Aust. J. Chem. 2012, 65, 91–94 http://dx.doi.org/10.1071/CH11378

Full Paper

Key Factors to Prepare Polyelectrolytes Showing Temperature-Sensitive Lower Critical Solution Temperature-type Phase Transitions in Water

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Tetrabutylphosphonium styrenesulfonate and its homopolymer showed a lower critical solution temperature-type phase transition in water. As the hydrophobicity of these monomeric and polymeric salts affects phase behaviour, the phase transition temperature of the polyelectrolyte was changed by the introduction of monomers having different alkyl chain length on the phosphonium cations.

Manuscript received: 25 September 2011. Manuscript accepted: 3 November 2011. Published online: 30 November 2011.

The solubility of molecules generally increases with heating of the solution. In contrast to this, some polymers are known to be miscible with certain solvents on cooling but become insoluble on heating. This unusual temperature-dependent phase behaviour is classified as a lower critical solution temperature (LCST)-type phase transition. Some polymers have been found to undergo an LCST-type phase transition with water, such as poly(*N*-isopropylacrylamide) (PNIPAAm),^[1,2] poly(ethylene glycol),^[3] elastin-like polypeptides,^[4–6] poly(2-oxazoline),^[7] and their copolymers.^[8] These polymers showing LCST-type phase transition have been designated as 'intelligent polymers', and have been applied in many areas, notably bioscience,^[9] including in drug delivery systems,^[10] cell cultures,^[11,12] magnetic colloids,^[13] and bioseparation.^[14] The LCST-type phase transition in polymer/water mixtures has hitherto been observed only for non-ionic polymers. Because of hydrophobic interaction being the driving force, the LCST-type phase transition has not been seen in hydrophilic and charged homopolymers. To introduce the capability for LCST-type phase transition into polyelectrolytes, copolymerization of ionic monomers and NIPAAm^[15–20] has generally been used. It has been reported to be effective to simply mix polyelectrolytes and the polymers mentioned above^[21] or others such as poly(vinyl alcohol).^[22] Ritter et al. reported that hydrophobic poly(1-butyl-3-vinylimidazolium bis(trifluoromethanesulfonyl)imide) exhibited pseudo-LCST behaviour with water in the presence of cyclodextrin (CD) by the formation of host-guest complexes between CD and the bis(trifluoromethanesulfonyl)imide anion.^[23] There has been no report of any authentic LCST-type phase transition in mixtures of polyelectrolytes and water. Novel and easily available polyelectrolytes showing a temperaturesensitive LCST-type phase transition will open new and widely varying interesting and advanced applications, such as dynamic control of the affinity between the polyelectrolytes and other polymers including biopolymers.

This decade, our group has designed several ionic liquids (ILs); these are organic salts having melting points below 100°C or preferably below room temperature.^[24,25] ILs have unique properties as liquids, and some of them behave totally differently from molecular liquids.^[26-28] As there is a structural diversity of available ions, it is possible to control their physicochemical properties through suitable design of the component ions. Our group has prepared ILs derived from amino acids (AAILs).^[29,30] Relatively hydrophobic AAILs were prepared by introducing a trifluoromethylsulfonyl group on the amino group^[31] and coupling with a tetrabutylphosphonium cation ($[P_{4444}]^+$). These ILs underwent a clear phase separation with water at room temperature, but they turned miscible on cooling by only a few degrees. On heating, the phase separation again took place; this phase transition was reversibly controlled by changing the temperature by only a few degrees. Reversible LCST-type phase behaviour of IL/water mixtures has not been reported previously. We recently analysed the phase behaviour of many ILs after mixing with water, and found that a few ILs exhibited a temperature-sensitive LCST-type phase transition.^[32]

We have previously reported some polyelectrolytes derived from ILs.^[33,34] These IL-based polyelectrolytes are readily prepared from IL monomers having polymerizable groups on the component ions. The resulting polyelectrolytes are characterized by their low glass transition temperature originated in the starting ILs. Our previous study strongly suggests that the polymerized ILs retain the basic properties of the corresponding monomeric ILs. According to our previous work, it should not be difficult to design polymerized ILs that undergo an LCSTtype phase transition with water. In the present study, we prepared IL monomers that undergo an LCST-type phase transition on mixing with water based on the relation between ion structure and the monomer's phase behaviour. Then, the IL-based polyelectrolytes were prepared by the polymerization of these IL monomers. Preliminarily, an IL composed of the



Scheme 1. Preparation of [P_{444n}][SS] and its polymers.

 $[P_{4444}]^+$ cation and tosylate anion ($[Tos]^-$) was found to undergo the LCST-type phase transition with water.^[32] We then selected styrenesulfonate ($[SS]^-$) as a polymerizable anion. As a counter-cation, we used two different phosphonium cations: $[P_{4444}]^+$ and $[P_{4446}]^+$ (Scheme 1). These ILs were prepared by anion exchange reaction of $[P_{4444}]Cl$ or $[P_{4446}]Br$ with sodium styrenesulfonate (Na[SS]). Thus prepared $[P_{4444}][SS]$ and $[P_{4446}]$ [SS] were obtained as a white solid and a clear viscous liquid, respectively. Direct neutralization of $[P_{4444}]OH$ with styrenesulfonic acid is also a convenient method to prepare target IL monomers. However, there was a fear of thermal polymerization during this process. We therefore did not use this step to avoid unexpected polymerization.

Next, we checked the phase behaviour of the IL monomers thus prepared. These were mixed with an equal weight of water (50 wt-%). [P4446][SS] was scarcely soluble in water, and no homogeneous phase was obtained even after heating or cooling. In contrast, [P₄₄₄₄][SS] formed a homogeneous mixture with water at low temperature. On gentle heating, a clear solution of this mixture became turbid and phase-separated. The phase transition temperature (T_c) of $[P_{4444}][SS]$ was a function of the amount of water added (see Fig. S1 in the Accessory Publication). The $T_{\rm c}$ was determined as the cloud point during heating of the homogeneous mixed solution. As shown in Fig. S1, the phase diagram for the [P₄₄₄₄][SS]/water mixture is a typical concave curve. When [P4444][SS] was mixed with an equal weight of water, the T_c of the mixture was 34°C. This value was much lower than that of the [P₄₄₄₄][Tos]/water mixture (56°C). It is not surprising that the introduction of the vinyl group in the anion has caused considerable change in the phase behaviour, because the LCST behaviour is affected by a subtle balance of hydrophobicity and hydrophilicity of ILs.[32]

Both [P₄₄₄₄][SS] and [P₄₄₄₆][SS] were polymerized by the suspension polymerization method (Scheme 1). The ILs were mixed with 1.0 mol-% of α, α' -azobis(isobutyronitrile) (AIBN), and the mixtures were suspended in degassed water. The solutions were stirred and heated at 80°C under an N2 atmosphere to start radical polymerization of the ILs, and the solutions were kept at 80°C for 3 h. After removal of water by evaporation, the products were dissolved in chloroform. The resulting solutions were then poured into hexane under vigorous stirring. The precipitates were collected and washed with hexane several times and then dried under vacuum at 60°C for 24 h. Both $poly([P_{4444}][SS])$ and $poly([P_{4446}][SS])$ were obtained as a white powder. The amount of monomers remaining in these solid samples was confirmed to be zero by attenuated total reflectance (ATR)-FTIR measurement (JASCO FT/IR 4200, ATR PRO410-S). Two typical bands at 1629 and 989 cm⁻¹ representing carbon–carbon double bonds disappeared completely in the solid samples (see Accessory

Publication, Figs S2 and S3). Complete polymerization was also confirmed by ¹H NMR measurement (JEOL ECX-400, 400 MHz). No signal for vinyl groups at 5.2 or 5.7 ppm was found in these polymers (see Accessory Publication, Figs S5 and S6).

We then analysed the phase behaviour of these polyelectrolytes after mixing them with pure water. Poly([P₄₄₄₆][SS]) was insoluble in water, and no phase transition was found in the mixture over the whole temperature range analysed. However, 10 wt-% poly([P₄₄₄₄][SS]) dissolved homogeneously in water at 25°C. On heating, the solution became turbid at 57°C. This turbid suspension became transparent again on cooling. It follows that poly([P₄₄₄₄][SS]) undergoes a reversible LCST-type phase transition after mixing with water as the corresponding monomer did. The transition temperature of the poly([P₄₄₄₄][SS]) in an aqueous phase greatly depended on the mixing ratio, just like the case for the aqueous solution of monomers. The T_c was 40 and 57°C for monomer and polymer (both containing 90 wt-% water). This certainly pointed out that the $T_{\rm c}$ of this polymer should be a function of the average molecular weight of the poly(IL). In spite of little data, it should be mentioned here that the increase in the average molecular weight of the polymers would raise the $T_{\rm c}$ of the mixture with the same amount of water.

The turbidity of an aqueous solution containing 10 wt-% of poly([P₄₄₄₄][SS]) was analysed by visible-light transmittance measurement (at 600 nm, Shimadzu UV-2550), with the solution temperature controlled with a water bath. The temperature was monitored with a thermocouple directly inserted into the solution. The phase transition temperature of the solution was evaluated as the temperature at which a transmittance of the mixture decreased to 90% during heating. On heating, the transmittance of the [P4444][SS]/water mixture dropped to 90% at 57°C (Fig. 1, black solid line). The transmittance of the solution decreased sharply on heating, and reached less than 1 % at 59°C. The turbid solution became transparent again on cooling (Fig. 1, black dotted line). As shown in Fig. 1, there is a small hysteresis observed. The transmittance of the solution increased sharply at 58°C, and the solution became transparent at 56°C. The LCST-type phase transition of the aqueous solution containing 10 wt-% poly([P4444][SS]) was controlled reversibly by a small change in temperature between 56 and 59°C. This very sharp transition found in this polyelectrolyte system will be applied for many fields.

We have already reported that the T_c of the IL/water mixtures is accurately and continuously controllable by mixing ILs having different hydrophobicity.^[32] When a more hydrophobic IL was added to the solution, the transition temperature fell. Based on these results, we expected that the T_c of the poly([P₄₄₄₄][SS])/water mixture would also be controlled by



Fig. 1. Turbidity change of an aqueous solutions containing 10 wt-% poly($[P_{4444}][SS]$) (black line) and poly($[P_{4444}][SS]_{0.7}$ -*co*- $[P_{4446}][SS]_{0.3}$; molar ratio of $[P_{4444}][SS]$ to $[P_{4446}][SS]$ was 7.0 to 3.0) (blue line); solid line: heating process, dotted line: cooling process.

adding a more hydrophobic IL into the polymer unit. We then prepared a copolymer containing both [P₄₄₄₄][SS] and [P₄₄₄₆][SS] (molar ratio of $[P_{4444}][SS]$ to $[P_{4446}][SS]$ was 7.0:3.0) by the same procedure as that for poly([P₄₄₄₄][SS]) (Scheme 1). The resulting poly([P₄₄₄₄][SS]_{0.7}-co-[P₄₄₄₆][SS]_{0.3}) was obtained as a white solid, and no residual monomer was found in the product (Figs S4 and S7, Accessory Publication). As expected, the T_c for this poly([P₄₄₄₄][SS]_{0.7}-co-[P₄₄₄₆][SS]_{0.3}) was lower (39°C) than that of poly([P₄₄₄₄][SS]) (Fig. 1, blue line). These results clearly show that the phase behaviour of the copolymer is controlled by the monomer ratio. These copolymerized poly([P444n][SS])/water mixtures have the capacity to widen the application of polyelectrolytes as novel temperatureresponsive polymers with a capability to control the hydration state of the polyelectrolytes by a small temperature change. It should be noted here that the hydrophobic and large cations are not always satisfactory for this purpose, but moderate hydrophobicity of the 'ion pair' is important.^[32]

In conclusion, we have prepared phosphonium styrenesulfonate-type ILs, $[P_{4444}][SS]$, which were confirmed to undergo an LCST-type phase transition after mixing with water. This LCST-type phase behaviour was maintained after polymerizing the $[P_{4444}][SS]$. The transition temperature of the mixture with water was dramatically lowered by the copolymerization of $[P_{4444}][SS]$ with more hydrophobic $[P_{4446}][SS]$. Hydrophobicity is the essential factor to control the LCST-type phase behaviour of IL-based polyelectrolytes.

Experimental

Synthesis of ILs

An aqueous solution of [P₄₄₄₄]OH (Hokko Chemical Industry Co.) was neutralized with hydrochloric acid in order to prepare [P₄₄₄₄]Cl. Next, [P₄₄₄₄]Cl or [P₄₄₄₆]Br (Hokko Chemical Industry Co.) was dissolved in water, and a slight excess of Na[SS] (Tokyo Chemical Industry Co.) was added to the solution. This solution was stirred for 24 h at room temperature. The product was extracted with dichloromethane, and the dichloromethane layer was washed repeatedly with water. The washed dichloromethane layer was evaporated, and residual liquid was

removed under vacuum for 24 h at room temperature. The structural characterization of $[P_{4444}][SS]$ and $[P_{4446}][SS]$ is summarized in the Accessory Publication.

Accessory Publication

The Accessory Publication contains the structural characterization of prepared ILs, phase diagram of the $[P_{4444}][SS]$ /water mixture, and ATR-FTIR spectra and ¹H NMR spectra for both $[P_{444n}][SS]$ and poly($[P_{444n}][SS]$).

Acknowledgement

This study was supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (no. 21225007).

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