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Upper critical solution temperature (UCST) phase transition of halide salts of branched polyethylenimine and methylated branched polyethylenimine in aqueous solutions

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The upper critical solution temperature (UCST) phase transition of halide salts of branched polyethylenimine (PEI) and methylated branched polyethylenimine (MPEI) is first reported in aqueous solutions. In particular, iodide counter-ions can introduce the UCST property in MPEI. The importance of the counter-ion composition of MPEI for UCST transition is discussed in detail.

Polymers with temperature responsiveness have been extensively researched in past decades. The temperature-responsive phase transition arises from different interactions between polymer and solvent molecules according to temperature variation. In a lower critical solution temperature (LCST) mixture, a polymer is miscible with a solvent below a certain temperature, but it is abruptly phase-separated above that temperature. On the other hand, an upper critical solution temperature (UCST) polymer-solvent mixture exhibits phase separation below the phase transition temperature. In particular, such phenomena in aqueous mixtures have been used in various fields, including hydrogels [1], drug delivery [2], chromatography [3], water purification [4], and optical devices [5].

In many cases, UCST phase transition occurs when solute-solute or solvent-solvent interactions dominate the solute-solvent interaction to generate the positive enthalpy of mixing ($\Delta H_m > 0$), unlike LCST phase transitions, which are more dependent upon the negative entropy of mixing ($\Delta S_m < 0$) due to the strong solute-solvent interaction [6]. In aqueous solution, examples of UCST polymers have been reported less frequently than those of LCST polymers, partially due to the characteristic strong interaction between polymers and water molecules with strong polarity and hydrogen-bonding capability [7]. Some selective polymers with hydrogen-bond-forming residues, such as urea [8] and amide [9], or zwitterion residues, such as sulfopropyl ammonium [10] and sulfopropyl imidazolium [11], exhibit UCST properties in water because the strong polymer-polymer interaction can overcome the polymer-water interaction to generate positive $\Delta H_m$. It was also reported that complex coacervate micelles composed of oppositely charged polymeric ions showed UCST-like behaviour in aqueous solutions [12].

Because the strong electrostatic interaction between polymer residues can induce UCST phase transition, we hypothesized that simple polymer-monomeric ion salts, not zwitterionic polymers or oppositely charged polymeric ion-based coacervates, could also exhibit a similar transition in aqueous solution. Of course, a separate monomeric ionic salt has a larger positive statistical $\Delta S_m$ due to a larger increase of the degree of freedom during the solvation process compared to the corresponding zwitterion or polymer-polymer ionic salt. Because the phase transition occurs when the Gibbs free energy of mixing ($\Delta G_m = \Delta H_m - T\Delta S_m$) becomes zero at a certain polymer-ion salt/water composition [13], the phase transition temperature ($T = \Delta H_m / \Delta S_m$) of the separate polymer-monomeric ionic salt might be lower than that of the zwitterionic or polymer-polymer ion salt if we assume that other conditions are equal in both polymers. Therefore, if we want to obtain UCST characteristics of a separate polymer-monomeric ionic salt in an appropriate temperature range, $\Delta H_m$ should be increased to compensate for the increase of $\Delta S_m$.

As a model polymer backbone for UCST transition, we chose branched polyethylenimine (b-PEI) with a high amine density (1 amine residue per 43 Da). Primary, secondary, and tertiary amines of b-PEI were gradually protonated with the addition of hydrogen halide, and the resulting ammonium residues could interact with halide counter-ions (Fig. 1A). If the interaction was strong enough to overcome the water-ion interaction, a positive $\Delta H_m$ could be generated to show UCST phase transition. As shown in Fig. 1 and Fig. S1, ESi*, various polyethylenimium (PEI) halide salts exhibited UCST phase transition in the temperature range between 0 °C and...
50 °C, UCST phase transition of PEI halide is quite sensitive to the amount of hydrogen halide. Phase transition temperature of PEI bromide (PEIB) increased as the HBr/ammine (N) ratio increased (Fig. 1B). Excessive HBr might have induced the further protonation of internal tertiary amines in PEI [14], and the electrostatic interaction between ammonium and halide ions increased to elevate ΔH_m and the phase transition temperature. Excessive HBr might also elevate the phase transition temperature by salting-out type effect. Phase transition temperature of PEIB was also dependent on the composition (Fig. 1C). Both PEI chloride (PEIC) and PEI iodide (PEII) exhibited the UCST phase transition, although it was observed at a very narrow range of the composition and halide/N ratio (Fig. S1, ESI†). The UCST phase transition of simple polymer-halide salts in aqueous solutions is reported here for the first time, although the UCST phase transition of polymer-complex ions was reported in a few previous papers [15].

However, UCST phase transition of PEI halide can be observed only under extreme pH conditions (Table S1, ESI†), probably because a considerable number of cationic ammonium residues, which interact with halide anions, can be generated only under those conditions. To obtain polymeric salts, which can show the UCST phase transition, we prepared a methylated PEI possessing permanent cationic ammonium residues. To investigate the effect of counter-ions, the phase transition of PEI halide was observed by varying the counter-ion composition (Fig. 1C). Both PEI chloride (PEIC) and PEI iodide (PEII) exhibited the UCST phase transition, although it was observed at a very narrow range of the composition and halide/N ratio (Fig. S1, ESI†). The UCST phase transition of simple polymer-halide salts in aqueous solutions is reported here for the first time, although the UCST phase transition of polymer-complex ions was reported in a few previous papers [15].

We could obtain a methylated PEI possessing permanent cationic ammonium residues (MPEII). The methylated polyethyleniminium iodide (MPEII) was prepared by the nucleophilic substitution between primary, secondary, and tertiary amine residues of b-PEI and methyl iodide (CH3I) [16]. The quaternary ammonium degree of each polymer salt was determined by the inverted gate (INVGATE) 13C NMR technique [17]. We could obtain an MPEII of which 35-38% of the total amine residues were quaternized (MPEII0.35 or MPEII0.38) using the 5.0 equivalent of CH3I (Fig. S2, ESI†). Most of the quaternary ammoniums originated from more-exposed primary amines on the external part of b-PEI through methylation reactions. Excess iodide salts were removed or exchanged into chloride or bromide to produce methylated polyethyleniminium chloride (MPEIC) or bromide (MPEIB) by dialysis (Fig. 2A).

Interestingly, unlike the unmethylated correspondents, only MPEII exhibited UCST phase transition in the temperature range of 0–20 °C (Fig. 2B). Marginal hysteresis (AT = 1.2°C) was observed in the phase transition of MPEI (Fig. S3, ESI†), which is a typical characteristic of temperature-sensitive phase transition of polymers [18]. Both MPEIC and MPEIB are miscible with water in the temperature range of 0–100 °C. In case of MPEI, the hydrophobic interaction between the methylated ammonium residues (NR4+) and the halide ions might also have been an important factor as well as the electrostatic interaction. The molar Gibbs free energies of the hydration of Cl−, Br−, and I− are -340, -315, and -275 kJ/mol, respectively [19]. Due to the more hydrophobic character of I− compared with other halide ions, the interaction of I− with NR4+ is fairly higher than Cl− and Br− [20]. The stronger interaction between NR4+ and I− can dominate the interaction between water molecules and ions to generate positive ΔH_m and give the UCST property to MPEI. However, the water-ion interaction might be stronger than the weaker interaction between NR4+ and other halide ions to generate negative ΔH_m and negative ΔG_m (=ΔH_m - TΔS_m) in the temperature range.

The composition-temperature phase diagram of MPEI/water mixtures showed a typical convex shape that has been observed in many other UCST mixtures [Fig. 2C] [21]. Fig. 2C also shows the effect of molecular weight on the phase transition temperature. High-molecular-weight MPEII0.35 (25 kDa) has a higher phase transition temperature than low-molecular-weight MPEII0.38 (0.80 kDa). High-molecular-weight MPEI has a less-positive ΔS_m than low-molecular-weight MPEI due to a smaller combinatorial entropy gain during mixing. Therefore, MPEII0.35 (25 kDa) showed a higher phase transition temperature (T =ΔH_m/ΔS_m) than MPEII0.38 (0.80 kDa), assuming that both derivatives have a similar ΔH_m at similar degrees of quaternization (35% vs 38%). To investigate the effect of counter-ions, the phase transition of MPEI halide was observed by varying the counter-ion composition...
polymers. However, the hydrophobicity of counter-ions seemed to be an important factor for the introduction of the UCST property into alkylated quaternary ammonium polymers.

In conclusion, we demonstrated that the simple polymer-ion salt such as the halide salts of PEI and MPEI could show the UCST phase transition in aqueous solutions if the polymer-ion interaction is strong enough to overcome the solute-water interaction. Without the complex synthesis of polymers containing zwitterionic or hydrogen bonding moieties, the simple exchange of counter-ions or methylation could introduce the UCST property into pre-existing polymers. After future research varying the cationic and anionic parts of polymers and ions, the characteristics of temperature-responsive polymeric salts will be understood in more detail, and they will be more helpful in the development of practical temperature-responsive smart materials for various applications.

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Experimental section

Measurement of the UCST phase transition

The phase transition was monitored by a V-650 UV/vis spectrophotometer (Jasco, Japan) equipped with an STR-707 water thermostatted cell holder. Each sample was completely dissolved in aqueous solution above phase transition temperature and then positioned in the temperature-controlled holder. The phase transition temperature was determined as the temperature showing 50% of the transmittance when the cooling rate was set at a 1 °C/min. For the adjustment of total anionic concentration in Fig. 3A, NaCl and NaI were added to the mixture of MPEI and MPEI at a specific [I⁻]/[A⁺] ratio.

Preparation of MPEI halide

A solution of b-PEI (Mθ = 25,000 (PD(Mθ/Mn)=2.5) or Mθ = 800 (PD(Mθ/Mn)=1.3)) in N,N-dimethylformamide (DMF) was added to a stirred solution of N,N-diisopropylethylamine in DMF at 30 °C. CH₃Cl (5.0 eq. of total amines in b-PEI) was slowly added to the solution. After 48 h of stirring, ammonium hydroxide solution was added to the solution for quenching. For the purification of MPEI (25 kDa), the reaction mixture was dialyzed against ethanol (+3) and deionized water (+5) using a membrane (Spectrum Laboratories, Inc., USA; MWCO =6-8 kDa). MPEI (0.80 kDa) was purified by ethanol precipitation. The purified MPEI was lyophilized to prepare the product as a pale yellow powder. The structure was characterized using the inverted gate (INVGATE) 1H NMR technique (Agilent 400-MR D20 (400 MHz)). Other MPEI salts were obtained by exhaustive dialysis of MPEI against corresponding sodium salt solutions (NaCl, NaBr, NaSCN, or NaBF₄).

Notes and references


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