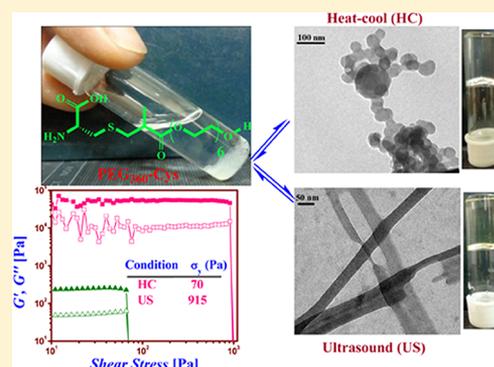


## Ultrasound-Induced Gelation of Organic Liquids by L-Cysteine-Derived Amphiphile Containing Poly(ethylene glycol) Tail

Rita Das Mahapatra and Joykrishna Dey\*

Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur 721 302, India

**ABSTRACT:** Amphiphile containing L-cysteine covalently linked with poly(ethylene glycol) (PEG) chain (PEG<sub>360</sub>-Cys) was observed to produce transparent gel at room temperature in polar aprotic solvents not only by heating-cooling (HC) but also when subjected to ultrasound (US). It was observed that a suspension of PEG<sub>360</sub>-Cys when treated with US readily formed gel at much lower critical gelation concentration. US irradiation has been established to control the gel properties at the molecular level. The morphological change of the organogels produced by the HC and US methods was confirmed from scanning as well as transmission electron microscopy. The organogels produced by the two external stimuli (HC and US) were characterized in detail by FTIR spectroscopy, differential scanning calorimetry, and rheology to shed light on the molecular packing during gelation. It is important to note that the US-induced organogels showed almost 13-fold increase in gel strength compared to the organogels obtained by the HC method. Further, US-induced gels were found to be thermally more stable than the heat-set gels. All these studies clearly demonstrate that hydrogen-bonding interaction is the main driving force for both the gelation processes, but the mode of hydrogen bonding at the molecular level is different.



## 1. INTRODUCTION

Supramolecular gels, owing to their soft nature, have been used in tissue engineering,<sup>1</sup> optical and electric devices,<sup>2</sup> and drug delivery.<sup>3</sup> These soft materials are formed by self-assembly of low-molecular-mass gelators (LMMGs) through noncovalent forces, such as hydrogen-bonding (H-bonding), electrostatic forces,  $\pi$ - $\pi$  stacking, and London dispersion forces.<sup>4-10</sup> These weak forces cause molecular interactions among the gelator molecules in the molecular level to form one-dimensional (1D) aggregate at the micrometer length scale,<sup>11</sup> which upon further entanglement led to the formation of three-dimensional (3D) network structure causing entrapment of solvents.<sup>12</sup> The macroscopic flow of the solvents is thus prevented by the 3D network structures through surface tension and capillary forces.<sup>13</sup> To date, numerous efforts have been made to understand the mechanism of formation of supramolecular gels. Literature reports reveal that factors that induce/enhance gelation are chirality, H-bonding,  $\pi$ - $\pi$  stacking, van der Waals interaction, etc. But interestingly none of these are self-sufficient or mandatory for gelation. Taken into consideration of all these factors, prediction about gelation behavior of any substance in terms of the structure-property relationship (SPR) is a fundamental aspect but still remains challenging.

Research on the behavior of supramolecular aggregates reveals that there are several kinds of stimuli, such as heat,<sup>14</sup> and solvent polarity,<sup>15</sup> light,<sup>16</sup> ultrasound,<sup>17,18</sup> ions,<sup>19</sup> and so forth which precisely manipulate the supramolecular self-aggregation at the molecular level. Among these stimuli, ultrasound (US) is a very common tool for dispersion of particles in food and cosmetic industries. US is generally used

for dissolution or dispersion of a compound in a liquid by disruption of weak intermolecular forces. In recent literature, there is a surge of interest in the use of US waves in medical diagnosis and transdermal drug delivery.<sup>20</sup> Owing to the more viscous nature and having great media to convey ultrasound energy, gels are more useful material in medical treatment than water. Besides, US is gradually being endorsed as a new energy source to reorganize the molecules for supersaturation during crystallization process.<sup>21</sup> Actually several contributions are likely to be responsible for the mentioned changes. They can be recognized as (1) US-induced shockwaves have been shown to shorten the time gap between achievement of supersaturation and initiation of nucleation, thereby favoring crystallization process, and (2) having excellent mixing property, US indeed weakens crystal aggregation with the aid of controlling nucleation population, approving the crystals to grow larger. In addition, the US has been observed to cause mechano-<sup>22</sup> and sonoluminescence<sup>23-25</sup> or to change reaction pathways to produce unexpected products.<sup>26,27</sup> Despite common belief that US breaks supramolecular assemblies in the liquid state, Naota and Koori<sup>28</sup> and Zhang and co-workers<sup>29</sup> first showed gelation of organic liquids in the presence of LMMGs when subjected to US. Such an unusual way to induce gelation attracted attention of the chemists. After these early works, a number of reports on the gelation of liquids by a gelator molecule that is activated by US have appeared in the

Received: June 19, 2015

Revised: July 16, 2015

Published: July 16, 2015

literature.<sup>30–38</sup> It is believed that US cleaves self-locked intramolecular hydrogen bonds<sup>34,35</sup> or  $\pi$ -stacking<sup>36–38</sup> to form interlocked structures through intermolecular interactions, but these are not the only mechanisms. For instance, Halder and co-workers have witnessed amyloid-like instant fibril formation by a terminally protected tripeptide in a variety of solvents under the influence of ultrasonic sound waves.<sup>39</sup> Some studies have shown US triggered gelation of different organic solvents by cholesterol based molecules.<sup>40,41</sup> Pan et al. have demonstrated US accelerated gelation of water by L-lysine derived gelator.<sup>42</sup>

Amidst a number of gelators reported to date, amino acid and peptide based LMMGs have earned a great attention owing to their inherent biocompatibility, effortless functionalization for tuning the gelation properties, and easy availability.<sup>43</sup> These features greatly spread out their potential application in biological sensing,<sup>44</sup> cell culture,<sup>45</sup> and biomedical area.<sup>46</sup> The gelation abilities of amino acid-derived LMMGs or amphiphiles demand careful balance between hydrophilic head and hydrophobic tail in order to form self-assembly. In other words, any substance that contained both hydrophilic head and hydrophobic tail would never form self-assembly. There are many reports on amphiphilic gelators containing a hydrocarbon tail.<sup>47,48</sup> But it is not known what will happen if the hydrocarbon tail is replaced by a PEG chain. There are only very few reports on organogelation by PEG containing derivatives where PEG group acts as a polymeric entity.<sup>49,50</sup> It is obvious from the literature reports that PEG chain behaves like a polar entity<sup>34</sup> (introduction of one  $-O-$  group by replacing a  $-CH_2-$  in hydrophobic long chain makes it polar). Hence, previously nonionic surfactants were synthesized by covalently attaching the PEG chain with hydrophobic molecules. Tween-20, Triton-X-100, etc., are well-known nonionic surfactants in which PEG chain acts as a polar head group. But for the first time, our group has reported self-assembly formation in organic solvents<sup>51</sup> as well as in water<sup>52–55</sup> by a number of molecules with polar head linked to PEG tail. Recently, we have reported gelation behavior of an amphiphile, PEG<sub>360</sub>-Cys, containing PEG tail (Figure 1) covalently linked to L-cysteine in different organic solvents. We had demonstrated that PEG<sub>360</sub>-Cys amphiphile spontaneously formed organogels in chloroform, dichloromethane, and benzene at room temperature (25 °C) with gelation time of ca. 14, 7, and 24 h, respectively, without the aid of any

external stimulus. The amphiphile was also able to solidify some polar aprotic solvents like DMF and propylene carbonate (PC) by the HC process.

While doing gelation test it was accidentally found that PEG<sub>360</sub>-Cys organogel in DMF produced by the HC method shrunk by expelling some amount of solvent when subjected to US treatment for 3–4 min in a bath type sonicator. However, upon standing at room temperature for 1–2 min, it produced again a transparent gel. Indeed, only 5 min US irradiation of a suspension of PEG<sub>360</sub>-Cys in DMF produced a clear solution, which on standing for 15 min at 25 °C (see Figure 1) transformed into a transparent gel. This phenomenon motivated us to test the gelation ability of the amphiphile in other polar solvents, including alcohols, N-methyl-2-pyrrolidone (NMP), and dimethylacetamide (DMA) by HC as well as US treatment. Thus, the present work is an extension of our previous work. Here we intend to explore what effect of US can have on the self-assembly formation by the gelator. In this paper, we show that suspension of PEG<sub>360</sub>-Cys amphiphile exhibits gelation in NMP, DMF, and DMA solvent by US treatment at room temperature as well as at 37 °C. As the synthesized amphiphile was also observed to gelate these solvents by HC treatment, the gels in the two process are characterized in detail through various techniques, and finally, the results are compared.

## 2. EXPERIMENTAL SECTION

**2.1. Materials.** Poly(ethylene glycol) methacrylate (MW-360), tetrabutylammonium fluoride (TBAF), and L-cysteine (99%) (Sigma-Aldrich, Bangalore, India) were used without further purification. Triethylamine, TEA (SRL), was procured locally and was dried and distilled before use. DMF, DMA, formamide (FA), and NMP were of good quality and were purified and dried whenever necessary.

The amphiphile PEG<sub>360</sub>-Cys was synthesized and purified following the same procedure as already reported.<sup>51</sup> The amphiphile was synthesized as the charge neutral form.

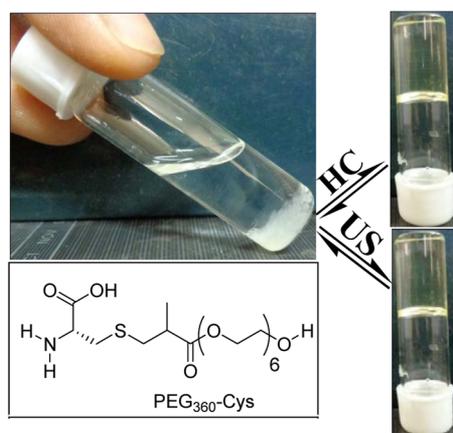
**2.2. Instrumentation and Methods.** Melting points of the solid samples were measured using the Instind (Kolkata) melting point apparatus with open capillaries. Specific rotation was measured with a digital polarimeter (Jasco P-1020). FT-IR spectra were measured with a PerkinElmer (model spectrum Rx1) spectrometer. The <sup>1</sup>H NMR spectra were recorded on an AVANCE DAX-400 (Bruker, Sweden) 400 MHz NMR spectrometer in D<sub>2</sub>O solvent.

Melting temperature of the gels were measured by inverted-tube experiment putting the screw-cap vial containing the gel in a temperature-controlled water bath (JULABO, model F12). The gel was slowly heated at a rate of 1 °C/min until the gelled mass starts to flow on tilting of the vial.

For scanning electron micrographs, the hot sample solution was placed on the aluminum or copper foil, allowed to cool, and air-dried at room temperature. The gel cast films (xerogels) were further dried in desiccators for 24 h. A layer of gold was sputtered on top to make conducting surface, and finally the specimen was transferred onto the field emission scanning electron microscope (FESEM, Zeiss, Supra-40) operating 5–10 kV to get the micrograph. The transmission electron micrographs (TEM) were taken with a transmission electron microscope (FEI-TECNAI G2 20S-TWIN, FEI, USA) operating at an accelerating voltage of 120 kV.

Differential scanning calorimetry (DSC) measurements were carried out on a PerkinElmer Pyris Diamond DSC calorimeter. The gel samples for DSC were placed in hermetically sealed Tzero lids and pans. The sample was then placed in the DSC apparatus together with an empty sample pan as reference. Then heating scan was recorded at heating rate 5 °C/min.

All the rheology measurements were performed on a Bohlin RS D-100 (Malvern, UK) rheometer using parallel-plate (PP-20) geometry with a constant tool gap of 100  $\mu$ m. The rheometer is fitted with a



**Figure 1.** Chemical structure of the amphiphiles showing gelation upon HC and US treatment.

solvent trap and Peltier device that controls temperature within  $25 \pm 0.1$  °C. An equilibration time of 30 min was allowed before measurements were taken for each sample. All measurements were performed with a matured gel after 10 h cooling. Oscillatory stress sweep measurements were carried out at a constant frequency of 1 Hz to obtain storage modulus ( $G'$ ) and loss modulus ( $G''$ ).

For sonication a bath type sonicator (Bandelin Sonorex Super RK 100/H) of frequency 35 kHz and ultrasound peak output 320 W was used.

### 3. RESULTS AND DISCUSSION

**3.1. US-Induced Gelation.** The gelation behavior of PEG<sub>360</sub>-Cys in the solvents employed in this study is summarized in Table 1. It was observed that in polar protic

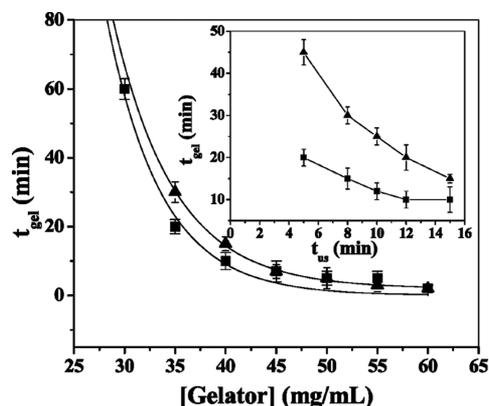
**Table 1. Gelation Behavior of PEG<sub>360</sub>-Cys in NMP, DMF, and DMA Solvent upon HC and US Treatment<sup>a</sup>**

sample	solvent	condition	heating/sonication temp (°C)	resting temp (°C)	remarks (CGC % w/v)
PEG <sub>360</sub> -Cys	NMP	HC	70	25	TG (2.2)
		US	25	25	TG (3.0)
		US	37	37	TG (3.0)
	DMF	US	25	37	TG (3.5)
		US	25	25	TG (1.6)
		US	25	37	TG (1.8)
	DMA	HC	70	25	TG (2.6) <sup>b</sup>
		US	70	25	TG (2.1)
		US	25	25	TG (1.6)

<sup>a</sup>Number in the parentheses represents corresponding CGC value ( $\pm 0.1\%$ , w/v) at 25 °C. <sup>b</sup>Data were taken from ref 51; TG = transparent gel.

solvents such as alcohols US-induced gelation was hard to achieve due to their insolubility. Interestingly, in NMP, DMF, and DMA solvents gelation was achieved by HC as well as by US treatment. The HC method also produced a transparent gel in all the solvents tested. It is important to note that US-induced gelation by the PEG<sub>360</sub>-Cys amphiphile was achieved only in amide type solvents, particularly in tertiary amide type solvent. To confirm this peculiar behavior, the gelation test was performed in FA solvent which has a primary amide group. As expected, FA solubilized the amphiphile almost immediately at room temperature. This is probably due to the increase of solvent–solute interaction, since the free  $-\text{NH}_2$  group present in FA offers its own H atoms to form intermolecular H-bond(s) with the gelator molecule. In order to better understand the role of US and gelation of the amphiphile, the gelation test of PEG<sub>360</sub>-Cys was monitored in NMP solvent by varying sonication bath temperature ( $T_{\text{us}}$ ), sonication period ( $t_{\text{us}}$ ), gelator concentration, etc., and the results are presented in Figure 2; the relevant data are included in Table 1.

The US treatment of the suspension of PEG<sub>360</sub>-Cys gelator (30 mg/mL) in NMP for a period of 15 min at 25 °C furnished a transparent gel after 1 h of resting at 25 °C. The increase of gelator concentration was observed to reduce the gelation time ( $t_{\text{gel}}$ ) exponentially as shown in Figure 2. In fact, gelation becomes almost instantaneous when gelator concentration was doubled to 60 mg/mL. Further, both  $t_{\text{us}}$  and  $T_{\text{us}}$  of sonication were found to have a significant effect on the gelation process. For example, with PEG<sub>360</sub>-Cys gelator (40 mg/mL), for a given sonication time ( $t_{\text{us}} = 15$  min), higher bath temperature ( $T_{\text{us}} = 37$  °C) required a longer time ( $t_{\text{gel}} \sim 15$  min) (Figure 2) to



**Figure 2.** Plot of gelation time ( $t_{\text{gel}}$ ) vs [gelator] for PEG<sub>360</sub>-Cys organogel in NMP at 25 °C (■,  $R^2 = 0.976$ ) and 37 °C (▲,  $R^2 = 0.996$ ). All the suspensions were sonicated (at 35 kHz, 320 W) for 15 min. Inset: plot of gelation time ( $t_{\text{gel}}$ ) vs sonication time (at 35 kHz, 320 W) ( $t_{\text{us}}$ ) of PEG<sub>360</sub>-Cys (40 mg/mL) organogel in NMP at 25 °C (■) and 37 °C (▲).

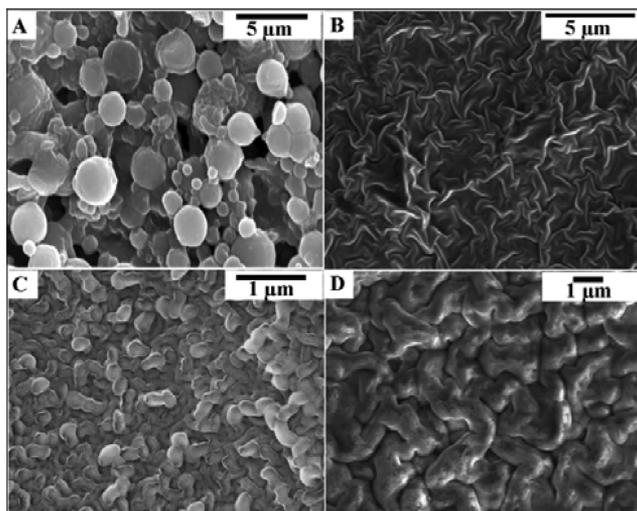
achieve a stable gel in comparison to that at 25 °C (inset, Figure 2). However, at both temperatures (25 and 37 °C) the  $t_{\text{gel}}$  value decreased with the increase of sonication time. This observation suggests that sonication at higher temperatures slows down the self-association process essential for the gelation. Indeed, no gelation was observed by US treatment of PEG<sub>360</sub>-Cys gelator in DMF at 37 °C. The CGC value was measured under different conditions, and the data are listed in Table 1. The data suggest that it requires a less amount of gelator and shorter sonication time to immobilize DMF in comparison to NMP.

#### 3.2. Effect of US on the Properties of the Organogels.

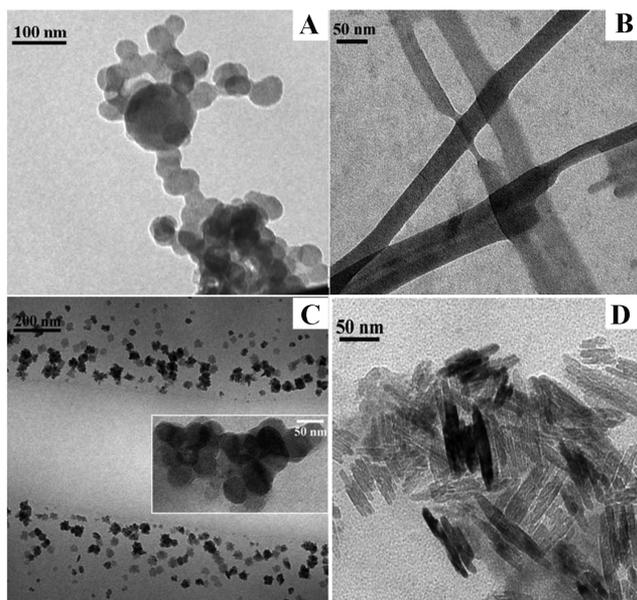
To study how the US-induced organogels differ from that produced by HC treatment, and hence to understand the effect of US on self-association process, the NMP and DMF organogels of PEG<sub>360</sub>-Cys produced by the two procedures HC and US treatment were characterized thoroughly.

**Morphology.** The morphology of the organogels was investigated by field emission scanning electron microscopy (FESEM). Figure 3 shows the FESEM images of the PEG<sub>360</sub>-Cys organogels produced by HC and US treatment in DMF and NMP. The images demonstrate that there is a marked difference in morphology of the organogels prepared by HC and US treatments. As can be seen, both DMF and NMP gels obtained by HC treatment exhibit small disk-like aggregates, whereas DMF gel produced upon US treatment shows large ribbon-like 1D supramolecular self-assemblies forming 3D network structures. The NMP gel prepared after US treatment also exhibit well-defined regular thick ribbon like network which entangled further into 3D network to arrest the solvents in it.

To further get a better insight into the change in morphology of the organogels under two different conditions, transmission electron microscopic (TEM) measurements were conducted with the unstained xerogels of DMF and NMP solvents obtained by the two experiments HC and US treatment. The micrographs are presented in Figure 4. It can be seen that the self-assembled network of DMF xerogel obtained by HC treatment displays spherical disk-like aggregates, whereas a dramatic change in morphology can be observed with the organogel obtained by US treatment. After 5 min US treatment, the micrograph exhibit 1D nanoribbons of average diameter



**Figure 3.** FESEM images of PEG<sub>360</sub>-Cys gel (30 mg/mL) in DMF by (A) HC and (B) US (25 °C) and in NMP obtained by (C) HC and (D) US (25 °C) method. In all the cases sonication period (frequency = 35 kHz, 320 W) was 15 min.

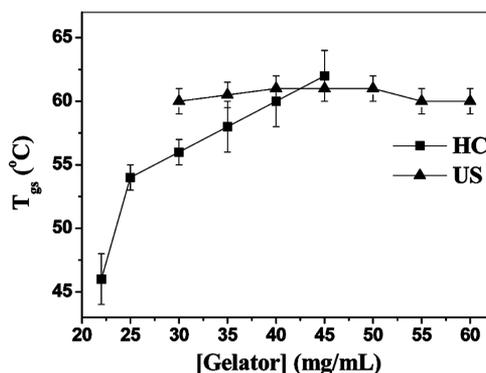


**Figure 4.** TEM images of PEG<sub>360</sub>-Cys gel (30 mg/mL) in DMF by (A) HC and (B) US (25 °C) in NMP obtained by (C) HC and (D) US (25 °C) method. In all the cases sonication period (frequency = 35 kHz, 320 W) was 15 min.

around 50 nm, which cross-linked further into 3D network (Figure 4B). The results observed from TEM experiment remains essentially similar in appearance to the FESEM experiments. The TEM images was also captured for NMP gels under two conditions. The HC process offered a self-assembled network composed of small disk-like aggregates (Figure 4C), and the elongation of the microdisks is clearly visible in the TEM pictures (Figure 4D) under US treatments. This dramatic change in the gel morphology induced by US facilitates gelation process reducing  $t_{gel}$  value. It has been well established fact that gelation of low-molecular-weight gelators in a given solvent is a result of gelator–gelator and solvent–gelator interaction, and strong gelator–gelator interaction leads to bigger well-ordered aggregates. Thus, the presence of large

aggregates in the US-induced organogels suggests that the gelator–gelator intermolecular interaction is much stronger than in the organogels formed by conventional HC method. This is elaborated in a latter section.

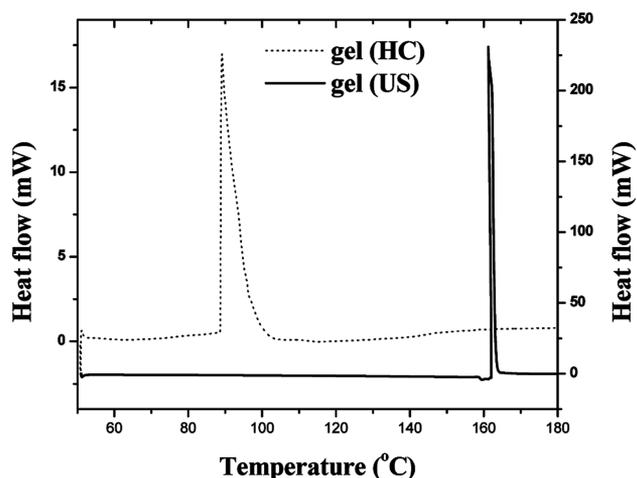
**Thermal Stability.** The change in morphology of the self-assemblies is also reflected in the gel-to-sol transition temperature ( $T_{gs}$ ) values. The DMF organogels of PEG<sub>360</sub>-Cys produced by HC and US treatment exhibit  $T_{gs}$  values at 70 and 78 °C, respectively. Further, a detail study of thermal stability of the organogels in NMP was also done. The results demonstrate that the gel produced by US treatment has higher  $T_{gs}$  values (60 °C) compared to the gel obtained by HC treatment 55 °C at a [gelator] < 45 mg/mL. It is interesting to note that in NMP solvent the  $T_{gs}$  values are independent of gelator concentration (Figure 5) for the gels obtained by US



**Figure 5.** Variation of gel melting temperature ( $T_{gs}$ ) with [gelator] for PEG<sub>360</sub>-Cys organogels in NMP produced by HC and US (15 min; 35 kHz, 320 W) treatments.

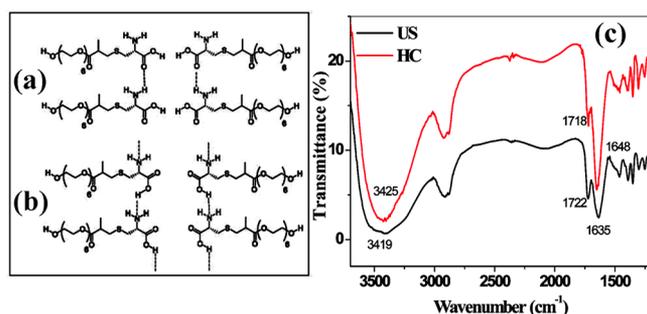
treatment. In contrast, for the gels produced by thermal stimuli, the  $T_{gs}$  value increases nonlinearly with the gelator concentration reaching plateau at [gelator] > 45 mg/mL. This clearly indicates that there is a difference in the nature of molecular interactions that are responsible for self-assembly formation induced by the two types of stimuli.

To get better insight into the thermal stability, and hence molecular packing of the gelators in the self-assembled structure causing gelation, measurements using differential scanning calorimeter (DSC) were performed with the DMF organogels prepared by the two processes. The thermograms are depicted in Figure 6, which show broad endothermic peak at 89 °C in the case of HC treated gel corresponding to its melting. In contrast, the gel prepared by US treatment exhibits a very sharp endothermic peak at 161 °C which is very relative to the former gel. It is important to note that the gel-to-sol phase transition temperature ( $T_{gs}$ ) as obtained from the above section does not match with the DSC results in either case. This is because DSC measurement is related to the complete transition from a heterogeneous gel state to a homogeneous solution state, whereas determination of  $T_{gs}$  is associated with the temperature at which the number density of fibers falls below a critical density for solvent immobilization.<sup>52</sup> However, these results clearly demonstrate that the nature of the molecular interactions are not identical in the two processes. The US treatment facilitates stronger interaction among gelator molecules in the self-assembled structure. In other words, US treatment to the gelators lead to well-organized molecular self-assembly. We have shown in our earlier publication<sup>51</sup> that the gelator molecules self-assemble through N–H⋯O=C inter-



**Figure 6.** DSC profiles of the gels of PEG<sub>360</sub>-Cys in DMF formed by HC and US effect.

molecular H-bonding interactions between head groups as shown in Figure 7a. In the case of US-treated organogel, either this intermolecular H-bonding interaction becomes stronger or some other kind of molecular interaction(s) is introduced.



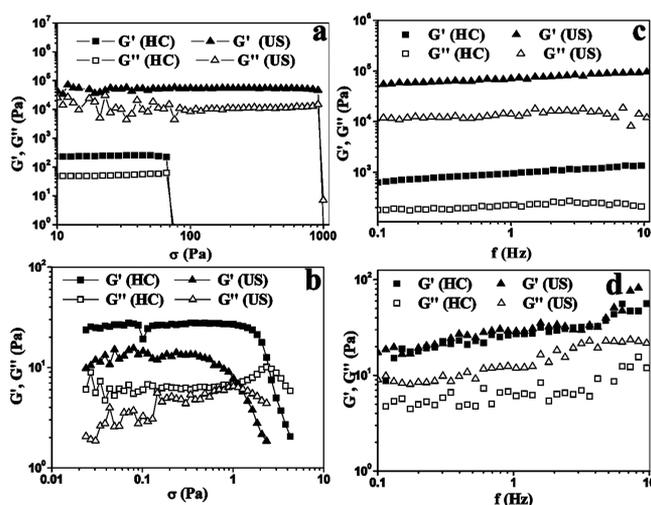
**Figure 7.** Schematic presentation of the mode of H-bonding of the gels of PEG<sub>360</sub>-Cys formed by (a) HC, (b) US effect, and (c) FT-IR spectroscopy of the xerogels of PEG<sub>360</sub>-Cys in DMF by HC and US treatment.

**Molecular Arrangement in the Gel State.** The role of intermolecular H-bonding interaction on the organogelation was confirmed by the disruption of gel structure upon addition of TBAF. Addition of 10  $\mu$ L of TBAF to 1 mL of thermal gels in DMF or NMP solvent caused disruption of the gel structure within 10 s, owing to the stronger H-bonding ability of the F<sup>-</sup> ion with the gelator molecules. It is interesting to note that in the case of US-induced organogel disruption of gel structure occurred after ca. 4 h of addition of TBAF. This suggests that H-bonding interaction in the self-assembled structure is stronger in the US-treated organogel. The above results drive us to predict that US treatment changes the mode of H-bonding interaction that produced stronger H-bond(s) and thereby stronger gel. Since the N–H $\cdots$ O=C H-bond (ca. 8 kJ/mol)<sup>56</sup> is weaker than O–H $\cdots$ N H-bond (29 kJ/mol),<sup>56</sup> we propose latter type of H-bonding in the self-assembly formation as shown in Figure 7b. This type of H-bonding interaction is expected to facilitate 1D growth of the molecular self-assembly forming ribbon-like structures and hence quicker and stronger gel formation.

The different mode of hydrogen-bonding interaction was confirmed by the FTIR spectra (Figure 7c) of the xerogels.

FTIR spectroscopy is the best technique to distinguish the noncovalent interactions involved in the self-association process. Therefore, to ascertain the new H-bonding pattern induced by the US treatment, FTIR spectra of PEG<sub>360</sub>-Cys in the xerogels of DMF solvent obtained by the two procedures US and HC treatment were measured. The spectrum of HC treated xerogels shows an intense peak at 1648 cm<sup>-1</sup> characteristic of the N–H bending vibration, whereas the same N–H bending vibration in the case of US-induced xerogel appeared at 1635 cm<sup>-1</sup>. This sort of red-shift of the N–H bending vibration clearly suggests formation of stronger H-bonds upon US treatment. Further, significant differences are observed for O–H stretching band of the carboxylic acid in both the xerogels. The broad O–H stretching band shifts to lower wavenumber (from 3425 to 3419 cm<sup>-1</sup>) in going from HC-treated gel to US-treated gel. This is because the O–H group of the carboxylic acids takes part in the new H-bonding pattern after US treatment.

**Rheology.** The rheological properties of the organogels obtained by the two methods were also compared. Rheological measurements for the gels are generally done in order to determine the stress required to deform the supramolecular network structure. It is well-known that there is a great dependence of the gel strength with the gelator concentration, with increasing gelator concentration gel strength increases. Therefore, to compare the mechanical strengths of different self-assembled network in different gels, all the rheological measurements were performed at CGC. The results are summarized in Figure 8. The storage modulus ( $G'$ ) of both



**Figure 8.** Variation of  $G'$  and  $G''$  with shear stress ( $\sigma$ ) of PEG<sub>360</sub>-Cys organogel in (a) DMF (39 mg/mL), (b) NMP (35 mg/mL); variation of  $G'$  and  $G''$  of PEG<sub>360</sub>-Cys organogel with frequency ( $f$ ) in (c) DMF and (d) NMP. In all the cases the samples were subjected to US (frequency 35 kHz, 320 W) treatment for 5 min at 25 °C.

organogels was higher than their corresponding loss modulus ( $G''$ ) in the applied frequency range, suggesting solid-like behavior of the gels. However, the  $G'$  ( $\sim 4 \times 10^4$  Pa) value of the organogel obtained by US treatment was much higher than that of the organogel obtained by HC treatment ( $G' \sim 20$  Pa). This implies that the mechanical strength of the US-treated organogel is higher than that obtained by HC treatment. This result is consistent with the results of FESEM and TEM images. The longer entangled fibrils in the US-treated organogel led to

higher storage modulus. That the US-treated organogel is stronger than the HC-treated gel is further substantiated by yield stress ( $\sigma_y$ ) value of the US-induced DMF gel ( $\sigma_y = 915$  Pa) which is much higher than that of the HC-treated DMF gel ( $\sigma_y = 70$  Pa). However, the NMP gel is much weaker ( $\sigma_y = 2.0$  Pa) than the DMF gel, irrespective of the nature of stimuli. This means that solvophobic interaction also plays a role in the self-assembly formation leading to gelation. DMF being less polar ( $\pi^* = 0.88$ )<sup>57</sup> and weaker H-bond acceptor ( $\beta = 0.69$ )<sup>57</sup> than NMP ( $\pi^* = 0.92$ ;  $\beta = 0.77$ )<sup>57</sup> the gelation is more favored in DMF solvent as indicated by the relatively lower CGC value (see Table 1).

#### 4. CONCLUSIONS

We have demonstrated organogelation of aprotic polar organic solvents in the presence of PEG<sub>360</sub>-Cys upon US irradiation. We have shown how US treatment changes the gel structure formed by PEG<sub>360</sub>-Cys gelator in DMF and NMP. FESEM and TEM images of the organogels in the two process revealed that the US treatment results in a dramatic morphological change from that observed with thermal gels. The organogels obtained by HC treatment exhibit small disk-like aggregates, whereas the organogels produced upon US treatment show large ribbon-like 1D supramolecular self-assemblies forming 3D network structures. The morphological change is manifested by the large increase of thermal and mechanical strength of the organogels. DSC measurement of the organogels clearly demonstrates appearance of a sharper endothermic peak at a much higher temperature for the US-treated gels. The mechanical strength of the US-treated DMF organogel ( $\sigma_y = 915$  Pa) was observed to be higher than that of HC-treated gel ( $\sigma_y = 70$  Pa). FTIR spectra of the xerogels in the two processes confirm stronger H-bonding interaction in the case of US-treated gels. All these results led us to conclude a US-induced conformational change of the head group favoring intermolecular H-bonding interactions to initiate self-assembly process which is likely to be an important factor for the gelation. The molecular arrangement in the self-assembly is shown to switch due to the switch of the mode of H-bonding upon energy input by US, which favored stronger intermolecular H-bonding interactions, thus facilitating rapid 1-D growth of the self-assembly. It seems that US bias thermodynamic self-assembly to ribbons with gelator molecules in a more tightly packed situation. In fact, it changes the successive self-assembly events and leads to the formation of 1-D ribbon-like structures, which is responsible for immobilization of the solvent.

#### AUTHOR INFORMATION

##### Corresponding Author

\*Fax (+) 91-3222-255303; e-mail [joydey@chem.iitkgp.ernet.in](mailto:joydey@chem.iitkgp.ernet.in) (J.D.).

##### Notes

The authors declare no competing financial interest.

#### ACKNOWLEDGMENTS

We thank the Indian Institute of Technology Kharagpur for partial support of this work. R.D.M. thanks CSIR, New Delhi, for a research fellowship (09/081(1157)/2012-EMR-I). The authors are thankful to Mr. Kiran Patruni, Department of Agricultural Science, IIT Kharagpur, for his assistance with the rheological measurements.

#### REFERENCES

- (1) Li, J.-L.; Liu, X.-Y. Architecture of Supramolecular Soft Functional Materials: From Understanding to Micro-/Nanoscale Engineering. *Adv. Funct. Mater.* **2010**, *20*, 3196–3216.
- (2) Ajayaghosh, A.; George, S. J. First Phenylenevinylene Based Organogels: Self-Assembled Nanostructures via Cooperative Hydrogen Bonding and  $\pi$ -Stacking. *J. Am. Chem. Soc.* **2001**, *123*, 5148–5149.
- (3) Banerjee, S.; Das, R.; Maitra, U. Supramolecular gels 'in action'. *J. Mater. Chem.* **2009**, *19*, 6649–6687.
- (4) Yu, G.; Yan, X.; Han, C.; Huang, F. Characterization of supramolecular gels. *Chem. Soc. Rev.* **2013**, *42*, 6697–6722.
- (5) Terech, P.; Weiss, R. G. Low Molecular Mass Gelators of Organic Liquids and the Properties of Their Gels. *Chem. Rev.* **1997**, *97*, 3133–3160.
- (6) Sangeetha, N. M.; Maitra, U. Supramolecular gels: Functions and uses. *Chem. Soc. Rev.* **2005**, *34*, 821–836.
- (7) Ajayaghosh, A.; Praveen, V. K.  $\pi$ -Organogels of Self-Assembled *p*-Phenylenevinylenes: Soft Materials with Distinct Size, Shape, and Functions. *Acc. Chem. Res.* **2007**, *40*, 644–656.
- (8) Kartha, K. K.; Mukhopadhyay, R. D.; Ajayaghosh, A. Supramolecular Gels and Functional Materials Research in India. *Chimia* **2013**, *67*, 51–63.
- (9) Babu, S. S.; Praveen, V. K.; Ajayaghosh, A. Functional  $\pi$ -Gelators and Their Applications. *Chem. Rev.* **2014**, *114*, 1973–2129.
- (10) Abdallah, D. J.; Weiss, R. G. n-Alkanes Gel n-Alkanes (and Many Other Organic Liquids). *Langmuir* **2000**, *16*, 352–355.
- (11) Burch, R. M.; Weitzberg, M.; Blok, N.; Muhlhauser, R.; Martin, D.; Farmer, S. G.; Bator, J. M.; Connor, J. R.; Ko, C.; Kuhn, W.; McMillan, B. A.; Raynor, M.; Shearer, B. G.; Tiffany, C.; Wilkins, D. E. N-(Fluorenyl-9-methoxycarbonyl) amino acids, a class of anti-inflammatory agents with a different mechanism of action. *Proc. Natl. Acad. Sci. U. S. A.* **1991**, *88*, 355.
- (12) Yang, Z.; Gu, H.; Zhang, Y.; Wang, L.; Xu, B. Small molecule hydrogels based on a class of anti-inflammatory agents. *Chem. Commun.* **2004**, 208–209.
- (13) Esch, J. H.; Schoonbeek, F.; Loos, M. D.; Veen, E. M.; Kellog, R. M.; Feringa, B. L. Low Molecular weight Gelators for Organic solvents. In *Supramolecular Science: Where It Is and Where It Is Going*; Ungaro, R., Dalcanele, R., Eds.; NATO ASI Series C; 1999; Vol. 527, pp 233–259.
- (14) Chen, Q.; Lv, Y.; Zhang, D.; Zhang, G.; Liu, C.; Zhu, D. Cysteine and pH-Responsive Hydrogel Based on a Saccharide Derivative with an Aldehyde Group. *Langmuir* **2010**, *26*, 3165–3168.
- (15) Zhou, Y.; Yi, T.; Li, T.; Zhou, Z.; Li, F.; Huang, W.; Huang, C. Morphology and Wettability Tunable Two-Dimensional Superstructure Assembled by Hydrogen Bonds and Hydrophobic Interactions. *Chem. Mater.* **2006**, *18*, 2974–2981.
- (16) Xiao, S.; Zou, Y.; Yu, M.; Yi, T.; Zhou, Y.; Li, F.; Huang, C. A photochromic fluorescent switch in an organogel system with non-destructive readout ability. *Chem. Commun.* **2007**, 4758–4760.
- (17) Bardelang, D. Ultrasound induced gelation: a paradigm shift. *Soft Matter* **2009**, *5*, 1969–1971.
- (18) Komiya, N.; Muraoka, T.; Iida, M.; Miyayama, M.; Takahashi, K.; Naota, T. Ultrasound-Induced Emission Enhancement Based on Structure-Dependent Homo- and Heterochiral Aggregations of Chiral Binuclear Platinum Complexes. *J. Am. Chem. Soc.* **2011**, *133*, 16054–16061.
- (19) Isozaki, K.; Takaya, H.; Naota, T. Ultrasound-Induced Gelation of Organic Fluids with Metalated Peptides. *Angew. Chem., Int. Ed.* **2007**, *46*, 2855–2857.
- (20) Watson, T. Ultrasound in contemporary physiotherapy practice. *Ultrasonics* **2008**, *48*, 321–329.
- (21) Luque de Castro, M. D.; Priego-Capote, F. Ultrasound-assisted crystallization (sonocrystallization). *Ultrason. Sonochem.* **2007**, *14*, 717–724.
- (22) Eddingsaas, N. C.; Suslick, K. S. Mechanoluminescence: Light from sonication of crystal slurries. *Nature* **2006**, *444*, 163.
- (23) Suslick, K. S.; Flint, E. B. Sonoluminescence from non-aqueous liquids. *Nature* **1987**, *330*, 553–555.

- (24) Didenko, Y.; McNamara, W. B., III; Suslick, K. S. Molecular emission from single-bubble sonoluminescence. *Nature* **2000**, *407*, 877–879.
- (25) Flannigan, D. J.; Hopkins, S. D.; Camara, C. G.; Putterman, S. J.; Suslick, K. S. Measurement of Pressure and Density Inside a Single Sonoluminescing Bubble. *Phys. Rev. Lett.* **2006**, *96*, 204301.
- (26) Hickenboth, C. R.; Moore, J. S.; White, S. R.; Sottos, N. R.; Baudry, J.; Wilson, S. R. Biasing reaction pathways with mechanical force. *Nature* **2007**, *446*, 423–427.
- (27) Cravotto, G.; Cintas, P. Forcing and Controlling Chemical Reactions with Ultrasound. *Angew. Chem., Int. Ed.* **2007**, *46*, 5476–5478.
- (28) Naota, T.; Koori, H. Molecules That Assemble by Sound: An Application to the Instant Gelation of Stable Organic Fluids. *J. Am. Chem. Soc.* **2005**, *127*, 9324–9325.
- (29) Wang, C.; Zhang, D.; Zhu, D. A Low-Molecular-Mass Gelator with an Electroactive Tetrathiafulvalene Group: Tuning the Gel Formation by Charge-Transfer Interaction and Oxidation. *J. Am. Chem. Soc.* **2005**, *127*, 16372–16373.
- (30) Malicka, J. M.; Sandeep, A.; Monti, F.; Bandini, E.; Gazzano, M.; Ranjith, C.; Praveen, V. K.; Ajayaghosh, A.; Armaroli, N. Ultrasound Stimulated Nucleation and Growth of a Dye Assembly into Extended Gel Nanostructures. *Chem. - Eur. J.* **2013**, *19*, 12991–13001.
- (31) Yu, X.; Chen, L.; Zhang, M.; Yi, T. Low-molecular-mass gels responding to ultrasound and mechanical stress: towards self-healing materials. *Chem. Soc. Rev.* **2014**, *43*, 5346–5371.
- (32) Anderson, K. M.; Day, G. M.; Paterson, M. J.; Byrne, P.; Clarke, N.; Steed, J. W. Structure Calculation of an Elastic Hydrogel from Sonication of Rigid Small Molecule Components. *Angew. Chem., Int. Ed.* **2008**, *47*, 1058–1062.
- (33) Park, S. M.; Kim, B. H. Ultrasound-triggered water gelation with a modified nucleoside. *Soft Matter* **2008**, *4*, 1995–1997.
- (34) Wu, J.; Yi, T.; Shu, T. M.; Yu, M. X.; Zhou, Z. G.; Xu, M.; Zhou, Y. F.; Zhang, H. J.; Han, J. T.; Li, F. Y.; Huang, C. Ultrasound Switch and Thermal Self-Repair of Morphology and Surface Wettability in a Cholesterol-Based Self-Assembly System. *Angew. Chem., Int. Ed.* **2008**, *47*, 1063–1067.
- (35) Wang, Y.; Zhan, C.; Fu, H.; Li, X.; Sheng, X.; Zhao, Y.; Xiao, D.; Ma, Y.; Ma, J. S.; Yao, J. Switch from Intra- to Intermolecular H-Bonds by Ultrasound: Induced Gelation and Distinct Nanoscale Morphologies. *Langmuir* **2008**, *24*, 7635–7638.
- (36) Cravotto, G.; Cintas, P. Molecular self-assembly and patterning induced by sound waves. The case of gelation. *Chem. Soc. Rev.* **2009**, *38*, 2684–2697.
- (37) Bardelang, D.; Camerel, F.; Margeson, J. C.; Leek, D. M.; Schmutz, M.; Zaman, M. B.; Yu, K.; Soldatov, D. V.; Ziessel, R.; Ratcliffe, C. I.; Ripmeester, J. A. Unusual Sculpting of Dipeptide Particles by Ultrasound Induces Gelation. *J. Am. Chem. Soc.* **2008**, *130*, 3313–3315.
- (38) Zhang, Y.; Ding, H.; Wu, Y.; Zhang, C.; Bai, B.; Wang, H.; Li, M. Ultrasound-induced controllable morphology and growth dimension in a dihydrazide-based self-assembly system. *Soft Matter* **2014**, *10*, 8838–8845.
- (39) Maity, S.; Kumar, P.; Haldar, D. Sonication-induced instant amyloid-like fibril formation and organogelation by a tripeptide. *Soft Matter* **2011**, *7*, 5239–5245.
- (40) Yu, X.; Liu, Q.; Wu, J.; Zhang, M.; Cao, X.; Zhang, S.; Wang, Q.; Chen, L.; Yi, T. Sonication-Triggered Instantaneous Gel-to-Gel Transformation. *Chem. - Eur. J.* **2010**, *16*, 9099–9106.
- (41) Dou, C.; Li, D.; Gao, H.; Wang, C.; Zhang, H.; Wang, Y. Sonication-Induced Molecular Gels Based on Mono-Cholesterol Substituted Quinacridone Derivatives. *Langmuir* **2010**, *26*, 2113–2118.
- (42) Pan, S.; Luo, S.; Li, S.; Lai, Y.; Geng, Y.; He, B.; Gu, Z. Ultrasound accelerated gelation of novel L-lysine based hydrogelators. *Chem. Commun.* **2013**, *49*, 8045–8047.
- (43) Briggs, B. D.; Knecht, M. R. Nanotechnology Meets Biology: Peptide-based Methods for the Fabrication of Functional Materials. *J. Phys. Chem. Lett.* **2012**, *3*, 405–418.
- (44) Zhang, Y.; Gu, H.; Yang, Z.; Xu, B. Supramolecular Hydrogels Respond to Ligand–Receptor Interaction. *J. Am. Chem. Soc.* **2003**, *125*, 13680–13681.
- (45) Galler, K. M.; Aulisa, L.; Regan, K. R.; D'Souza, R. N.; Hartgerink, J. D. Self-Assembling Multidomain Peptide Hydrogels: Designed Susceptibility to Enzymatic Cleavage Allows Enhanced Cell Migration and Spreading. *J. Am. Chem. Soc.* **2010**, *132*, 3217–3223.
- (46) Slaughter, B. V.; Khurshid, S. S.; Fisher, O. Z.; Khademhosseini, A.; Peppas, N. A. Hydrogels in Regenerative Medicine. *Adv. Mater.* **2009**, *21*, 3307–3329.
- (47) Ghosh, A.; Dey, J. pH-Responsive and Thermoreversible Hydrogels of N-(2-hydroxyalkyl)-L-valine Amphiphiles. *Langmuir* **2009**, *25*, 8466–8472.
- (48) Patra, T.; Pal, A.; Dey, J. A Smart Supramolecular Hydrogel of N $\alpha$ -(4-n-Alkyloxybenzoyl)-L-histidine Exhibiting pH-Modulated Properties. *Langmuir* **2010**, *26*, 7761–7767.
- (49) Fan, J.; Zou, J.; He, X.; Zhang, F.; Zhang, S.; Raymond, J. E.; Wooley, K. L. Tunable mechano-responsive organogels by ring-opening copolymerizations of N-carboxyanhydrides. *Chem. Sci.* **2014**, *5*, 141–150.
- (50) Zou, J.; Zhang, F.; Chen, Y.; Raymond, J. E.; Zhang, S.; Fan, J.; Zhu, J.; Li, A.; Seetho, K.; He, X.; Pochan, D. J.; Wooley, K. L. Responsive organogels formed by supramolecular self assembly of PEG-*block*-allyl-functionalized racemic polypeptides into  $\beta$ -sheet-driven polymeric ribbons. *Soft Matter* **2013**, *9*, 5951–5958.
- (51) Ghosh, S.; Das Mahapatra, R.; Dey, J. Thermoreversible as Well as Thermoirreversible Organogel Formation by L-Cysteine-Based Amphiphiles with Poly(ethylene glycol) Tail. *Langmuir* **2014**, *30*, 1677–1685.
- (52) Dey, J.; Shrivastava, S. Can molecules with an anionic head and a poly(ethylene glycol) methyl ether tail self-assemble in water? A surface tension, fluorescence probe, light scattering, and transmission electron microscopic investigation. *Soft Matter* **2012**, *8*, 1305–1308.
- (53) Dey, J.; Shrivastava, S. Physicochemical Characterization and Self-Assembly Studies on Cationic Surfactants Bearing mPEG Tail. *Langmuir* **2012**, *28*, 17247–17255.
- (54) Ghosh, R.; Dey, J. Vesicle Formation by L-Cysteine-Derived Unconventional Single-Tailed Amphiphiles in Water: A Fluorescence, Microscopy, and Calorimetric Investigation. *Langmuir* **2014**, *30*, 13516–13524.
- (55) Ghosh, R.; Dey, J. Aggregation behavior of poly(ethylene glycol) chain-containing anionic amphiphiles: Thermodynamic, spectroscopic and microscopic studies. *J. Colloid Interface Sci.* **2015**, *451*, 53–62.
- (56) Fang, Y. *Thermodynamics - Fundamentals and Its Application in Science*; Morales Rodriguez, R., Ed.; 2012, Chapter 3, p 70; <http://dx.doi.org/10.5772/S2410>.
- (57) Kamlet, M. J.; Abboud, J. L. M.; Abraham, M. H.; Taft, R. W. Linear solvation energy relationships. 23. A comprehensive collection of the solvatochromic parameters,  $\pi^*$ ,  $\alpha$ , and  $\beta$ , and some methods for simplifying the generalized solvatochromic equation. *J. Org. Chem.* **1983**, *48*, 2877–2887.