 (2019) 4051–4054.
[9] A. Halperin, M. Kröger, F.M. Winnik, Poly(N-isopropylacrylamide) phase diagrams fifty years of research, Angew. Chem. Int. Ed. 54 (2015) 15342–15367.
[10] C. Li, Y. Ma, Z. Tian, Thermal switching of thermoresponsive polymer aqueous solutions, ACS Macro Lett. 7 (2018) 53–58.
[11] R. Hoogenboom, H. Schlaad, Thermoresponsive poly(2-oxazoline)s, polypeptoids, and polypeptides, Polym. Chem. 8 (2017) 24–40.
[12] R. Hoogenboom, H.M.L. Thijs, M.J.H.C. Jochems, B.M. van Lankvelt, M.W.M. Fijten, U.S. Schubert, Tuning the LCST of poly(2-oxazoline)s by varying composition and molecular weight: alternatives to poly(N-isopropylacrylamide)? Chem. Commun. 44 (2008) 5758–5760.
[13] J. Seuring, S. Agarwal, Polymers with upper critical solution temperature in aqueous solution: unexpected properties from known building blocks, ACS Macro Lett. 2 (2013) 597–600.
[14] M. Noh, S. Kang, Y. Mok, S.J. Choi, J. Park, J. Kingma, J.-H. Seo, Y. Lee, Upper critical solution temperature (UCST) phase transition of halide salts of branched polyethylenimine and methylated branched polyethylenimine in aqueous solutions, Chem. Commun. 52 (2016) 509–512.
[15] Q. Zhang, R. Hoogenboom, Polymers with upper critical solution temperature behavior in alcohol/water solvent mixtures, Prog. Polym. Sci. 48 (2015) 122–142.
[16] J. Seuring, S. Agarwal, Polymers with upper critical solution temperature in aqueous solution, Macromol. Rapid. Commun. 33 (2012) 1898–1920.
[17] R.B. Grubbs, Z. Sun, Shape-changing polymer assemblies, Chem. Soc. Rev. 42 (2013) 7436–7445.
[18] A.H. Gröschel, A. Walther, T.I. Löbling, F.H. Schacher, H. Schmalz, A.H.E. Müller, Guided hierarchical co-assembly of soft patchy nanoparticles, Nature 503 (2013) 247.
[19] M. Arotçaréna, B. Heise, S. Ishaya, A. Laschewsky, Switching the inside and the outside of aggregates of water-soluble block copolymers with double thermoresponsivity, J. Am. Chem. Soc. 124 (2002) 3787–3793.
[20] L. Makinen, D. Varadharajan, H. Tenhu, S. Hietala, Triple hydrophilic UCST-LCST block copolymers, Macromolecules 49 (2016) 986–993.

[21] X. Liang, F. Liu, V. Kozlovskaya, Z. Palchak, E. Kharlampieva, Thermoresponsive micelles from double LCST-poly(3-methyl-N-vinylcaprolactam) block copolymers for cancer therapy, ACS Macro Lett. 4 (2015) 308–311.

[22] J.V.M. Weaver, S.P. Armes, V. Butun, Synthesis and aqueous solution properties of a well-defined thermo-responsive schizophrenic diblock copolymer, Chem. Commun. 18 (2002) 2122–2123.

[23] F. Kaefer, F. Liu, U. Stahlschmid, V. Jerome, R. Freitag, M. Karg, S. Agarwal, LCST and UCST in one: double thermoresponsive behavior of block copolymers of poly(ethylene glycol) and poly(acrylamide-co-acrylonitrile), Langmuir 31 (2015) 8940–8946.

[24] H. Zhang, J. Zhang, W. Dai, Y. Zhao, Facile synthesis of thermo-, pH-, CO2- and oxidation-responsive poly(amido thioether)s with tunable LCST and UCST behaviors, Polym. Chem. 8 (2017) 5749–5760.

[25] X. Jiang, C. Feng, G. Lu, X. Huang, Thermoresponsive homopolymer tunable by pH and CO2, ACS Macro Lett. 3 (2014) 1121–1125.

[26] Q. Zhang, F. Tosi, S. Ugduler, S. Maji, R. Hoogenboom, Tuning the LCST and UCST thermoresponsive behavior of poly(N, N-dimethylaminoethyl methacrylate) by electrostatic interactions with trivalent metal hexacyano anions and copolymerization, Macromol. Rapid. Commun. 36 (2015) 633–639.

[27] F.A. Plamper, A. Schmalz, A.H.E. Müller, Tuning the thermoresponsiveness of weak polyelectrolytes by pH and light: lower and upper critical-solution temperature of poly(N, N-dimethylaminoethyl methacrylate), J. Am. Chem. Soc. 129 (2007) 14538–14539.

[28] B. Peng, N. Grishkewich, Z. Yao, X. Han, H. Liu, K.C. Tam, Self-Assembly behavior of thermoresponsive oligo(ethylene glycol) methacrylates random copolymer, ACS Macro Lett. 1 (2012) 632–635.

[29] V.R. de la Rosa, R. Hoogenboom, Solution polymeric optical temperature sensors with long-term memory function powered by supramolecular chemistry, Chem. Eur. J. 21 (2015) 1302–1311.

[30] K. Matyjaszewski, N.V. Tsarevsky, Macromolecular engineering by atom transfer radical polymerization, J. Am. Chem. Soc. 136 (2014) 6513–6533.

[31] K. Matyjaszewski, Advanced materials by atom transfer radical polymerization, Adv. Mater. 30 (2018).

[32] V.R. de la Rosa, P. Woisel, R. Hoogenboom, Supramolecular control over thermoresponsive polymers, Mater. Today 19 (2016) 44–55.

[33] H. Huo, T. Tan, L. Gou, L. Chen, L. Zhang, Q. Zhang, F. Liu, Single-chain tethered nanoparticles with tunable softness: scalable synthesis and unique self-assembly behavior, Polym. Chem. 10 (2019) 6183–6190.

[34] S.J. Holder, N.A.J.M. Sommerdijk, New micellar morphologies from amphiphilic block copolymers: disks, toroids and bicontinuous micelles, Polym. Chem. 2 (2011) 1018–1028.

[35] L. Zhang, J. Su, W. Zhang, M. Ding, X. Chen, Q. Wu, Temperature-sensitive phase transition of dendritic polyethylene amphiphiles with core−shell architecture revealed by a rayleigh scattering technique, Langmuir 26 (2010) 5801–5807.

[36] H. Hong, Y. Mai, Y. Zhou, D. Yan, J. Cui, Self-assembly of large multimolecular micelles from hyperbranched star copolymers, Macromol. Rapid. Commun. 28 (2007) 591–596.

[37] B. Trzebicka, N. Koseva, V. Mitova, A. Dworak, Organization of poly(2-ethyl-2-oxazoline)-block-poly(2-phenyl-2-oxazoline) copolymers in water solution, Polymer 51 (2010) 2486–2493.

[38] C. Allen, Y. Yu, D. Maysinger, A. Eisenberg, Polycaprolactone-b-poly(ethylene oxide) block copolymer micelles as a novel drug delivery vehicle for neurotrophic agents FK506 and L-685,818, Bioconjugate Chem. 9 (1998) 564–572.

[39] M.V. Rekharsky, Y. Inoue, Complexation thermodynamics of cyclodextrins, Chem. Rev. 98 (1998) 1875–1918.