

Controlled thermoreversible transfer of poly(oxazoline) micelles between an ionic liquid and water†

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Poly(2-nonyl-2-oxazoline-*block*-2-ethyl-2-oxazoline) block copolymer micelles were investigated as an alternative system to the approach proposed by He and Lodge (Y. He and T. P. Lodge, *J. Am. Chem. Soc.*, 2006, 128, 12666) for the thermoreversible transfer of micelles between a hydrophobic ionic liquid phase and an aqueous phase; this work describes the possibility of thermally triggering and controlling this process.

The use of ionic liquids (ILs), substances composed entirely of ions which are in the liquid state below 100 °C, as potential and novel replacements of volatile organic solvents in various chemical and physical processes, has been a topic of great interest in recent years.¹ This is mainly due to the intriguing properties of ILs, such as their capability to dissolve diverse substances,² their special surface active properties,³ as well as their potentially “environmentally-friendly” characteristics (*e.g.*, negligible vapor pressure, negligible flammability, and stability over a broad temperature range).^{1a,b} Unlike conventional solvents, the properties of ILs can be tuned by varying the composition of their ions.^{1a,b} ILs have also been used in combination with polymers to prepare a wide range of materials with novel properties,^{2b} and as reaction media for polymer synthesis.⁴ Thus, polymerizations have been performed using ILs as reaction media in heterogeneous^{3b,5} and homogeneous⁶ processes implying that ILs can act as thermodynamically bad and good solvents for the respective polymers. Consequently, the micellization of block copolymers in ILs has been considered: when a block copolymer with incompatible blocks is dissolved in an IL that is a thermodynamically good solvent for one of the blocks and a bad solvent for the other block, the copolymer chains associate to form micelles.⁷ Moreover, the thermoreversible transfer of the micelles between two different phases (IL and aqueous phases) has been achieved without

perturbing the micellar structures.⁸ In this regard, the thermoreversible transport of micelles formed by poly(1,2-butadiene-*block*-ethylene glycol) (PB-*b*-PEG) block copolymers between 1-butyl-3-methylimidazolium hexafluorophosphate (BMI-PF₆) (a hydrophobic IL) and water has been recently described.⁸ Indeed, PB-*b*-PEG block copolymer micelles originally prepared in BMI-PF₆ migrate to an aqueous phase at room temperature (rt) (water and BMI-PF₆ form a two phase system) due to the fact that PEG chains show more affinity for the aqueous phase than for the IL phase at these conditions. However, when this biphasic system is heated at temperatures higher than 70 °C, the micelles return to the IL phase as a consequence of the well-known lower critical solution temperature (LCST) phenomenon observed for PEG chains.⁹ The LCST behavior of PEG in water provokes the rupture of the hydrogen bonds between the ethylene glycol units and water molecules; thereafter the coalescence of the micelles in the aqueous phase occurs due to the fact that they are not stabilized by their corona (PEG block) any longer. At this stage, the micelles are precipitated in the aqueous phase and transferred back into the IL phase to complete the thermoreversible cycle. It is thought that this kind of stimuli-responsive multi-phase system might find important applications, for example, in micellar reactions¹⁰ where chemical micelles could be reversibly transported from one phase to another and recovered after accomplishing specific tasks.¹¹ A special emphasis was made on the peculiarity of the aforementioned micellar system because it relies on the remote possibility of finding a polymer (PEG) that is nearly equally soluble in two immiscible solvents of a completely different nature (BMI-PF₆ and water).

However, a recent publication describes the homogeneous synthesis of poly(2-ethyl-2-oxazoline) (PEtOx) in the hydrophobic IL BMI-PF₆ as well as the isolation of the polymer by an extraction process with water.^{6b} In that work, it was demonstrated that the PEtOx has more affinity for water than for BMI-PF₆ at rt. Hence, PEtOx originally synthesized in BMI-PF₆ could be successfully extracted into an aqueous phase, resulting in a biphasic system with an aqueous upper phase containing the extracted polymer while the lower phase consists of polymer-free IL BMI-PF₆. These findings^{6b} suggest that amphiphilic block copolymers containing a PEtOx block might show a similar phase transfer behavior as described before for amphiphilic block copolymers with PEG blocks.⁸ Based on these considerations, this contribution demonstrates that poly(2-nonyl-2-oxazoline-*block*-2-ethyl-2-oxazoline)¹² (PNonOx-*b*-PEtOx) block copolymers self-assemble into nanostructures (“micelles”)¹³ in

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Table 1 Molecular characteristics of the investigated block copolymer systems in BMI-PF₆. Sub-indices indicate the average number of monomer units incorporated into each block which were estimated by GPC in combination with ¹H NMR spectroscopy; hence the average molecular weights (M_n) and composition of the block copolymers can be obtained (see ESI†)

Sample	Block copolymer	M_n /kDa
M1	PNonOx ₂₀ - <i>b</i> -PEtOx ₈₀	11.9
M2	PNonOx ₄₀ - <i>b</i> -PEtOx ₆₀	13.8
M3	PNonOx ₅₀ - <i>b</i> -PEtOx ₅₀	14.8
M4	PNonOx ₆₀ - <i>b</i> -PEtOx ₄₀	15.8
M5	PNonOx ₈₀ - <i>b</i> -PEtOx ₂₀	17.8

the presence of BMI-PF₆ and that they also show a behavior similar to the thermoreversible phase transfer of micelles described above between BMI-PF₆ and water.⁸ Moreover, the phase transfer of the nanostructures was also investigated by turbidity measurements, which demonstrated that the process is fully reversible and that it can be selectively triggered and controlled.

For the purpose of this contribution a block copolymer library of PNonOx-*b*-PEtOx¹² with a constant total degree of polymerization and variable block copolymer composition has been utilized to prepare self-assembled nanostructures in BMI-PF₆, which acts as a thermodynamically good solvent for the PEtOx block and as a bad solvent for the PNonOx block as reported elsewhere^{6b,7c} (or observed in this study). Table 1 summarizes the molecular characteristics of the investigated block copolymer systems in BMI-PF₆. The used experimental procedures are described in the ESI.†

Fig. 1 displays images of the thermoreversible transfer phenomenon between BMI-PF₆ and an aqueous phase of nanostructures formed by selected PNonOx-*b*-PEtOx block copolymers of Table 1, while in Fig. 2 the results of the turbidity measurements (% transmittance) correlated with temperature for the two-phase system formed by sample M4 (Table 1) are shown. The thermoreversible phase transfer process of the nanostructures of Fig. 1 is quantitatively displayed in Fig. 2. Fig. 2a shows that at the onset of the measurements at 25 °C, the transmittance in the IL phase is close to 100% indicating the absence of nanostructures (the turbidity sensor is located at the IL phase (lower phase in Fig. 1)). This means that, after a considerable period of time at rt (at least 3 days before performing the measurements of Fig. 2), the biphasic system

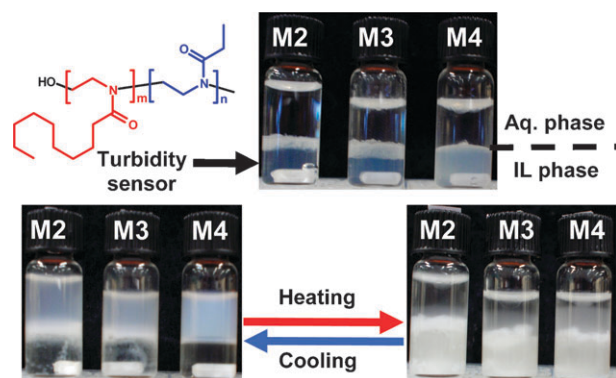


Fig. 1 Overview of the thermoreversible phase transfer of block copolymer nanostructures between an aqueous phase and a hydrophobic IL phase (BMI-PF₆). This phenomenon was investigated by turbidity measurements. M2–M4 correspond to nanostructures formed by PNonOx-*b*-PEtOx block copolymers (Table 1).

has reached a thermodynamic equilibrium, and the nanostructures are only present in the aqueous phase. The aqueous phase is a cloudy dispersion at 25 °C due to the presence of the nanostructures, whereas the IL phase is almost transparent at 25 °C due to the absence of the nanostructures (Fig. 1). Thereafter, as soon as the temperature is increased up to 95 °C (at a rate of 5 °C min⁻¹), the transmittance in the IL phase rapidly decreases to 0%. This corresponds to the situation where the nanostructures have migrated to the IL phase due to the LCST behavior shown by the PEtOx¹⁴ blocks in the investigated systems. At this condition (95 °C), the IL phase becomes cloudy while the aqueous solution, now free of nanostructures, becomes transparent (Fig. 1). According to the aforementioned transfer mechanism, the nanostructures must eventually return to the aqueous phase upon cooling the system below the LCST of PEtOx (60 °C). However, this process is rather slow and can take a considerable period of time to reach the new equilibrium state as shown in Fig. 2a, where after the first heating-cooling cycle the system is kept at 25 °C for 30 min and no significant increase in the transmittance is revealed, confirming that the nanostructures are still present in the IL phase. It was observed that when the system is kept at 25 °C long enough, from 3 to 5 days, the equilibrium state is eventually reached and the nanostructures are transferred back to the aqueous phase. Nevertheless, it was found that the transfer of the

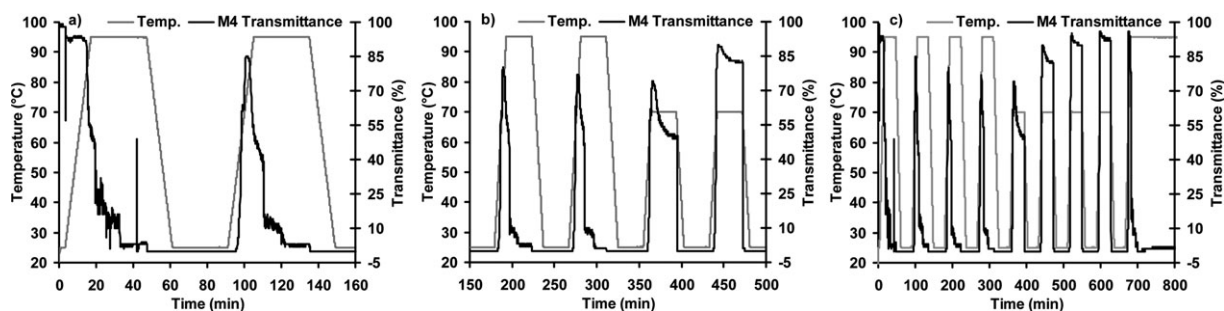


Fig. 2 Thermoreversible phase transfer experiments of PNonOx-*b*-PEtOx block copolymer nanostructures between an aqueous phase and a hydrophobic IL phase (BMI-PF₆). Turbidity measurements (as functioned by light transmission) are plotted as a function of temperature and time for the IL phase (lower phase in the systems shown in Fig. 1) of sample M4 (Table 1). (a) and (b) are close-ups of (c), whereas (b) is the continuation in time of (a).

nanostructures from the IL phase to the aqueous phase can be immediately achieved and triggered by supplying heat to the system. For instance in Fig. 2a, it is observed that after the 30 min period at 25 °C, the system was again heated up to 95 °C causing a sudden increase in the transmittance of the IL phase up to 85%, and immediately followed by a decrease to 0% when the system is kept at 95 °C. This observation is confirmed in further heating-cooling cycles as revealed in Fig. 2b and c.

In Fig. 2b, it is also observed that when the system is exposed to cycles between 70 and 25 °C, the phase transfer of the nanostructures differs from the case of heating-cooling cycles between 95 and 25 °C. Fig. 2b reveals that when the system is heated only up to 70 °C and kept at this condition for 30 min, the transmittance only slightly decreases and does not completely drop to 0% within this 30 min period. This observation suggests that the transfer of the nanostructures from the aqueous phase to the IL phase at 70 °C considerably slows down (or does not occur at the investigated conditions) when compared to the case at 95 °C. After 30 min at 70 °C, the system is then subjected to a cooling process and it is observed that the transmittance drops immediately to 0%, which indicates that the nanostructures were transferred from the aqueous to the IL phase. This suggests that the transfer of the nanostructures from the aqueous to the IL phase at this condition (70 °C) can also be achieved and triggered by removing heat from the system. It is thought that this effect may be related to the fact that when the temperature of the system is close to the LCST value of the hydrophilic corona, LCST of PEtOx (60 °C), the nanostructures have equal preference for one or the other phase, which allows that the phase transfer of the nanostructures can be triggered by sudden changes in temperature. Several repetitions of the investigated heating-cooling cycles confirmed the reproducibility of the described observations as fully displayed in Fig. 2c. Additional measurements also demonstrated that the variation of the heating-cooling rates from 5 to 1 °C min⁻¹ during the phase transfer experiments had almost no influence on the aforementioned results. The stirring speed during the experiments was also found to be an important factor for the phase transfer process. For instance, higher stirring speeds cause a faster phase transfer of the nanostructures. Even though the obtained results provide a good insight into the analyzed systems, it is clear that the investigated phenomenon is a very complex process influenced by many variables, which must be further investigated to fully understand these systems. For example, the diffusion processes of the nanostructures in each phase and at the interface, and the kinetic processes of formation and rupture of the hydrogen bonds related to the LCST behavior of the investigated polymers, might be crucial aspects to understand the transfer process. Furthermore, this phenomenon will also be strongly affected by many other variables (*e.g.*, viscosity of the phases, interfacial tension, temperature, molecular properties of the block copolymers, *etc.*)

The self-assembly of the PNonOx-*b*-PEtOx block copolymers of Table 1 into nanostructures in the presence of the hydrophilic IL 1-butyl-3-methylimidazolium trifluoromethanesulfonate was additionally investigated by dynamic light scattering and compared to the case of the hydrophobic IL BMI-PF₆. The results revealed that the nature of the IL can significantly influence the size of the nanostructures as well (see ESI†).

In this work PNonOx-*b*-PEtOx block copolymers were proposed as a new system for the thermoreversible phase transfer of block copolymer nanostructures between the hydrophobic IL BMI-PF₆ and water. It was found that the transfer of the nanostructures between the two phases is a fully reversible process and can be triggered (or controlled) by heating or cooling the system. This work demonstrates the existence of at least one alternative polymer (PEtOx) that shows characteristics similar to the (PB-*b*-PEG) system,⁸ which was thought to be rather unusual because the PEG block shows nearly equal solution properties in two solvents of completely different nature. Nevertheless, it is known that other water soluble and non-ionic polymers (*e.g.*, poly(*N*-isopropylacrylamide))^{9a} have a LCST which may show a similar behavior to the cases described herein. Future investigations on this topic may be focused on block copolymer nanostructures in which the corona is formed by other polymers with a LCST to investigate whether other systems can show a similar behavior to the one addressed in this work. In addition, the search for other solvents of different nature to form multi-phase systems with the approach presented herein might also be considered.

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- The self-assembled nanostructures investigated herein had relatively large sizes as measured by dynamic light scattering (see ESI†). One may estimate that the size of self-assembled core-shell micelles even with fully stretched macromolecules will not match the sizes of the nanostructures of this work (at least not in the case of BMI-PF₆; see Table A in ESI†). For this reason and for scientific formality the term “nanostructures” is preferred instead of the term “micelles” throughout the discussion of the results of this contribution.
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