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Reversible Nanoparticle-Micelle Transformation of Ionic Liquid-Sulfonatocalix[6]arene Aggregates

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Abstract

The effect of temperature and NaCl concentration variations on the self-assembly of 1-methyl-3-tetradecylimidazolium ($C_{14}mim^+$) and 4-sulfonatocalix[6]arene (SCX6) was studied by dynamic light scattering and isothermal calorimetric methods at pH 7. Inclusion complex formation promoted the self-assembly to spherical nanoparticles (NP), which transformed to supramolecular micelles (SM) in the presence of NaCl. Highly reversible, temperature-responsive behavior was observed, and the conditions of the NP–SM transition could be tuned by the alteration of $C_{14}mim^+$:SCX6 mixing ratio and NaCl concentration. The association to SM was always exothermic with enthalpy independent on the amount of NaCl. In contrast, NPs were produced in endothermic process at low temperature, and the enthalpy change became less favorable upon increase of NaCl concentration. The NP formation was accompanied by negative molar heat capacity change, which further diminished when NaCl concentration was raised.

Key words: Nanoparticle, supramolecular interaction, self-assembly, macrocycle, surfactant

1. INTRODUCTION

Supramolecular amphiphiles, the surfactants composed of noncovalently bound constituents, have their versatile applications and easily tunable properties.¹⁻³ Host-guest complex formation with macrocyclic compounds was often used to alter the thermodynamics of association and the morphology of the product. Inclusion of a surfactant in the cavity of cyclodextrins usually increases the critical micelle concentration.⁴ The confinement of the dominant component of mixed cationic–anionic surfactant systems in β -cyclodextrin promoted aggregate growth leading to micelle-to-vesicle transition.⁵ Spontaneous formation of giant vesicles was found upon coinclusion of methylviologen substituted with a long alkyl chain and 2,6-dihydroxynaphthalene inside cucurbit[8]uril.⁶ This host induced vesicle formation by ternary complex formation with pyrene-functionalized peptide and N-methyl-N'-octadecyl viologen.⁷ The dynamic character of noncovalent interactions was exploited to create stimuli-responsive self-assembled systems. Cyclodextrins were most frequently used as host macrocycles in associates exhibiting structure alteration controllable by pH,⁸ redox reaction,⁹ temperature¹⁰ or photoirradiation.^{11,12}

Because of their flexible π -electron-rich cavity and negative charge, 4-sulfonatocalix[n]arenes (SCXn) are particularly beneficial building elements for the creation of diverse nanostructures.¹³⁻¹⁵ The role of SCXn in the design of fluorescent sensing systems, pesticide detoxification, drug delivery,¹⁶ biochemistry,^{17,18} crystal engineering^{13,19} and supramolecular polymerization²⁰ has been reviewed. In contrast to cyclodextrins or cucurbiturils, which induces the dissociation of aggregates by host-guest complexation,²¹ the binding to SCXn promotes the aggregation of aromatic or amphiphilic compounds.²²⁻²⁵ We have demonstrated the inclusion of 1-alkyl-3-methylimidazolium ($C_n\text{mim}^+$) type of ionic liquids in SCXn²⁶ and unraveled the alteration of the binding thermodynamics with the length of the 1-alkyl substituent on the methylimidazolium moiety.^{27,28} When the aliphatic

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3 chain was composed of $n = 12, 14$ or 16 C atoms, $C_n\text{mim}^+$ cations and SCX6 spontaneously
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5 organized to spherical nanoparticles (NPs) possessing dense multilayered structure and 7:1
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7 stoichiometry.²⁹ The main objectives of the present work were to demonstrate the stimuli-
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9 responsive behavior of these NPs, and to reveal the major factors affecting their
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11 thermal-induced structural change. We focus on the self-assembly of $C_{14}\text{mim}^+$ and SCX6
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13 (Scheme 1) in solutions neutralized by NaOH.
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26 **Scheme 1.** Formulas of ionic liquid cation and 4-sulfonatocalix[6]arene
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30 2. EXPERIMENTAL SECTION

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32 **Materials.** 1-Methyl-3-tetradecyl-imidazolium bromide ($C_{14}\text{mim}^+\text{Br}^-$) was synthesized by
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34 the previously published procedure.³⁰ 4-Sulfonatocalix[6]arene (SCX6) (Acros Organics)
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36 contained 1:13 stoichiometric amount of water in its crystal structure.³¹ SCX6 solutions were
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38 always neutralized by the minimum volume of concentrated NaOH. Water of ultrapure
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40 quality was used as solvent. 2-Hydroxy-substituted Nile Red (HONR), also called 9-
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42 diethylamino-2-hydroxy-5*H*-benz[*a*]phenoxazin-5-one (Aldrich) was employed without
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44 further purification.
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48 **Sample preparation.** Stock solutions of $C_{14}\text{mim}^+\text{Br}^-$ (2 mM) and SCX6 (1 mM, pH 7) were
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50 prepared. NPs were obtained by mixing the required amounts of these solutions under stirring
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52 at 150 rpm at 25°C. SCX6 concentration was kept constant (0.1 mM) unless otherwise noted.
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54 Ionic strength was varied by addition of small volume (<50 μl) of concentrated solution of
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56 NaCl. The solutions were usually equilibrated 200 min at 25°C before measurements.
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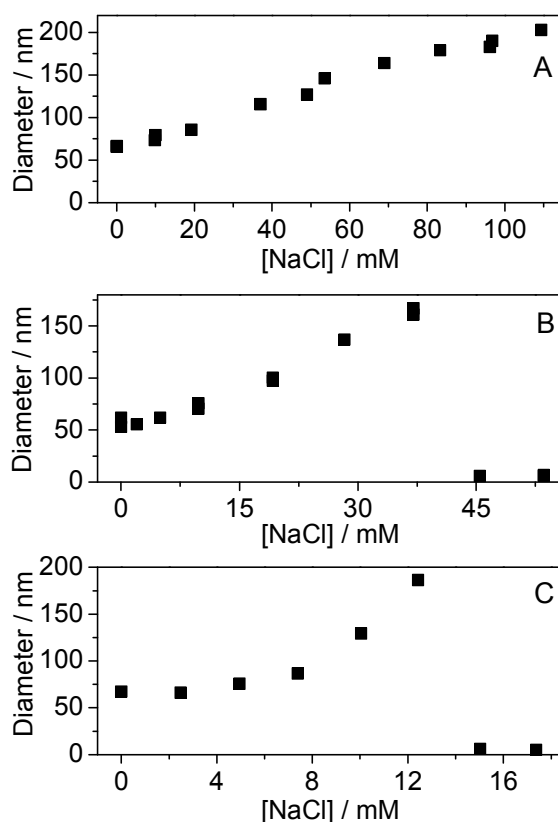
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3 **Utilization of fluorescent probe.** 23 nmol HONR in methanol was added to 5 ml flask and
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5 the solvent was evaporated by letting nitrogen flow over the solution. After adding the
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7 supramolecular surfactant aqueous solution, the sample was equilibrated for 2 days in the
8
9 dark.

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11 **Instrumentation.** The absorption spectra were recorded on an Agilent Technologies Cary60
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13 spectrophotometer. Particle size was determined by dynamic light scattering on a Zetasizer
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15 Nano-ZS (Malvern Instrument) equipped with a He-Ne laser ($\lambda = 633$ nm, scattering angle
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17 173°). Each measurement was the average of 12 runs of 10 seconds. Data were analyzed with
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19 the software developed by the manufacturer using a distribution analysis (General Purpose
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21 analysis). The mean diameter of the NPs was calculated on the basis of number distribution.
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23 Experiment was repeated at least twice. NPs were separated from the liquid phase by an
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25 ultracentrifuge from Beckman Coulter (Optima Max-XP, type TLA 110 rotor). Total carbon
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27 analyses were performed on a Shimadzu TOC-L CSN instrument, which was calibrated by a
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29 potassium hydrogen phthalate solution in ultrapure water (2.125 g dm^{-3} corresponding to
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31 1000 mgC dm^{-3}). ITC measurements were carried out with a MicroCal VP-ITC
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33 microcalorimeter. 10 μl of 3.4 mM ionic liquid solutions were injected from the computer
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35 controlled microsyringe at an interval of 180 s into the cell (volume = 1.4569 ml) containing
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37 0.1 mM SCX6 solution at pH 7, while stirring at 450 rpm. Cryo-TEM images were taken on
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39 an Ultrascan 2 k CCD camera (Gatan, USA), using a LaB₆ JEOL JEM 2100 (JEOL, Japan)
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41 cryo-microscope operating at 200 kV with a JEOL low dose system (Minimum Dose System,
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43 MDS) to protect the thin ice film from any irradiation before imaging and to reduce the
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45 irradiation during the image capture. The images were recorded at 93 K and digitally
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47 corrected using the ImageJ software. The samples were prepared as follows. A drop of the
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49 suspension was deposited on a Quantifoil grid (Micro Tools GmbH, Germany). The excess
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51 of solution was then blotted out with a filter paper, and before evaporation the grid was
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3 quench-frozen in liquid ethane to form a thin vitreous ice film. The grid was mounted in a
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5 Gatan 626 cryo-holder cooled with liquid nitrogen and transferred in the microscope.
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8 9 10 3. RESULTS

11 **NaCl-promoted NP–micelle transition.** In accordance with previous findings in acidic
12 solutions,²⁹ NPs of negative ζ potential were produced when $C_{14}mim^+$ was added to the
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14 neutralized solution of 0.1 mM SCX6 in 6 - 2 molar excess at 298 K. The initial points in
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16 Figure 1 and Supporting Information Figure S1 demonstrate that the NP size ($d \sim 60$ nm) is
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18 independent on the $C_{14}mim^+ : SCX6$ molar ratio (r) in the absence of NaCl. However, the
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20 gradual increase of NaCl concentration in mixtures of different r brought about two types of
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53 **Figure 1.** Mean particle diameter as a function of NaCl concentration for $C_{14}mim^+ : SCX6$
54 solution of molar ratio (A) 6 (B) 4 and (C) 2 at 298 K. Measurement was performed
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56 immediately after each successive NaCl addition. $[SCX6] = 0.1$ mM
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3 behaviors. At $r = 5 - 6$, the initial mean NP diameter steadily increased until a fast coalescence
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5 occurred around 150 mM NaCl concentration. Contrarily, NP size growth followed by a
6
7 sudden considerable size diminution was observed at $2 \leq r \leq 4$. The abrupt structure change
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9 took place around 40, 25, and 15 mM NaCl concentration in the case of $r = 4, 3,$ and 2,
10
11 respectively. This phenomenon was attributed to the reassembly of the NP components to
12
13 supramolecular micelles (SM) of 6.0 ± 0.3 nm mean diameter. When r is low, smaller number
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15 of SM is produced at constant SCX6 concentration. Consequently, less NaCl can ensure SM
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17 formation, and the NP–SM transition occurs at lower NaCl concentration. The SM size did
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19 not vary significantly under our experimental conditions. In the absence of SCX6, micelles of
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21 4.5 ± 0.3 nm mean diameter was found in 2.5 mM $C_{14}mim^+Br^-$ and 20 mM NaCl solution at
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23 298 K and 277 K alike. The larger size of SM could indicate the incorporation of SCX6
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25 macrocycles. NPs formed at $r \leq 6$ are negatively charged because the outer layer of the NPs is
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27 mainly composed of SCX6.²⁹ For example, the zeta potential (ζ) is -43 mV or -60 mV for
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29 NPs formed at $r = 3$ without or with 15 mM NaCl, respectively. The more negative ζ in the
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31 presence of NaCl probably arises from the NP size increase. NPs coalesced quickly at $r = 8$
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33 due to a ζ value close to zero, whereas positively charged NPs were produced at $r \geq 9$ because
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35 the outer layer of NPs is composed mainly of $C_{14}mim^+$ at large excess of ionic liquid over
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37 SCX6. The addition of at least 50 and 70 mM NaCl brought about precipitation at $r = 12 - 15$
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39 and $r = 18$, respectively.
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48 **Thermal-induced reversible SM–NP interconversion.** At constant $C_{14}mim^+ : SCX6$ molar
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50 ratio, the onset temperature of SM–NP transformation can be tuned by the variation of NaCl
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52 concentration. Figure 2 displays the results achieved in the solution of 0.2 mM $C_{14}mim^+$ and
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54 0.1 mM SCX6. The SMs were stable till higher temperature when more NaCl was added to
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56 the solution, and NPs were not produced below 300 and 306 K in the presence of 15 and 50
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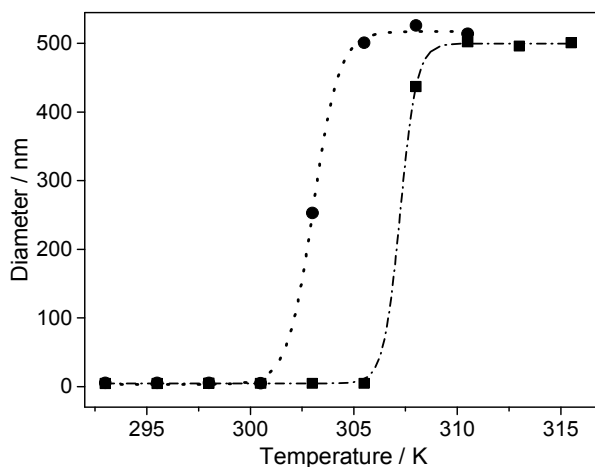


Figure 2. Effect of NaCl addition on the particle mean diameter at various temperatures for $C_{14}mim^+ : SCX6$ solution of molar ratio 2 with 15 mM NaCl (\bullet) and 50 mM NaCl (\blacksquare). $[SCX6] = 0.1$ mM.

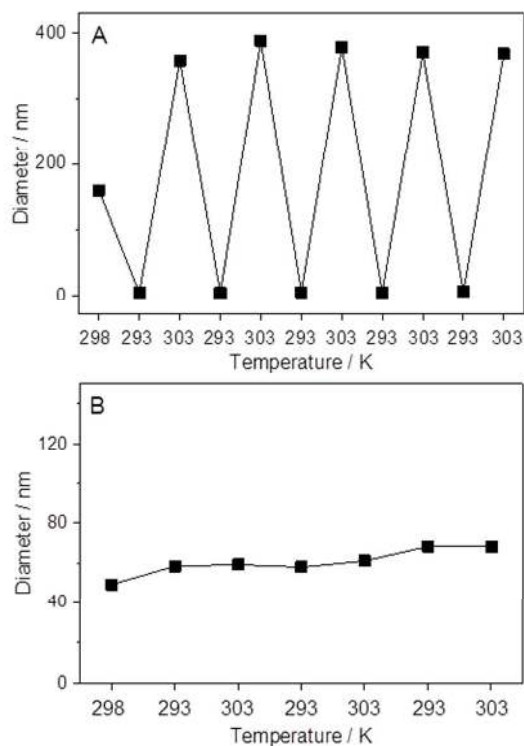
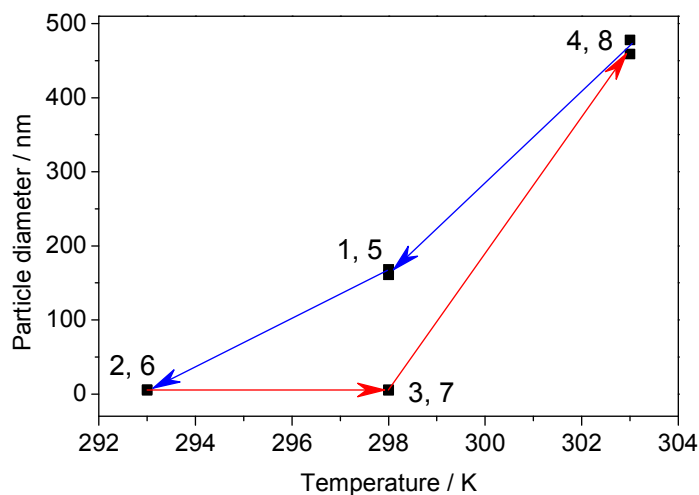


Figure 3. (A) Mean diameter of particles for $C_{14}mim^+ : SCX6$ solution of molar ratio 3 with 15mM NaCl measured 20 min after repeated switch of temperature between 293 and 303 K. (B) Results of an analogous experiment in the absence of NaCl. $[SCX6] = 0.1$ mM

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3 mM NaCl concentrations, respectively. Above these temperatures, the initial growth of NPs
4 leveled off. The type of aggregates produced by self-assembly could be controlled by
5 temperature. As a representative example, Figure 3A presents how the cycling of temperature
6 between 293 and 303 K influenced the mean particle diameter (d). The initial NPs of $d = 160$
7 nm vanished upon cooling to 293 K, and SMs of 6 nm diameter emerged. The temperature
8 rise to 303 K resulted in NP solution ($d = 370$ nm). The size of aggregates was constant
9 within the limits of experimental errors even after several temperature variation cycles.
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11 Similar NP–SM interconversion was observed at $[C_{14}mim^+]/[SCX6] = 2$ or 4. At reactant
12 ratio 2, NP–SM transformations were observed at temperature alteration between 298 and
13 303 K, whereas switching between 293 and 298 K was needed at $[C_{14}mim^+]/[SCX6] = 4$.
14 Noteworthy, no thermal-induced SM formation occurred in the absence of NaCl in the 293–
15 303 K temperature range (Figure 3B).



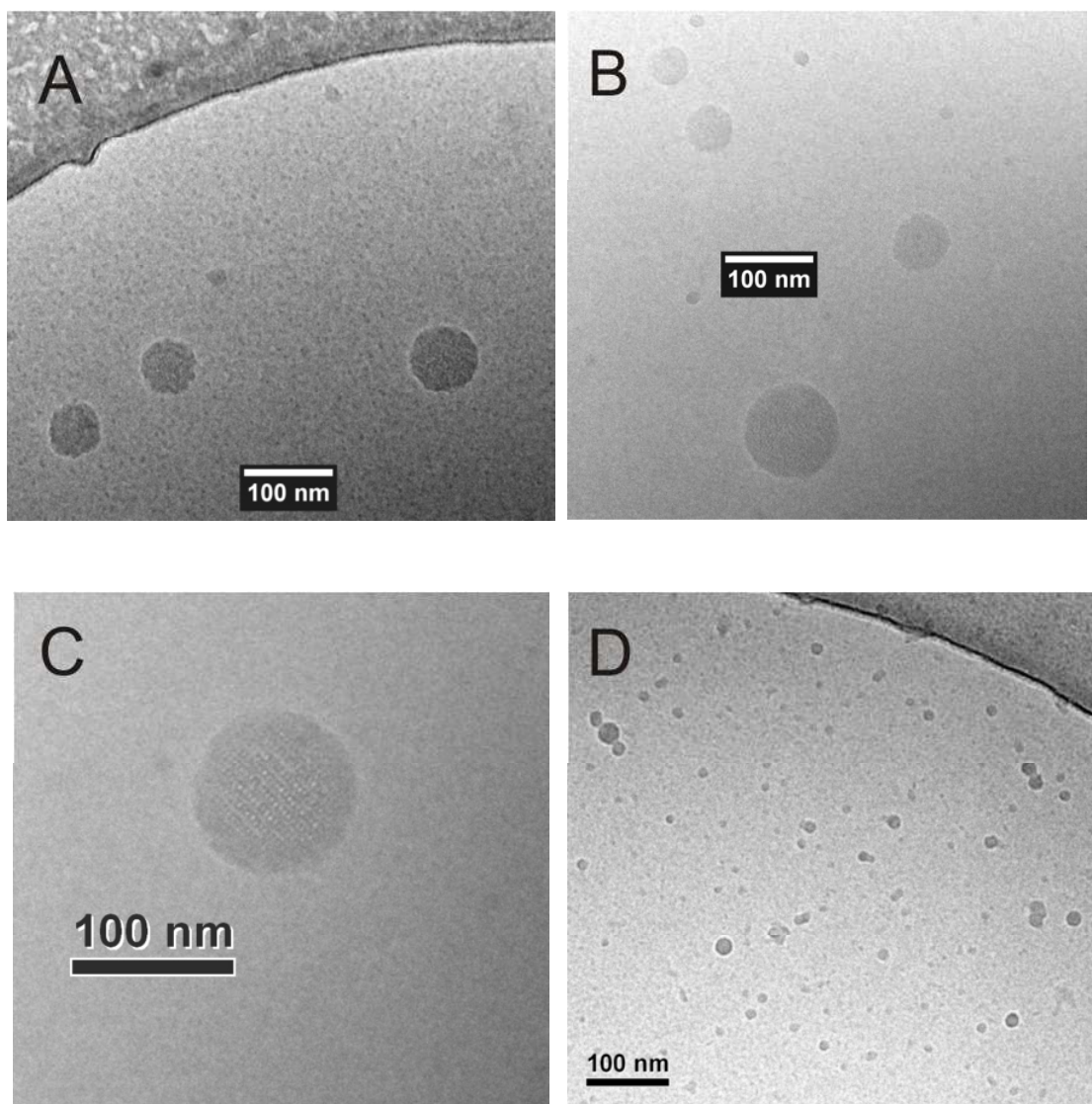
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50 **Figure 4.** Mean particle diameter for $C_{14}mim^+ : SCX6$ solution of molar ratio 3 with 15 mM
51 NaCl after 40 min equilibration time. The temperature was changed in the order of the
52 numbers as shown by the arrows. $[SCX6] = 0.1$ mM
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3 Repeating the experiment whose results are presented in Figure 3A using temperature
4 intervals of 5 K, a hysteresis was found that remained even when 40 min equilibration time
5 was employed (Figure 4). This indicates that the rearrangement of SMs into NPs is slower
6 than the reverse process.
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14 **Stoichiometry of the components in NPs.** The amounts of the components in the NPs were
15 obtained as a difference between the total concentrations and the concentrations in the
16 aqueous phase. The NPs were separated from the solutions by ultracentrifugation, and the
17 supernatants were analyzed by total carbon content measurement and spectrophotometric
18 determination of SCX6 concentration as previously described.²⁹ In the mixture of 0.4 mM
19 $C_{14}mim^+$ and 0.1 mM SCX6 at 298 K, $C_{14}mim^+ : SCX6$ molar ratio in NPs were found to be
20 7.4 ± 0.5 and 7.2 ± 0.5 at $[NaCl] = 0$ and 15 mM, respectively. These values indicate that the
21 presence of 15 mM NaCl insignificantly modified the stoichiometry of association although it
22 induced a slight increase in the NP diameter (Figure 1B).
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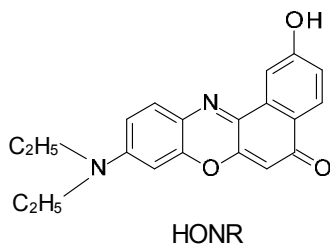
36 **Nanoparticle Structure.** The morphology of the NPs was characterized by cryo-TEM and as
37 a representative example, we studied the NPs at molar ratio of 4 (Figure 5A-C) and the
38 corresponding SMs obtained after adding 53 mM NaCl into the NPs suspension (Figure 5D).
39 The observed NPs are spherical with diameter varying between 45 and 120 nm. The average
40 diameter is around 71 ± 20 nm from 45 measurements, which is in agreement with the results
41 of the DLS studies. Few smaller aggregates ($d \sim 7$ nm) are also observed (Figure 5A-B),
42 corresponding to SMs. Interestingly, NPs show internal structure (Figure 5C). The core of the
43 NPs exhibits parallel lines made of smaller units suggesting lamellar structure for the NP
44 core; each unit has a size around 2 nm and could correspond to one SCX6 associated with 7
45 $C_{14}mim^+$. An amorphous shell of 10-12 nm appears around the structured core. The image of
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3 the SMs at ratio 4 shows many well-separated aggregates inside the thin vitreous ice film
4 (Figure 5D). The SMs are spherical with diameters mainly below 15 nm in accordance with
5 the DLS results. Among the numerous images recorded for this sample, it should be noted that
6 no NPs were observed.
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53 **Figure 5** Cryo-TEM images of (A-C) $C_{14}mim^+$:SCX6 solution of molar ratio 4 and (D)
54 $C_{14}mim^+$:SCX6 solution of molar ratio 4 with 53 mM NaCl. [SCX6] = 0.2 mM.
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3 **Critical aggregation concentration (cac) of supramolecular micelle.** The solubility
4 enhancement of 2-hydroxy-substituted Nile Red (HONR, Scheme 2), a highly fluorescent,
5 solvatochromic dye³² has been successfully employed as an environmental sensitive
6 fluorescent probe for the determination of critical micelle concentration of ionic liquids.^{30,33}
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21 **Scheme 2** Formula of 2-hydroxy-substituted Nile Red fluorescent probe

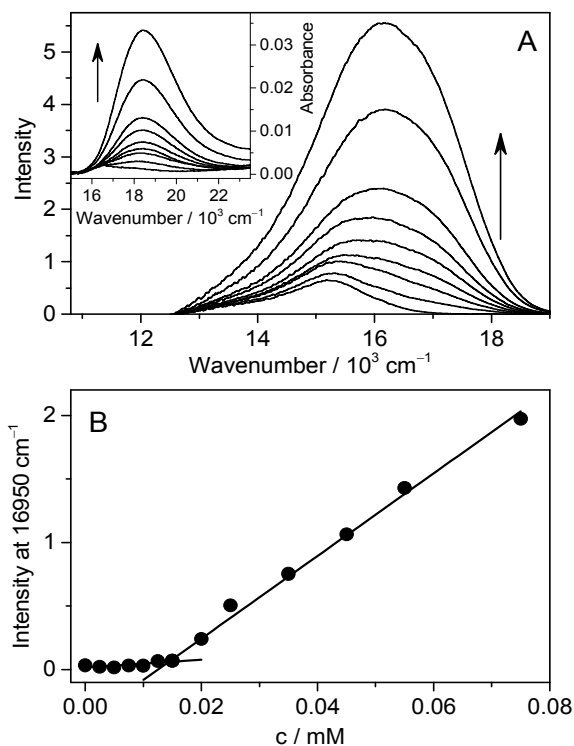


Figure 6. (A) Alteration of fluorescence and absorption (inset) spectra for saturated HONR solutions of $C_{14}mim^+$:SCX6 (molar ratio 2) and 50 mM NaCl at pH 7 ($[C_{14}mim^+] = 0, 0.02, 0.025, 0.035, 0.045, 0.055, 0.075, 0.0135, \text{ and } 0.175 \text{ mM}$). Temperature was 296 K. Excitation took place at 510 nm. (B) Fluorescence intensity at 16950 cm^{-1} as a function of $C_{14}mim^+$ concentration at $C_{14}mim^+$:SCX6 molar ratio of 2 in 50 mM NaCl solution at pH 7.

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3 Its solubility is very low in water and SCX6 aqueous solution, but significantly grows upon
4 binding to micelles. Figure 6A displays the change of the fluorescence and absorption (inset)
5 spectra upon parallel increase of the $C_{14}mim^+$ and SCX6 concentration keeping their molar
6 ratio $r = 2$ in 50 mM NaCl solution. The HONR spectra remain unaltered up to 0.015 mM
7 $C_{14}mim^+$ concentration because neither $C_{14}mim^+$ nor SCX6 enhance HONR solubility in this
8 concentration range. However, further increase of the amounts of additives leads to SM
9 formation. As the number of SMs grows, more HONR can be encapsulated and the
10 absorbance and the fluorescence intensity gradually grow. Figure 6B clearly shows a break in
11 the plot of the fluorescence intensity at 590 nm vs $C_{14}mim^+$ concentration. From the location
12 of the abrupt intensity enhancement, a value of 0.015 mM is obtained for the cac of $C_{14}mim^+$
13 at $r = 2$ in 50 mM NaCl solution at pH 7. The presence of SCX6 causes about 48-fold
14 diminution in cac. $C_{14}mim^+$ association into micelles begins at 0.72 mM under analogous
15 experimental conditions (50 mM NaCl). The binding to SCX6 polyanion lessens the
16 electrostatic repulsion among the imidazolium headgroups of $C_{14}mim^+$ and promotes the self-
17 organization of the alkyl chains thereby facilitating SM formation. The experiment was
18 repeated in 30 and 75 mM NaCl solutions at $r = 2$. The cac value insignificantly altered with
19 NaCl concentration. When 50 mM NaCl concentration was kept constant and
20 $[C_{14}mim^+]:[SCX6]$ ratio was varied, cac remained about 0.015 mM at $r = 1, 2, 3$ and 3.6
21 molar ratios alike.
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45 The marked hypsochromic shift of the spectra upon inclusion in SM implies that
46 HONR is situated in a microenvironment of moderate polarity where it is less accessible to
47 interaction with water. Figure S2 in Supporting Information displays the change of the
48 fluorescence maximum of HONR with the $E_T(30)$ solvent polarity parameter.^{32,34} The data
49 measured in neat solvents are fitted with a polynom. The obtained function serves as a
50 calibration for the characterization of the surroundings around the dye in micelles. The
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triangles indicate the substantial diminution of the local polarity compared to that in water. HONR senses microenvironment of 189 and 225 kJ mol⁻¹ E_T(30) values in SM and C₁₄mim⁺ micelle in 50 mM NaCl solution, respectively. The latter quantity corresponds to that reported for HONR bound to C₁₄mim⁺ micelle in the absence of NaCl.³⁰ The surroundings of HONR were also insensitive to NaCl concentration in SMs. On the basis of the derived E_T(30) parameters we conclude that the environment around the probe in C₁₄mim⁺ micelle closely resembles that of diethylene glycol, whereas in SM the polarity is lower, and similar to that of dimethylformamide and acetonitrile. The binding site in SM provides larger protection against water compared to that in conventional C₁₄mim⁺ micelle.

Isothermal titration calorimetry (ITC). To get insight into the thermodynamics of the association processes, ITC measurements were performed. A solution of 3.4 mM C₁₄mim⁺ with 15 mM NaCl was injected into 0.1 mM SCX6 and 15 mM NaCl mixture at pH 7. The dilution heat of the titrant, which was determined by the titration of 15 mM NaCl, was always

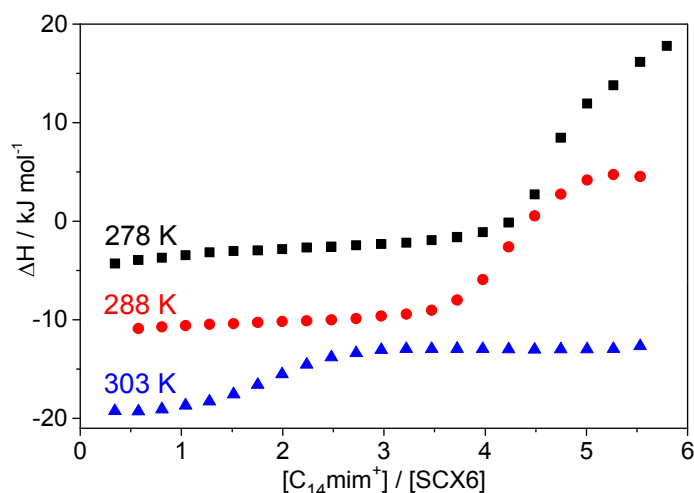


Figure 7 Enthalpograms after correction with the dilution heat of the titrant solution at various temperatures. 3.4 mM C₁₄mim⁺ solution was added to 0.1 mM SCX6 keeping 15 mM NaCl concentration constant.

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3 subtracted. Representative results are presented in Figure 7, whereas enthalpograms at 0 and
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5 50 mM NaCl concentrations are displayed in Supporting Information Figure S3 and S4.
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7 Figure S5 demonstrates that the same enthalpy gain is obtained irrespective of whether the
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9 concentration of $C_{14}mim^+$ is above or below cmc in the titrant solution. The heat evolution at
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11 low $C_{14}mim^+ : SCX6$ ratios (ΔH_{SM}) in 15 mM NaCl solution (Figure 7) is due to formation of
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13 inclusion complexes and self-assembly to SM. These two types of processes cannot be
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15 separated due to the small critical aggregation concentration (cac) of SMs. Since the heat
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17 evolution is constant at low ratios, this indicates that SMs are already formed after the first
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19 $C_{14}mim^+$ addition, showing that cac are very low (lower than 0.04 mM $C_{14}mim^+$ in 0.1 mM
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21 SCX6). This is in accordance with the 0.015 mM cac of $C_{14}mim^+$ in 0.1 mM SCX6
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23 determined by HONR fluorescence probe (vide supra). At 278 and 288 K, the consecutive
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25 injections at low $[C_{14}mim^+] : [SCX6]$ ratios increase only the number of SMs, therefore the
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27 produced heat barely varies. At larger $[C_{14}mim^+] : [SCX6]$ ratios, the enthalpy change
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29 becomes less negative or even positive because of the transformation of SMs to NPs. The
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31 shift of the inflexion point of the enthalpograms (Figure 7) indicates that smaller amount of
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33 $C_{14}mim^+$ is sufficient to induce SM–NP conversion at higher temperature. The plateau of the
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35 sigmoid curves at large $[C_{14}mim^+] : [SCX6]$ ratios corresponds to the enthalpy of NP
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37 formation (ΔH_{NP}). The endothermic association to NPs at low temperature turns into
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39 exothermic above 292 K, whereas the enthalpy of SM formation from the components is
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41 always negative and diminishes with the increase of temperature. Figure 8A presents the
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43 temperature dependence of ΔH_{SM} and ΔH_M , the enthalpy of $C_{14}mim^+$ conventional micelle
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45 formation, at 15 and 50 mM NaCl concentrations. ΔH_M was calculated from the results of the
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47 titration of NaCl solution with 20 mM $C_{14}mim^+$ as described by Blume and coworkers.³⁵ The
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49 enthalpy changes showed linear correlations with temperature, and the slopes provided the
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51 molar heat capacity changes (ΔC_p). Neither ΔH_M nor ΔH_{SM} displayed NaCl concentration
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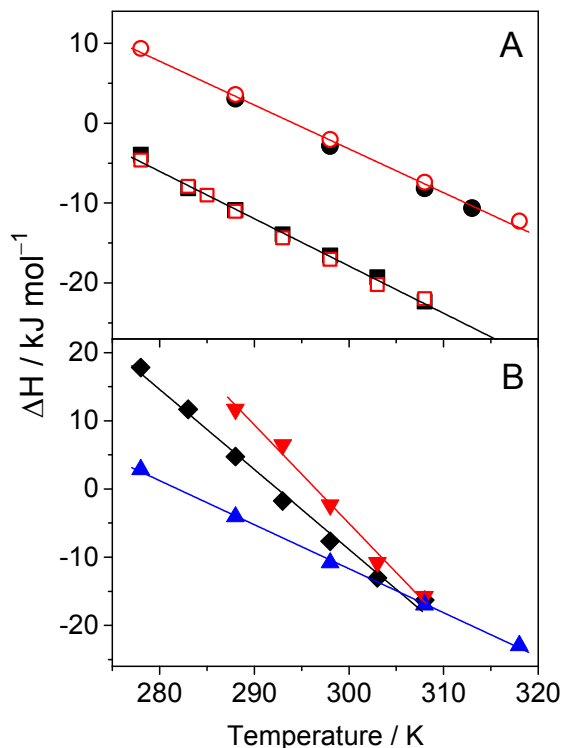


Figure 8 Enthalpy changes per mole of $\text{C}_{14}\text{mim}^+$ as a function of temperature (A) for $\text{C}_{14}\text{mim}^+\text{Br}^-$ micelle (circles) and SM (squares) formation in 15 mM (filled symbols) and 50 mM (empty symbols) NaCl solution; (B) for NP formation in 0 (\blacktriangle), 15 (\blacklozenge), and 50mM (\blacktriangledown) NaCl solution.

influence on their temperature dependence. The increase of NaCl concentration from 15 to 50 mM did not modify the temperature dependence of ΔH_M and ΔH_{SM} . The latter quantity is negative in the whole temperature range and about 14 kJ mol^{-1} smaller than the enthalpy change of the conventional $\text{C}_{14}\text{mim}^+$ micelle formation. As seen in Table 1, the ΔC_p values for conventional and supramolecular micelles barely differ, and are in accordance with that reported for $\text{C}_{14}\text{mim}^+\text{Cl}^-$ micelle in neat water.³⁶ In contrast to the behavior of ΔH_{SM} , a steeper and NaCl concentration sensitive temperature dependence was obtained for ΔH_{NP} (Figure 8B). ΔC_p of NP formation significantly decreased upon gradual increase of NaCl concentration.

Table 1 Results of the linear least-squares fit of the temperature dependence of enthalpy changes

Particle	[NaCl] / mM	ΔC_p / $\text{kJ mol}^{-1} \text{K}^{-1}$	Intercept / kJ mol^{-1}
$\text{C}_{14}\text{mim}^+\text{Cl}^-$ micelle ^a	0	-0.595 ^a	-
$\text{C}_{14}\text{mim}^+\text{Br}^-$ micelle	15	-0.54	161
$\text{C}_{14}\text{mim}^+\text{Br}^-$ micelle	50	-0.54	160
SM	15	-0.59	160
SM	50	-0.59	159
NP	0	-0.64	182
NP	15	-1.17	343
NP	50	-1.44	428

^a Reference³⁶

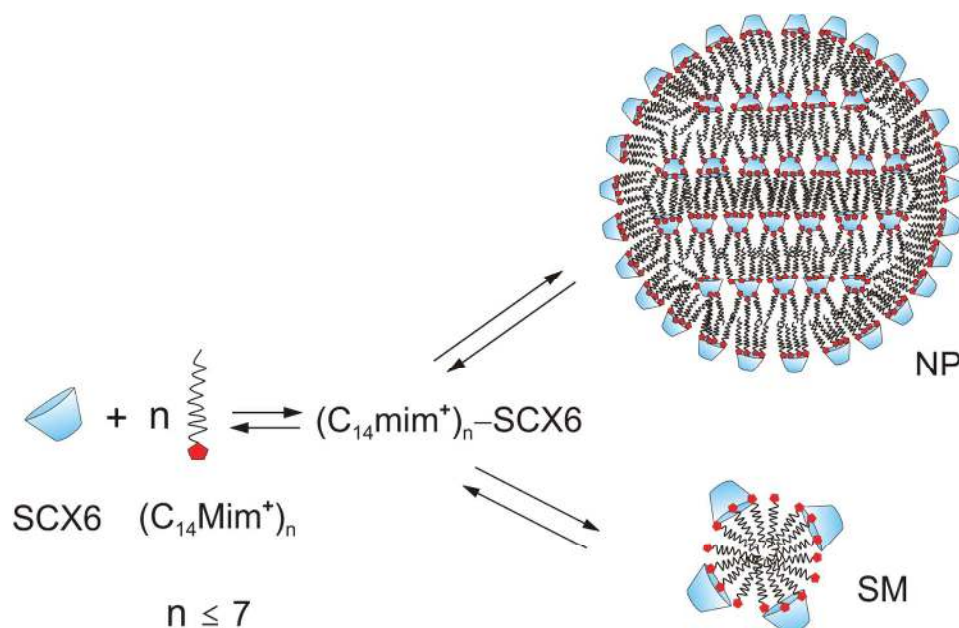
Noteworthily, the reversible transformation between SM and NP became equi-enthalpic around 308 K at various NaCl concentrations. The more negative ΔC_p for the association to NP compared with that for SM formation significantly contributes to the temperature-switchable character of SM–NP transition.

4. DISCUSSION

Our results demonstrate that three parameters, the molar ratio of the components, temperature, and NaCl concentration determine that either NPs or SMs are formed as a result of the self-assembly of $\text{C}_{14}\text{mim}^+$ and SCX6 in neutral solution. Since the critical micelle concentration of $\text{C}_{14}\text{mim}^+$ is 2.5 mM in neat water at 298 K,³⁰ the ionic liquid cations do not aggregate in the absence of SCX6 under the experimental conditions of our studies. The negative logarithm of the acid dissociation constants (pK_a) of the phenolic OH groups in

SCX6 are 3.29, 4.91, and 12.5 in 0.1 M NaCl solution at 298 K, and they shift to lower value in the presence of organic cations.³⁷ Therefore, most of SCX6 hosts contain two phenolate moieties, and the macrocycle has 8 negative charges at pH 7. Our results have shown that in the conditions where SMs are formed, cac is very low ($[C_{14}mim^+] = 0.015mM$) and depends neither on the mixing ratio r nor on NaCl concentration. Moreover, SM size ($d \sim 6$ nm) and structure are also independent on these two parameters, as shown by ITC and DLS measurements. When NPs are formed, their stoichiometry is around 7 with a negative surface charge suggesting a partial neutralization of the SCX6 negative charges, whatever the mixing ratio and NaCl concentration are. Contrary to SMs, ΔC_p of NPs depend on the salt concentration (ITC, Figure 8). TEM images have shown spherical particles with inner structure composed of building blocks of 2 nm size. The main change going from NP to SM

Scheme 3 Illustration of nanoparticle and supramolecular micelle formation^a



^aIn reality, the structure of SCX6 probably differs from the truncated cone shape. The counter-ions and charges were omitted for the sake of simplicity.

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3 suspension is the large increase in the specific surface area of the particles. This could be a
4
5 key parameter to understand the factors controlling the NP–SM transition.
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7
8 Scheme 3 outlines NP and SM formations. Below cac, 1:1 complexation occurs
9
10 between $C_{14}mim^+$ and SCX6. The equilibrium constant of this process (K) can be estimated
11
12 on the basis of the K values published for the association of various 1-alkyl-3-
13
14 methylimidazolium (C_nmim^+) with SCX6.²⁷ The extrapolation of the K dependence on the
15
16 number of carbon atoms in C_nmim^+ with a second order polynom provided $K = 1.9 \times 10^4 M^{-1}$
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18 for the 1:1 inclusion of $C_{14}mim^+$ in SCX6 cavity. Multiple binding of $C_{14}mim^+$ to SCX6
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20 macrocycle could also take place due to the electrostatic, host-guest and hydrophobic
21
22 interactions producing $(C_{14}mim^+)_n-SCX6$. Above cac, the $(C_{14}mim^+)_n-SCX6$ complexes
23
24 aggregate either to NPs or SMs depending on the experimental conditions. The reversible
25
26 transformation between NP and SM probably also occurs via $(C_{14}mim^+)_n-SCX6$. Only NPs
27
28 or SMs were observed experimentally.
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33 The NP–SM transition is markedly influenced by the NaCl concentration (Figure 1
34
35 and 2). This salt effect may arise from several factors. (i) Na^+ cations can competitively bind
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37 to the macrocycle. DOSY NMR measurements showed Na^+ association with SCX6.³⁸ The
38
39 analogous reaction of Na^+ with the smaller homologue, 4-sulfonatocalix[4]arene, has a low
40
41 association constant³⁹ of $183 M^{-1}$. This is probably not a predominant process. (ii) Na^+ ions
42
43 can screen the electrostatic repulsion among negatively charged species promoting thereby
44
45 their colloidal destabilization. This is observed for NPs at mixing ratios of 5 and 6. At lower
46
47 mixing ratios, the observed NP–SM transformation cannot be explained by screening effect.
48
49 (iii) Na^+ and Cl^- ions may interact with the first hydration shell of the ionic moieties and
50
51 interfere with the ordered hydrate structure around the hydrophobic chains. (iv) Na^+ cations
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53 can serve as loosely bound counterions for SM and NP alike. Adsorption of counterions in
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55 the Stern layer could partly explain the NP–SM transition. Because of the surface area
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3 difference, the number of bound cations should be much higher for SMs than for NPs at large
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5 salt concentration where saturation of Na^+ adsorption occurs.
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8 The transition between SMs and NPs also depends on the temperature and the mixing
9
10 ratio r at a given salt concentration. Due to the negative ΔH_{SM} and the endothermic character
11
12 of the self-assembly to NP (Figure 8), SM formation prevails at low temperature. The more
13
14 negative ΔC_p renders the enthalpy of NP formation more temperature sensitive than that of
15
16 SM production. Therefore, NP formation becomes energetically favorable at high
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18 temperature and mixing ratio. From the comparison of the data in Figure 7 and 8, we
19
20 conclude that NP can be formed even when ΔH_{NP} is positive. This indicates the substantial
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22 favorable entropy contribution to the driving force. The entropy increase arising from the
23
24 release of water molecules from the ordered hydrate structure around the individual
25
26 hydrophobic carbon chains⁴⁰ and from the solvate shell of the ionic moieties³⁹ is only partly
27
28 compensated by the entropy diminution due to association into NPs. As the temperature is
29
30 raised, the ordered aqueous region surrounding the aliphatic groups gradually vanishes and
31
32 the extent of hydration around the ionic groups diminishes leading to lessening entropy gain
33
34 for NP formation. The barely different ΔC_p for conventional $\text{C}_{14}\text{mim}^+$ micelles and SMs
35
36 indicates that the hydrophobic molecular surface exposed to water is the dominant factor
37
38 determining ΔC_p .³⁶ The presence of SCX6 in the headgroup region barely alters the degree of
39
40 water penetration into the micelles.
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48 5. CONCLUSIONS

49
50 Inclusion complex formation promotes the self-organization of $\text{C}_{14}\text{mim}^+$ and SCX6 ions
51
52 either to NP or SM in neutral solutions depending on temperature, mixing ratio of the
53
54 component and NaCl concentration. SMs are formed in an exothermic and practically NaCl
55
56 concentration independent process above 0.015 mM critical aggregation concentration. They
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3 are stable only in the presence of NaCl, at low temperature, and at $[C_{14}mim^+]:[SCX6] \leq 4$
4
5 mixing ratios. Otherwise spherical NP production has a larger driving force. At low
6
7 temperature, NPs do not exist because the entropy gain cannot overcompensate the
8
9 endothermicity of their formation. The salt sensitive and substantially negative molar heat
10
11 capacity change upon self-assembly to NPs plays important role in determining the
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13 conditions for NP stability. The reversible SM–NP transformation may find applications in
14
15 systems possessing thermally switchable optical properties and in stimuli-responsive
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17 assemblies capable of controlled release of substrates.
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23 **Supporting Information**

24
25 Figures S1 – S5. This material is available free of charge via the Internet at <http://pubs.acs.org>.
26
27

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29
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