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Lower critical solution temperature (LCST) phase behaviour of an imidazolium-based ionic liquid is reported, which can be controlled by concentration, the choice of cation, anion and solvent, and by supramolecular host–guest complex formation. Molecular dynamics simulations provide insight into the molecular basis of this LCST phenomenon. This thermo-responsive system has potential applications in cloud point extraction processes.

The implementation of controllable and programmable stimuli-responsiveness into materials is pivotal for smart function and the realization of applications.¹ Lower critical solution temperature (LCST) phase behaviour in solution is an intensely studied property of a series of thermo-responsive materials. They are miscible with solvents – in most cases water – only below a critical temperature.² So far, the investigation of LCST phase behaviour overwhelmingly focused on covalent polymers.² Classic examples such as poly(*N*-isopropylacrylamide) and its derivatives have many applications in the areas of nano- and biotechnology.^{2c,m} Comparably, much less attention has so far been paid to low molecular weight compounds exhibiting LCST behaviour, although such phenomena may have practical values for example in extraction processes.

Ionic liquids (ILs) are organic salts with melting points below 100 °C and offer unique physicochemical properties.³ They have gained importance for diverse areas such as green chemistry, supramolecular chemistry and catalysis.³ ILs are not only tunable solvents to promote the thermo-responsive behaviour of the solutes, but some of them display LCST-type phase transition in water or organic solvents themselves.⁴ Though ILs with LCST phase transition behaviour have been reported, attention is

Lower critical solution temperature (LCST) phase behaviour of an ionic liquid and its control by supramolecular host–guest interactions†

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mainly focused on the phase transition phenomena,⁴ while a mechanistic understanding of this behaviour at the molecular level still needs to be developed.^{2h,4,5} Furthermore, the parameters to fine-tune the LCST behaviour of ILs have been limited to concentration and solvent so far – a quite severe restriction for the implementation of applications. More options to tailor thermo-responsiveness would thus be a great advantage for function.^{2,6}

Here, we report the LCST phase behaviour of an ionic liquid, 1,3-dimethylimidazolium iodide, in acetone combining experiment and molecular dynamics (MD) simulations in order to get more detailed insight into the molecular basis of the phenomenon. As an additional tuning option, we introduce supramolecular control of the thermal behaviour and demonstrate that different hosts for the ionic liquid offer control over the phase transition temperature.

At room temperature, 1,3-dimethylimidazolium iodide (**IL-I**) is soluble in acetone and forms a transparent, light-yellow solution. When heated to 50 °C, the acetone solution of **IL-I** turns turbid first and then separates into an **IL-I** phase at the bottom of the vial and an acetone phase immiscible with it on top (Fig. 1). After cooling down the **IL-I**/acetone phase-separated mixture to room temperature, a single transparent phase forms again (Fig. 1). This temperature-induced mixing–demixing is thus fully reversible and has not been described for **IL-I**/acetone so far. In contrast, no such LCST behaviour was observed for **IL-I** in other solvents such as water, methanol, ethanol, acetonitrile, DMF and DMSO (Fig. S1 and S2, ESI†). These observations indicate that the LCST-type phase transition of **IL-I** is a unique, solvent-specific phenomenon in acetone.^{4a}

In order to obtain detailed insight into this LCST phase behaviour, cloud points were determined by light transmittance measurements at a wavelength (λ) of 550 nm for differently concentrated **IL-I**/acetone mixtures at various temperatures (Fig. 2a). At **IL-I** concentrations of 300, 400, and 500 mg mL⁻¹, the corresponding cloud point temperatures (T_{cloud}) defined as 50% of the initial transmittance at $\lambda = 550$ nm are 49.4, 46.5 and 44.8 °C, respectively. All transitions are sharp, typically within 1 °C from the beginning to the end of the transitions. At even higher **IL-I** concentrations (> 600 mg mL⁻¹), a reversed T_{cloud} /concentration relationship

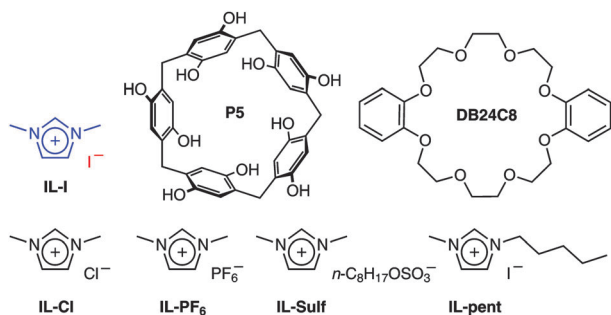
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Scheme 1 Chemical structures of ionic liquids, and two macrocyclic compounds (pillar[5]arene **P5** and crown ether **DB24C8**) which are known hosts for the imidazolium cation.

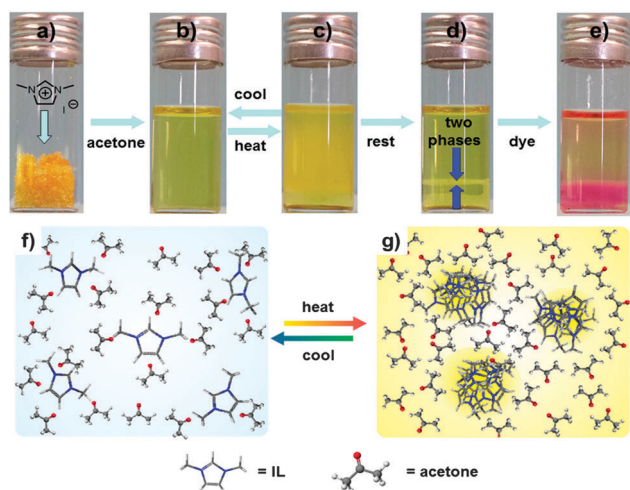


Fig. 1 Top: The reversible LCST phase behaviour of **IL-I** in acetone: (a) pure ionic liquid, (b) clear solution (500 mg mL^{-1}) after acetone addition, (c) turbid dispersion and (d) phase separation after heating to and resting at 50°C . (e) To make the phase separation more clearly visible, rhodamine B is added to the solution. Bottom: Cartoon representation of the underlying clustering processes that cause the LCST behaviour: (f) situation at room temperature with **IL-I** dissolved uniformly in acetone. (g) Upon heating, the imidazolium salt clusters.

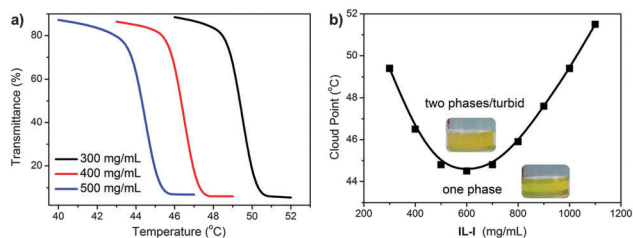


Fig. 2 (a) Temperature-dependence of light transmittance of mixtures of **IL-I** and acetone. (b) Concentration dependence of cloud point of **IL-I** in acetone.

is observed. The T_{cloud} /concentration phase diagram (Fig. 2b) exhibits a V-shaped curve separating the single-phase from the double-phase region. Such a V-shaped T_{cloud} curve is a typical feature of LCST-type ionic liquids and also typical for most polymer-based LCST systems.

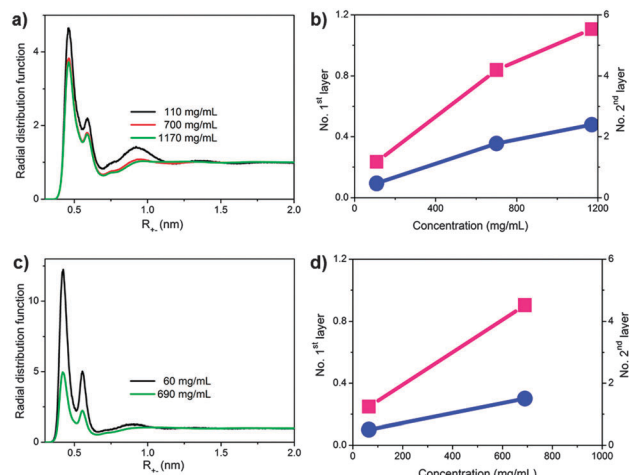


Fig. 3 (a) Strength of cation–anion affinity in **IL-I**. (b) The numbers of counterions in 1st (blue line) and 2nd (red line) shell of **IL-I**. (c) Strength of cation–anion affinity in **IL-Cl**. (d) The numbers of counterions in 1st (blue line) and 2nd (red line) shell of **IL-Cl**. Strength of cation–anion affinity is expressed in terms of cation–anion radial distribution function, at rising concentration of **IL**.

As ionic liquids are salts, the nature of the ions plays a crucial role for their solubility as well as their thermo-responsiveness.^{4g} Therefore, other counterions and a more lipophilic cation were examined. When I^- in **IL-I** was replaced by Cl^- , PF_6^- or $n\text{-C}_8\text{H}_{17}\text{OSO}_3^-$, respectively, or when 1-pentyl-3-methylimidazolium iodide was used, no LCST phase separations occurred. These results demonstrate both the cation and anion in **IL-I** to be important for thermo-responsiveness, *i.e.* the LCST behaviour of **IL-I** is structure-specific and depends on both the ion–solvent and anion–cation interactions.

All atom molecular dynamics (MD) simulations were performed to unravel the demixing mechanism at the molecular level and gain a more profound understanding into the microscopic processes occurring in **IL**/acetone mixtures (Fig. 3 and Fig. S4–S8, ESI[†]).⁷ More detailed insight into the role of the anions (Cl^- vs. I^-), **IL** concentration, and temperature were gained, as the simulations allowed measuring cation–anion affinity in terms of radial distribution functions. **IL-I** is more or less homogeneously dissolved in acetone at room temperature and the interactions among individual **IL-I** ion pairs are strengthened at higher temperatures, resulting in the aggregation of **IL-I**, the release of solvating acetone molecules into the bulk and, as a consequence, the observed LCST behaviour (Fig. S4, ESI[†]). Furthermore, the concentration of the ionic liquid has only a modest effect on the solution structure (the height of contact ion-pair peak decreases from 4.5 at 110 mg mL^{-1} only to 3.8 at 1170 mg mL^{-1} , Fig. S3a and S4, ESI[†]).

The same simulation protocol was applied to **IL-Cl** (1,3-dimethylimidazolium chloride).⁷ As shown in Fig. 3c and Fig. S5 (ESI[†]), in the diluted regime, the chloride anion has a strong affinity to 1,3-dimethylimidazolium (at any temperature), which can be attributed to its smaller size and its therefore ‘harder’ character. For solution thermodynamics of **IL-Cl**, an obvious difference to the iodide salt exists: the ionic liquid–ionic



liquid affinity decreases with growing temperatures, indicating that **IL-Cl** cannot form large-scale aggregates. The simulations thus agree with experiment in that no LCST behaviour of **IL-Cl** is observed in acetone and support the finding that the LCST phenomenon is sensitive to changes in the chemical nature of the ionic liquid involved.

The probabilities of contact ion pair formation at different concentrations were simulated and also gave us a clear comparison between different anions (Fig. 3a and c). The cation-Cl⁻ affinity is very strong at low concentration; however, it rapidly decreases when the concentration increases. In marked contrast, the cation-I⁻ affinity is virtually concentration-independent, having clear consequences for the aggregating and clustering abilities. In the case of **IL-I**, larger clusters (or mesoscopic, dense **IL-I** regions) form and lead to the clouding and subsequent demixing, while for **IL-Cl**, the cation-anion affinity substantially decreases with increased concentration, making the **IL-Cl** effectively increasingly miscible with acetone at higher **IL-Cl** concentrations thus prohibiting phase separation.

Imidazolium-based ILs have been reported to form host-guest complexes with macrocyclic hosts, including pillararenes such as **P5** and crown ethers like **DB24C8** (chemical structures in Scheme 1).⁸ Previous work demonstrated the important role of supramolecular interactions inducing LCST behaviour.^{6a} The introduction of supramolecular interactions in the LCST system under study here provides us with an additional tool to control the thermo-responsiveness beyond mere concentration, solvent and counterion changes. The addition of increasing amounts of **P5** leads to a clear decrease of T_{cloud} (Fig. 4). In the case of **DB24C8**, the opposite trend is observed. Upon increasing the concentration of **DB24C8** (**IL-I**: 500 mg mL⁻¹), T_{cloud} increases correspondingly. Supramolecular interactions can consequently be used to control the thermo-responsiveness^{6a} even in significantly different ways.

At present, we can only speculate, why the two complexes behave differently. With **DB24C8**, complexes with the ionic liquid form, which are more soluble and decompose at higher temperature. The higher the concentration of the crown, the

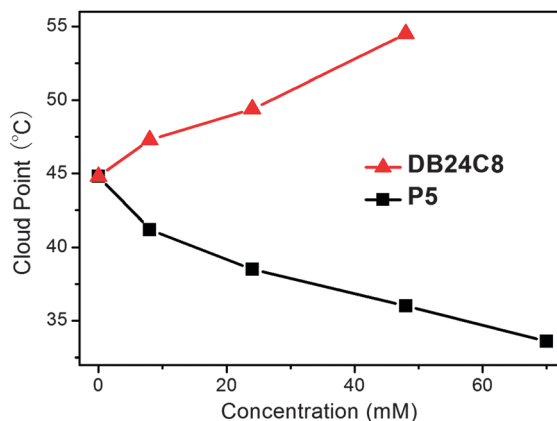


Fig. 4 Supramolecular control over the LCST-type phase behaviour through different macrocyclic compounds. The concentration of **IL-I** for each measurement is at 500 mg mL⁻¹, 2.2 M.

higher the concentration of complexes and the lower the concentration of native ionic liquid. Consequently, the cloud point temperatures increase with higher crown ether concentration as the dissociation of most of the complexes is required to generate enough free ionic liquid to induce the LCST transition. This mechanism does not easily rationalize the opposite trend observed for the pillararene. Here, two effects likely counterbalance each other. One is the host-guest complex formation as discussed for the crown ether. The second one is likely an effect on the solvent properties caused by the presence of many OH groups on the pillararene. At least, other OH-rich molecules such as different carbohydrates are also known to cause a downwards trend of cloud point temperatures in polymeric LCST materials.⁹ If this second effect over-compensates the host-guest effect, decreasing cloud point temperatures are expected, when the concentration of the host is increased. The host or the complex or both are thus directly involved in the LCST transition rather than being merely a modifying agent for the amount of ionic liquid.

Acetone is a common solvent in organic chemistry and the reversible thermo-responsive mixing and demixing processes in acetone might be useful to realize cloud point extraction (CPE) as a separation procedure (Fig. 5 and Fig. S3, ESI[†]). An organic dye, azure A, which is soluble in acetone, was applied as the organic model molecule. After the addition of azure A to acetone, the whole acetone solution becomes purple. When **IL-I** is added to this solution, the color turns green due to the mixing of the purple acetone and the yellowish **IL-I** phases at room temperature. Upon heating and resting, demixing leads to two immiscible layers, with the major fraction of the dye residing in the **IL-I** layer. After removal of dye-containing **IL-I** layer, fresh **IL-I** is added and the extraction repeated. After three cycles, virtually all the azure A is extracted from the acetone layer. These observations indicate that this **IL-I**-based LCST system is useful for applications in mixture separation and purification.^{4a,6a,9}

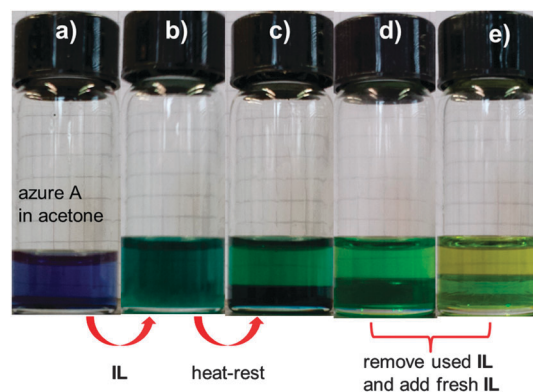


Fig. 5 Application of the LCST behaviour in the cloud point extraction of the model dye azure A. (a) Azure A in acetone, (b) addition of **IL-I** to solution (a) at room temperature, and (c) solution (b) after heating to 50 °C and resting at that temperature. (d) Second extraction cycle after removal of the azure A-containing **IL-I** layer from vial (c), addition of fresh **IL-I** (and heating/resting, 50 °C) and (e) third extraction cycle after repetition of the same **IL-I** replacement-heating-resting procedure.



In conclusion, a rather unique LCST phase behaviour of an imidazolium-based ionic liquid in acetone has been described. This LCST phase behaviour can be conveniently controlled by changing concentration, cation, anion and solvent. Supramolecular interactions between the ionic liquid and two macrocyclic hosts control the phase transition temperatures – surprisingly with opposite concentration dependences of the cloud temperatures. Molecular dynamics simulations are consistent with the observed thermo-responsiveness, and provide insight into the molecular basis of the observed thermo-responsive behaviour as well as the role of the counterions. Our very simple thermo-responsive system has potential for applications in separation processes. Considering the easy commercial availability of both acetone and **II-I**, this binary system is thus of practical importance.

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