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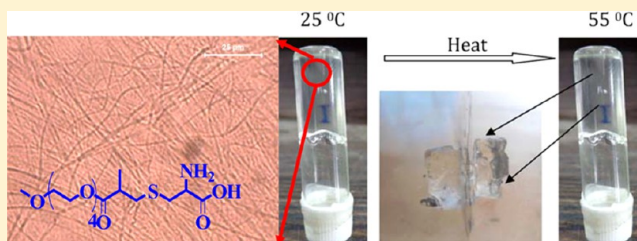
# Thermoreversible as Well as Thermoirreversible Organogel Formation by L-Cysteine-Based Amphiphiles with Poly(ethylene glycol) Tail

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## S Supporting Information

**ABSTRACT:** We report here the gelation behavior of two novel L-cysteine-based amphiphiles bearing a poly(ethylene glycol) tail. The amphiphiles were found to form transparent organogels in both apolar and aprotic polar solvents at reasonably low concentrations. In chloroform, dichloromethane, and benzene solvents, the organogels are formed at room temperature without the requirement of heating–cooling cycle due to strong hydrogen-bonding interaction between gelator molecules. The swelling kinetics, however, becomes faster on heating. Unlike most organogels of low-molecular-mass gelators, these organogels do not exhibit a gel-to-sol transition on heating but instead become rigid when heated. Surprisingly, in polar solvents, the gelation required a heating–cooling cycle, and the sol-to-gel transition was found to be reversible. The gelation abilities of the amphiphiles were correlated with the hydrogen-bonding parameters of the solvents. Intermolecular H-bonding interaction was found to be the major driving force for the organogelation. The morphology of the organogels was investigated by the use of optical as well as electron microscopy and was found to be dependent on the nature of solvent. The mechanical strengths of the organogels were studied by rheological measurements.



## INTRODUCTION

Supramolecular organogels are an important class of soft materials that can entrap a huge amount of organic liquids within the three-dimensional (3-D) network structure formed by the self-assembly of gelator molecules. In order to understand structure–property relationship in supramolecular gels, various low-molecular-weight gelators (LMWGs) of diverse molecular architectures have been studied in the past three decades.<sup>1–10</sup> Among these, amino acid-based amphiphilic LMWGs have attracted tremendous attention because of their facile synthesis and easy functionalization.<sup>11–28</sup> Further amino acid-based amphiphiles are biocompatible as well as biodegradable.<sup>29</sup> These amphiphilic molecules are known to self-associate in organic liquids through different noncovalent forces (e.g., van der Waals interactions,  $\pi$ – $\pi$  stacking, H-bonding, etc.) to form various nanostructures like ribbons, wires, and helical and twisted nanofibers.<sup>11–26</sup> It should be noted that in most of the amino acid-derived amphiphilic gelators, the acyl group is a hydrocarbon tail which is soluble in organic solvents. However, Dey and co-workers have shown that amphiphiles containing a poly(ethylene glycol) (PEG) tail can also self-assemble in water to form vesicles.<sup>30</sup> This, in contrast to literature reports, suggests that the PEG chain can play the role of a hydrophobic tail. Also, PEG-decorated amphiphilic polymers are known to be biocompatible.<sup>31</sup>

Among the natural amino acids, L-cysteine is an important essential amino acid. For example, S-allyl-L-cysteine is known to inhibit damage caused by oxidative stress in bovine endothelial

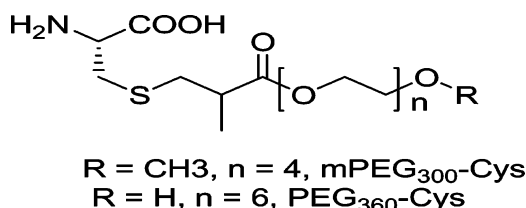
cells and also inhibits oxidation of low-density lipoprotein at an optimum concentration of 1 mM.<sup>32</sup> Therefore, attempts have been made to include L-cystein derivatives as one of the active ingredients in many pharmaceutical products. The *N,N'*-dibenzoylcysteine derivative has been shown to efficiently form hydrogels.<sup>33</sup> A cationic gemini surfactant based on L-cysteine has also been shown to form thermoreversible hydrogel.<sup>34</sup> The gelation of the aqueous L-cysteine/AgNO<sub>3</sub> system in the presence of different electrolytes has been reported.<sup>35,36</sup> More recently, our group has also designed a new L-cysteine-based amphiphile, L-(3-alkylcarbamoysulfanyl)-2-(3-alkylurido)-propionic acid, that produced organogels in pure organic solvents as well as in ethanol/water mixtures.<sup>37</sup> Although there are many reports on physical gelation by LMWGs, it is still not completely known the relationship between the molecular structure and gelation behavior.

Considering these, we have designed and synthesized two new amphiphiles, mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys (see Chart 1 for structures), by thiol–ene “click” chemistry using L-cysteine and poly(ethylene glycol) methacrylate (MW = 360) or poly(ethylene glycol) methyl ether methacrylate (MW = 300).<sup>38</sup> The amphiphiles, though structurally very similar, have different molecular weights. In contrast to *N*-acyl-amino acid gelators,<sup>11,16–20,39–44</sup> these amphiphiles have PEG chain

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**Chart 1. Chemical Structures of mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys Amphiphiles**

and have no amide functionality that is known to be responsible for gelation. Here we demonstrate that amino acid-derived amphiphiles with PEG tail can also self-assemble in organic liquids, producing organogels. The gels were characterized by a number of techniques including NMR spectroscopy, microscopy, and rheology.

## EXPERIMENTAL SECTION

**Materials.** Poly(ethylene glycol)methyl ether methacrylate (MW 300), poly(ethylene glycol) methacrylate (MW 360), and L-cysteine (99%) were obtained from Sigma-Aldrich (Bangalore, India) and were used without further purification. Triethylamine, TEA (SRL), was procured locally and was dried and distilled before use. Chloroform (CF), dichloromethane (DCM), 1,2-dichloroethane (DCE), benzene (BZ), 1,4-dioxane (DX), nitrobenzene (NB), dimethylformamide (DMF), and propylene carbonate (PC) were of good quality and were purified and dried whenever necessary.

**Synthesis.** Compound A was synthesized from poly(ethylene glycol)methyl ether methacrylate and L-cysteine by thiol-ene “click” chemistry following a method reported in the literature.<sup>38</sup> Briefly, poly(ethylene glycol)methyl ether methacrylate (2.1 g, 7 mmol) was reacted with L-cysteine (1.275 g, 10.5 mmol) in methanol at room temperature for 6 h in the presence of TEA. The product was obtained as white solid after evaporation of the solvent. To remove unreacted materials, the solid compound was dissolved in water and then reprecipitated by adding dry acetone. The compounds were isolated as hygroscopic solids. The chemical structure of the compounds was determined by FT-IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectroscopy. Representative FT-IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra of both mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys have been depicted in Figures S1–S8 of the Supporting Information. The spectral data are also included in the Supporting Information. The presence of strong peaks near 3411 cm<sup>−1</sup> (N–H and O–H stretching), 1725 cm<sup>−1</sup> (C=O stretching), and 1638 cm<sup>−1</sup> (N–H bending) in the FTIR spectrum of mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys (Figures S1 and S2) clearly suggests that the amphiphiles are isolated in the neutral form. This is also supported by the <sup>13</sup>C NMR spectra (Figures S5 and S8) which exhibit a peak near 172.3 ppm, corresponding to the undissociated COOH group. The amphiphilic molecules are therefore expected to be present in the neutral form in organic solvents. However, in D<sub>2</sub>O solvent, the <sup>13</sup>C peak of the COOH group shifts to 170.2 ppm (Figure S6), indicating the existence of the zwitterionic form.

**Methods and Instrumentation.** Carbon, hydrogen, and nitrogen contents were analyzed using a PerkinElmer 2400 Series II CHN analyzer. The measurements of optical rotations were performed on a Jasco P-1020 digital polarimeter. The FT-IR spectra were measured with a PerkinElmer (Model Spectrum Rx I) spectrometer. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on an AVANCE DAX-400 (Bruker, Sweden) 400 MHz NMR spectrometer in CDCl<sub>3</sub> or D<sub>2</sub>O solvent. All measurements were done at 298 K unless otherwise mentioned.

A Jasco J-810 spectropolarimeter was used to measure the circular dichroism (CD) spectra using quartz cells of 1 mm path length. Each spectrum was baseline corrected using appropriate reference solvent.

The gelation test was performed in 4 mL screw-capped vials containing 50 mg of the gelator under study. The compounds were dissolved in organic solvents at an elevated temperature and then were

left for cooling at 298 K in a thermostating water bath. The gelation was confirmed by the resistance to flow upon inversion of the vial.

The light micrographs were taken on a Leica-DMRXP microscope. The images taken by a video camera were analyzed by Leica Qwin software. For FESEM, the gel cast film on an aluminum foil was first air-dried at room temperature and stored in desiccators until before measurement. A layer of gold was sputtered on top, and the specimen was examined on a field emission scanning electron microscope (FESEM, Zeiss, Supra-40) operating at 5–10 kV.

Rheology measurements were performed on a Bohlin Gemini-200, (Malvern, UK) rheometer using parallel-plate (PP-20) geometry with a constant tool gap of 100 μm. The rheometer is fitted with a solvent trap and a Peltier device that controls temperature within 298 ± 0.1 K. An equilibration time of 30 min was allowed before measurement for each sample. All measurements were performed on matured gels. Oscillatory stress sweeps were measured at a constant frequency of 1 Hz. The frequency sweep measurements of storage modulus (*G'*) and loss modulus (*G''*) were performed at a constant stress of 2000, 30, and 75 Pa in CF, DX, and DMF, respectively, for PEG<sub>360</sub>-Cys and 80, 3, and 120 Pa in CF, DX, and BZ, respectively, for mPEG<sub>300</sub>-Cys.

## RESULTS AND DISCUSSION

**Gelation Behavior.** The gelation test was performed in various organic solvents of different polarities. The results are summarized in Table 1. The amphiphiles PEG<sub>360</sub>-Cys and

**Table 1. Critical Gelation Concentration (CGC) of PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys in Organic Solvents at 25 °C**

solvent	CGC (±0.2%, w/v)	
	PEG <sub>360</sub> -Cys	mPEG <sub>300</sub> -Cys
CF	5.2	5.3
DCM	3.8 <sup>a</sup>	2.0 <sup>a</sup>
DCE	3.0	3.8
TCM	I	I
CDS	I	I
DX	1.5	0.9 <sup>d</sup>
THF	Sw <sup>c</sup>	S
BZ	I	3.1
TL	I	Sw
NB	Sw	6.6 <sup>b</sup>
ACN	I	I
DMF	2.6 (71 °C)	P
DMSO	S	S
PC	3.9	I
MeOH	S	S

<sup>a</sup>MGC was measured without a heating-cooling cycle. <sup>b</sup>Gelation occurred after 18 h; S = soluble; I = insoluble; P = precipitate. <sup>c</sup>Sw = swelling. <sup>d</sup>Opaque.

mPEG<sub>300</sub>-Cys, however, were observed to produce organogels in chlorinated hydrocarbons (e.g., chloroform (CF), dichloromethane (DCM), and 1,2-dichloroethane (DCE)), benzene (BZ), 1,4-dioxane (DX), nitrobenzene (NB), dimethylformamide (DMF), and propylene carbonate (PC). Despite structural similarity, PEG<sub>360</sub>-Cys failed to gelate BZ. On the other hand, while PEG<sub>360</sub>-Cys can gelate DMF and PC, the mPEG<sub>300</sub>-Cys amphiphile remained insoluble in these solvents. However, both amphiphiles failed to gelate any protic solvent, such as methanol (MeOH). All organogels, except that of mPEG<sub>300</sub>-Cys in DX solvent, were observed to be transparent. Interestingly, in CF, DCM, and benzene the organogels are formed spontaneously at room temperature (25 °C) with gelation time of ca. 14 h in CF, ca. 7 h in DCM, and ca. 24 h in benzene for PEG<sub>360</sub>-Cys gelator. The gelation time, however,

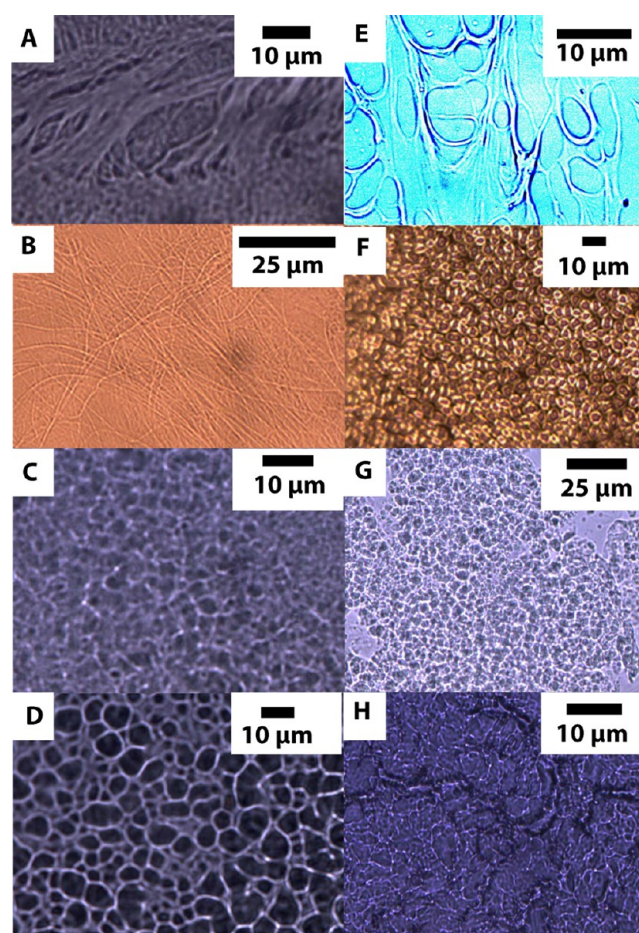


was found to be less (5 h in DCM) with mPEG<sub>300</sub>-Cys gelator. Also, the gelation time was observed to decrease with the increase of gelator concentration as well as with the increase of temperature. For example, the CF organogels of mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys are produced within 30 min and 5 h, respectively, at 37 °C. It is important to note that the CF organogels of mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys are produced almost immediately when heated above 50 °C; the gelation occurred even under the hot conditions. Similar behavior was also observed in DCM and BZ solvent. In other words, heat-set gels were formed in CF, DCM, and BZ solvents. In contrast, gelation in DCE, NB, DX, PC, and DMF required a heating-cooling cycle, and the resulting organogels were found to be thermoreversible. It is worth mentioning here that gelation in CF solvent could also be achieved in the presence of 1% (w/v) ibuprofen, a nonsteroidal anti-inflammatory drug, but at the cost of increased gelation time.

The gelation abilities of the amphiphiles in different solvents can be compared by using the values of critical gelation concentration (CGC) listed in Table 1. The data presented in the table suggest that the amphiphiles have CGC values <7% (w/v), indicating reasonably good gelation ability. In non-hydrogen-bonding solvents the CGC values are less compared to those in H-bonding solvents. CF, being a weak H-bond donor solvent, the CGC values of both amphiphiles are higher than those in DCM and DCE solvents. The gelation abilities of PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys were observed to be highest in DX, which is a weak H-bond acceptor. Increased H-bond accepting capacity of the solvent was found to decrease the gelation ability as the CGC values increased in the order DX < DMF < PC < NB. The effect of H-bonding on gelation is elaborated below in a separate section. It is observed that despite different PEG chain lengths, the gelation abilities of both PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys in a given solvent are similar.

**Optical Microscopy.** The morphology of the organogels was studied by optical microscopy (OM). Figure 1 shows the OM images of the mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys organogels in different solvents. The OM images, except that of PEG<sub>360</sub>-Cys in DCM (F), clearly exhibit fibrillar aggregates of high aspect ratio, forming 3-D network structures. The microstructures of the DCM (F) organogel of PEG<sub>360</sub>-Cys appear like small bowls. The resolution of the OM images being poor details microstructures could not be seen. In fact, no microstructures could be observed in the OM pictures of the organogels of PEG<sub>360</sub>-Cys amphiphile in DMF and PC solvents. This may be due to similarity of the refractive index values of the aggregates and the solvent.

**Electron Microscopy.** The field emission scanning electron microscopic (FESEM) pictures (Figure 2) of most of the air-dried organogels also show lamellar structures of high aspect ratio. The long ribbon-like aggregates might have formed through H-bonding interaction of the gelator molecules and one-dimensional growth as discussed below. However, the CF organogels of both mPEG<sub>300</sub>-Cys (B) and PEG<sub>360</sub>-Cys (G) amphiphiles have leaf-like flat lamellar structures of low aspect ratio and are different from the corresponding OM images. It appears that the lamellar aggregates in CF organogels of mPEG<sub>300</sub>-Cys have aspect ratios higher than those of PEG<sub>360</sub>-Cys. The morphology of the aggregates PEG<sub>360</sub>-Cys in DMF (K) and PC (L) are also different from those in the other solvents. The amphiphile in DMF forms flat disk-like aggregates while in PC solvent it forms long and thin fibers.

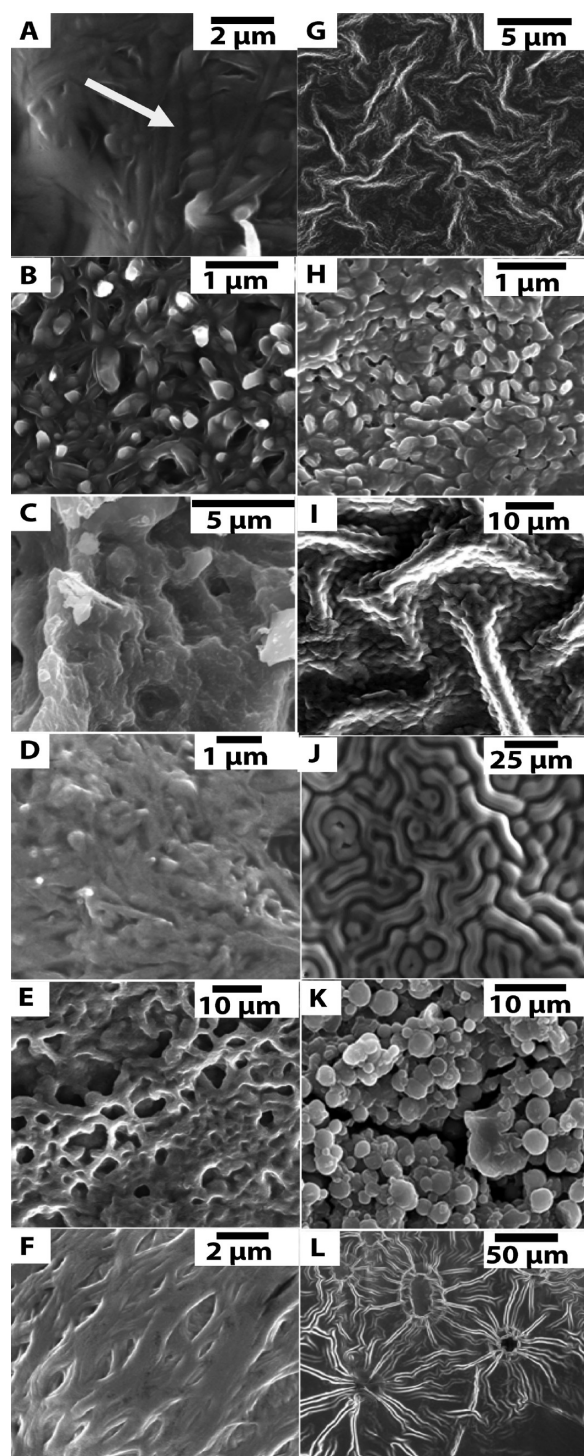


**Figure 1.** Optical microscopic images of the organogels of mPEG<sub>300</sub>-Cys in (A) DCM (2.0%), (B) CF (5.3%), (C) DX (0.9%), (D) BZ (3.1%), and (E) NB (6.6%) and of PEG<sub>360</sub>-Cys in (F) DCM (3.8%), (G) CF (5.2%), and (H) DX (1.5%).

The FESEM image of the DX organogel (J) of PEG<sub>360</sub>-Cys, however, is quite different from those of other organogels in the sense that the fibrils are not entangled with each other, but instead they exhibit branching of the fibres. It appears to us that the fibers are made of tubular aggregates which might have formed by either twisting or rolling of the lamellar structures. Such type of aggregate formation in water by amino acid-based amphiphiles has also been reported by others.<sup>45</sup> Indeed, the existence of helical or twisted ribbons (indicated by arrow) is observed in the FESEM image (A) of the DCM organogel of mPEG<sub>300</sub>-Cys amphiphile. The formation of such chiral aggregates is expected because the headgroup of the amphiphiles (L-cystein) is chiral. The existence of the chiral aggregates in the gel matrix is also suggested by the circular dichroism (CD) spectra of the organogel as discussed below.

**Circular Dichroism Spectra.** Since these amphiphiles have chiral centers, we have also measured CD spectra of the organogels. CD spectra of the organogels in DCM (Figure 3a) can be compared with those of molecular solutions in MeOH solvent (Figure 3b). A positive and a negative Cotton effect at ca. 280 and 235 nm, respectively, and a crossover at ca. 250 nm can be observed in the CD spectrum of DCM organogel of mPEG<sub>300</sub>-Cys. The spectrum is different from its solution spectrum in MeOH which shows one peak at ca. 230 nm and another very weak peak (hump) at around 280 nm corresponding to free molecules. This means that the CD





**Figure 2.** FESEM images of the organogels of (i) mPEG<sub>300</sub>-Cys in DCM (A), CF (B), DCE (C), DX (D), BZ (E), and NB (F) and (ii) PEG<sub>360</sub>-Cys in DCM (G), CF (H), DCE (I), DX (J), DMF (K), and PC (L).

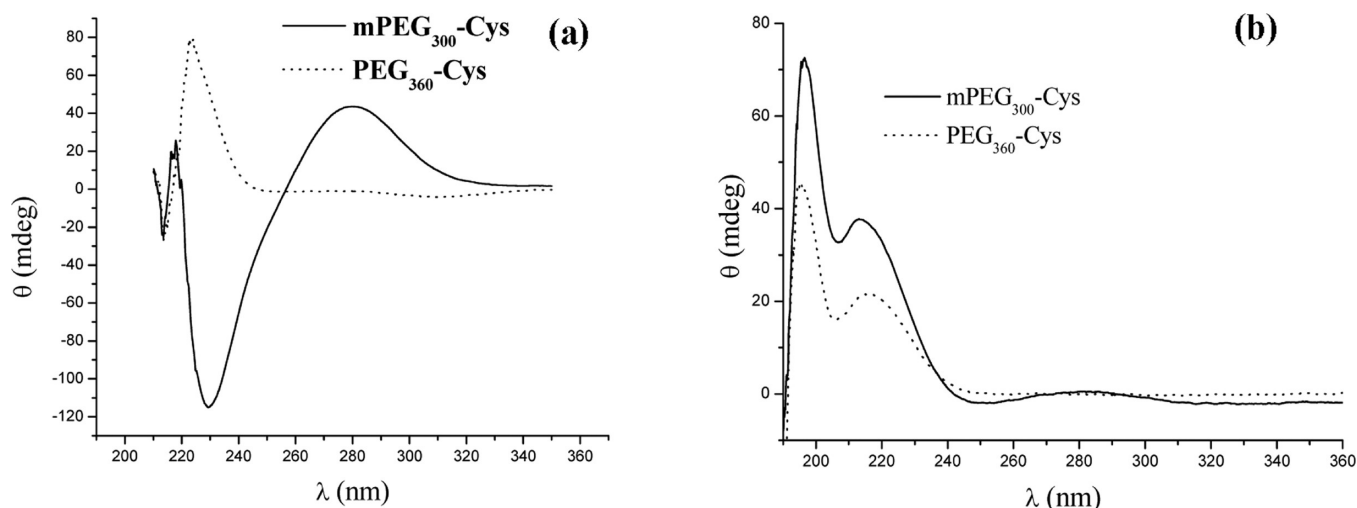
spectrum of the mPEG<sub>300</sub>-Cys organogel is due to supra-molecular chirality. This also suggests formation of chiral nanofiber (helical) in mPEG<sub>300</sub>-Cys organogel. We have also measured the temperature-dependent CD spectra of DCM organogel (Figure S9). As the gel does not melt at 35 °C, we could not get any change in the CD spectra. Since organogels in other solvents do not melt when heated, we were unable to perform variable temperature CD study. The CD spectrum of

the PEG<sub>360</sub>-Cys organogel, however, does not exhibit any Cotton effect. The positive band at ca. 230 nm closely similar to the CD spectrum in MeOH solution is due to molecular chirality, indicating formation of only achiral (straight) nanofibers. This means that the orientation of the gelator molecules in mPEG<sub>300</sub>-Cys organogel is different from that of PEG<sub>360</sub>-Cys gelator. This is very interesting because both amphiphiles have the same chiral headgroup. This difference in behavior may be due either to the  $-OCH_3$  group at the end of the PEG chain of mPEG<sub>300</sub>-Cys gelator molecule or to the longer and more polar PEG chain of PEG<sub>360</sub>-Cys gelator.

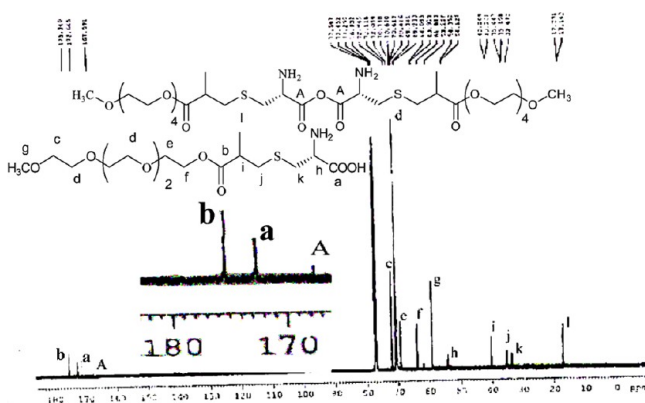
**Thermal Stability.** It should be noted that the organogels in chlorinated hydrocarbon solvents (except DCE) as well as in BZ do not exhibit gel-to-sol transition even when heated at the boiling point of the solvent (Figure S10). In fact, the gels become so strong on heating that they can be cut into small pieces (see inset of Figure S10). This means that these organogels are thermoirreversible in nature. The reverse thermoresponsiveness was found to be due to anhydride formation. The anhydride formation through elimination of water upon heating is demonstrated by the  $^{13}C$  NMR spectrum (Figure 4) of the heated BZ organogel of mPEG<sub>300</sub>-Cys in  $CDCl_3$  solvent. When benzene completely evaporated upon heating, we redissolved the sample again in  $CDCl_3$  solvent and measured the  $^{13}C$  NMR spectrum. It can be observed that a new peak at 167.591 ppm corresponding to a carbon of an anhydride appears along with the  $-COOH$  carbon peak. Therefore, it can be concluded that the  $-COOH$  group of the amino acid head transforms into the corresponding anhydride upon heating (see Figure 5b), which in turn stabilizes the aggregates and hence the 3-D network structure. The formation of anhydride prevents melting of the organogel.

**Driving Force for Gelation.** The nature of the driving force for organogelation can be understood by comparing gelation efficiency in different solvents. On the other hand, the gelation efficiency of the gelator can be judged by the values of CGC in different solvents. The CGC values of the amphiphiles in different solvents are listed in Table 1. The organogels formed in CF, DCM, and DCE are either transparent or translucent. It is observed that for both gelators the CGC value decreases in the order  $CF > DCM > DCE$ . This can be attributed to the H-bond donating ability ( $\alpha$ )<sup>46</sup> of the solvent molecules which decreases in the same order  $CF > DCM > DCE$ . Since the H-bonded structure of the gelators is more stable in non-hydrogen-bonding solvents, the gelation ability of the amphiphiles is higher in these solvents. In H-bond donor/acceptor solvents, both gelators have greater values of CGC. Thus, DX being weak H-bond acceptor has the lowest CGC value. On the other hand, NB being strong H-bond acceptor solvent has the highest CGC value. The gelation ability of the gelators is correlated with the H-bond acceptor ( $\beta$ ) and donor ( $\alpha$ ) parameters<sup>46</sup> in Figure 6. As observed, the CGC value linearly increases with the  $\alpha$  parameter in the case of PEG<sub>360</sub>-Cys gelator, which has a free  $-OH$  group at the end the PEG chain. Although no such correlation was observed with PEG<sub>360</sub>-Cys gelator, the CGC value increased with the  $\alpha$  parameter in the case of mPEG<sub>300</sub>-Cys gelator. Therefore, it can be concluded that H-bonding interaction of the solvent molecules with the  $-OH$  as well as with the cysteine headgroup affects gelation.

The role of H-bonding is further demonstrated by the failure to gelate the solvent in the presence of a small volume (8–10  $\mu L/mL$ ) of methanol (MeOH) or tetrabutylammonium

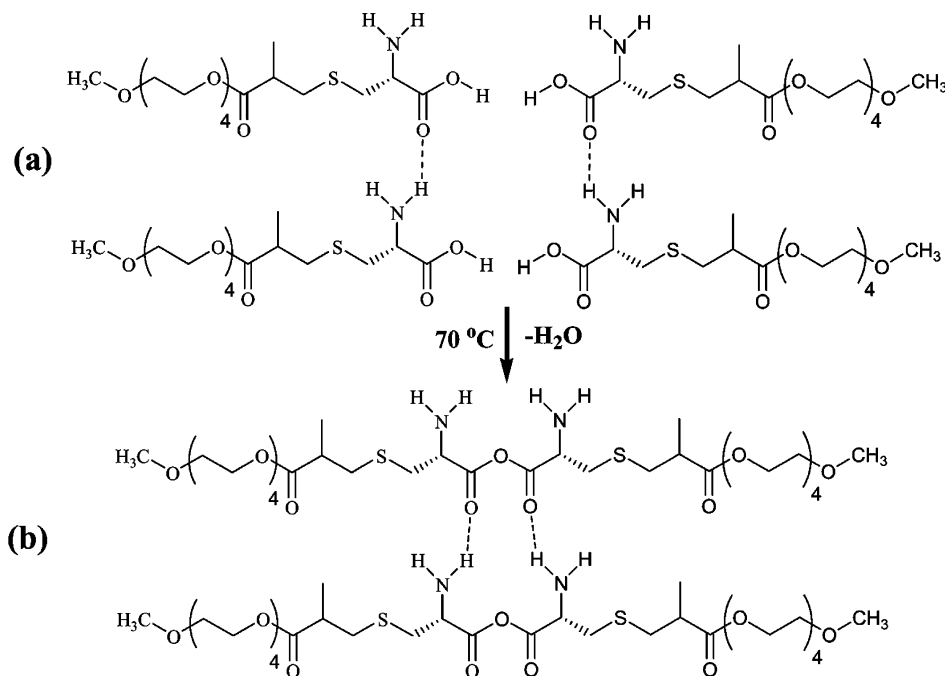


**Figure 3.** CD spectra of the (a) DCM organogels (38 mg/mL) and (b) MeOH solution (2 mg/mL) of PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys at 298 K.

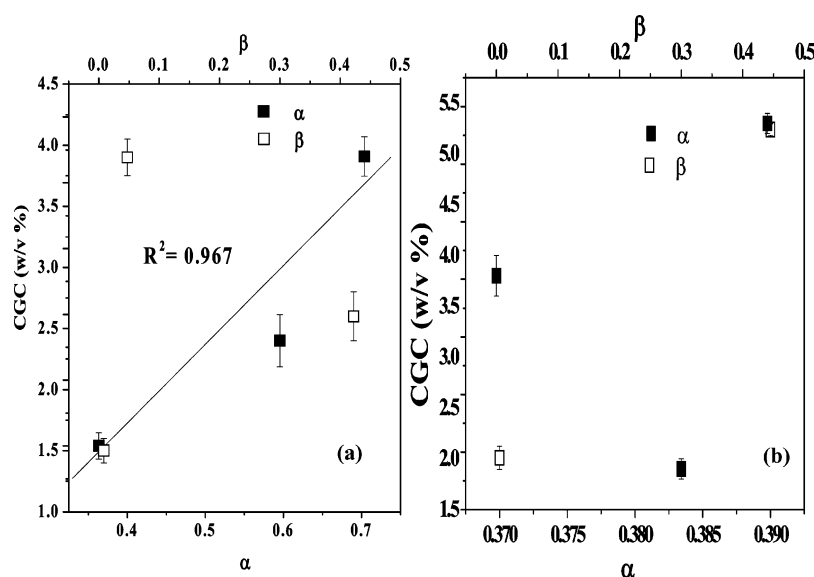


**Figure 4.** <sup>13</sup>C NMR spectrum of mPEG<sub>300</sub>-Cys powder (obtained after evaporation of benzene) in CDCl<sub>3</sub> solvent at 25 °C.

fluoride (TBAF). The presence of MeOH partially disrupts the interactions between gelator molecules by creating H-bonding with the latter, thereby inhibiting gelation. We have measured FTIR spectra (see Figure S3a,b) of mPEG<sub>300</sub>-Cys in dilute solution as well as in the gel state in DCE solvent. The FT-IR spectrum of the organogel shows peaks at 1618 and 1724 cm<sup>-1</sup> which are red-shifted in comparison to the corresponding vibration (1636 and 1735 cm<sup>-1</sup>) observed in dilute solution, suggesting H-bonding interactions between -COOH and -NH<sub>2</sub> groups of adjacent molecules. Strong H-bonding is further shown by the broadening of the peak due to O-H (-COOH group) stretching vibration in the gel state. The C-H (-CH<sub>2</sub>O) stretching vibration is also observed to shift toward lower wavenumber, indicating van der Waals interactions among PEG chains in the gel state. It appears that both -NH<sub>2</sub> and -COOH groups of the amino acid headgroup are involved in the H-bonding interaction as shown



**Figure 5.** Schematic presentation of the H-bonding interaction between gelator molecules (a) at room temperature and (b) at 70 °C.



**Figure 6.** Plot of CGC vs H-bonding parameters,  $\alpha$  and  $\beta$ , for (a) PEG<sub>360</sub>-Cys and (b) mPEG<sub>300</sub>-Cys gelators.

in Figure 5. This is indicated by the absence of peaks corresponding to  $-\text{NH}_2$  and  $-\text{COOH}$  protons in the  $^1\text{H}$  NMR spectrum (Figure S4) of mPEG<sub>300</sub>-Cys in  $\text{CDCl}_3$  solvent. It should also be noted that the peak due to  $-\text{CH}_2-$  protons of the PEG chain is broadened, indicating strong interaction among PEG chains within the aggregate. Although H-bonding interaction is the major driving force for the gelation process, the importance of van der Waals forces that enhance interaction between PEG chains in the aggregate cannot be neglected. This is confirmed by the fact that in polar and H-bonding solvents the organogelation required heating. Since upon heating the PEG chain becomes desolvated, van der Waals interactions are enhanced and thus facilitate aggregation.

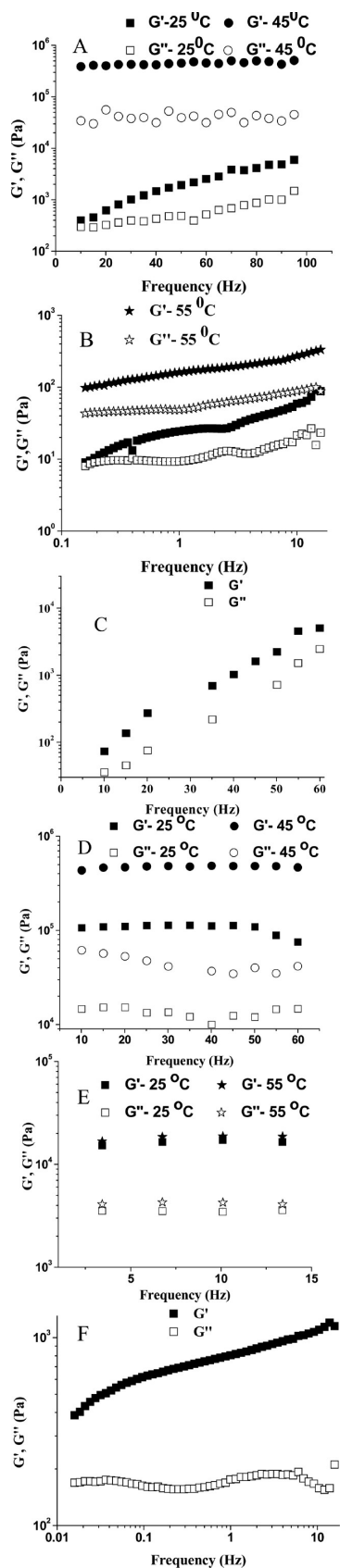
**Viscoelastic Behavior.** In order to measure mechanical strength, we performed rheology measurements of the organogels of both molecular gelators in different solvents and also at different temperatures. The variation of storage ( $G'$ ) and loss ( $G''$ ) moduli of the organogels of mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys with the oscillation frequency ( $f$ ) at two different temperatures (25, 45, or 55 °C) is shown in Figure 7. It can be seen that at any given temperature both  $G'$  and  $G''$  values of the organogels, except those in benzene, are nearly independent of frequency in the case of PEG<sub>360</sub>-Cys organogel, which is characteristic of gel structure. In the case of benzene gel, the linear dependence of  $G'$  and  $G''$  values on the frequency may be due to the difference in morphology of the aggregates. Indeed, the  $G'$  value is not large in comparison to  $G''$  value. On the other hand, for the other organogels, the  $G'$  value at any frequency is greater than  $G''$  value by 3 orders of magnitude, which implies elastic nature of the organogels. Further, it can be observed that the  $G'$  value of the organogels of both mPEG<sub>300</sub>-Cys and PEG<sub>360</sub>-Cys increases with increasing temperature, suggesting increase of mechanical strength upon heating. This is due to the decrease of CGC value as a consequence of stronger H-bond formation which leads to formation of fibers of high aspect ratio. The enhanced entanglement of the fibers thus formed increases rigidity of the solvent and hence the mechanical strength.

We also measured the variation of  $G'$  and  $G''$  as a function of shear stress ( $\sigma$ ) at room temperature as shown in Figure 8. It can be observed that above a critical  $\sigma$ -value the gel starts to

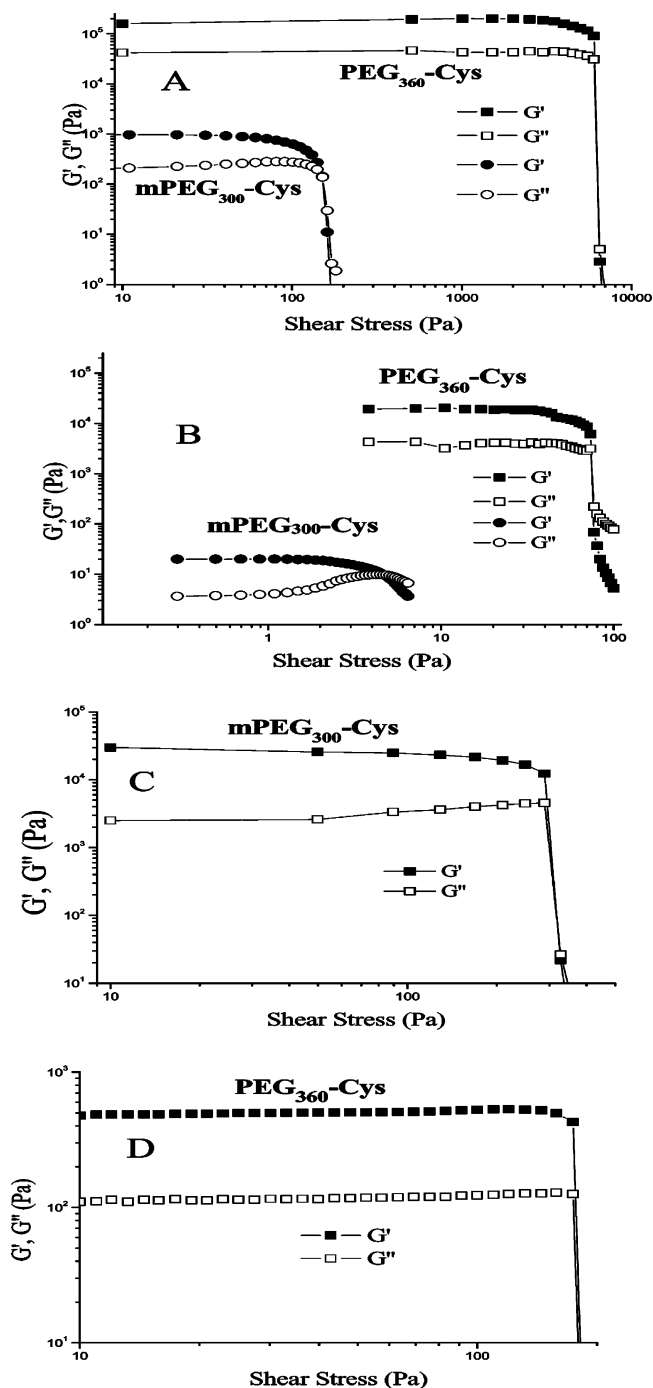
flow as indicated by the sharp fall of both  $G'$  and  $G''$  values. This critical stress is referred to as yield stress ( $\sigma_y$ ). In CF solvent, the  $\sigma_y$  value of the PEG<sub>360</sub>-Cys organogel (ca. 6000 Pa) is greater than that of mPEG<sub>300</sub>-Cys (ca. 150 Pa). This means that the former gel is much stronger than the latter gel at room temperature, which can be attributed to longer PEG chain of PEG<sub>360</sub>-Cys. A similar behavior is also observed with the organogels in DX solvent. It is important to note that the  $\sigma_y$  values of the DX organogel of PEG<sub>360</sub>-Cys (ca. 80 Pa) as well as of mPEG<sub>300</sub>-Cys (ca. 6 Pa) are much weaker than the corresponding gel in CF solvent. This must be due to the H-bond acceptor property of DX which inhibits one-dimensional growth of aggregates through H-bonding interaction. It should be noted that the  $\sigma_y$  value of the benzene organogel (ca. 300 Pa) of mPEG<sub>300</sub>-Cys is greater than that of CF organogel (ca. 150 Pa). This is consistent with the different morphology of the supramolecular gels.

## CONCLUSIONS

In summary, we have developed two novel and inexpensive amphiphiles, PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys, bearing a poly(ethylene glycol) tail that produce organogels in nonpolar as well as non-hydroxy polar organic solvents. Failure to gelate organic solvents in the presence of H-bonding additives, such as MeOH or TBAF, confirmed H-bonding as the major driving force for the gelation. It is important to note that in nonpolar solvents, such as CF, DCM, and benzene, the organogels are formed without the requirement of a heating–cooling cycle. To the best of our knowledge, this is the first report on organogel formation by low-molecular-weight amphiphilic gelators bearing a PEG tail without the requirement of heating–cooling cycle. However, the gelation process becomes faster with increasing temperature due to stronger H-bonding and van der Waals interactions. Consequently, the organogels of both PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys become much stronger upon heating above room temperature. At room temperature, however, the CF organogel of PEG<sub>360</sub>-Cys is stronger than mPEG<sub>300</sub>-Cys organogel which is associated with the H-bonding interaction due to the terminal  $-\text{OH}$  group of the former gelator. Because of the stronger H-bonding interaction at higher temperatures, the gel-to-sol transition temperature of



**Figure 7.** Variation of  $G'$  and  $G''$  vs frequency ( $f$ ) for mPEG<sub>300</sub>-Cys organogels in (A) CF, (B) DX, and (C) BZ and for PEG<sub>360</sub>-Cys organogels in (D) CF, (E) DX, and (F) DMF solvents at different temperatures.



**Figure 8.** Variation of  $G'$  and  $G''$  vs shear stress ( $\sigma$ ) of PEG<sub>360</sub>-Cys (77 mg/mL) organogels in (A) CF, (B) DX, and (C) mPEG<sub>300</sub>-Cys in BZ and (D) PEG<sub>360</sub>-Cys in DMF.

the organogels was observed to be very high. In fact, in chlorinated hydrocarbons, the organogels were not observed to melt even at the boiling point of the solvent as a result of anhydride formation. The morphologies of the organogels of both PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys were observed to be dependent on the nature of the solvent. Unlike molecular solutions, the organogel fibers of mPEG<sub>300</sub>-Cys exhibit supramolecular chirality. The absence of any supramolecular chirality of the gel fibers of PEG<sub>360</sub>-Cys gelator is due to the strong intermolecular H-bonding interaction of the terminal -OH group in the PEG tail.



Since the organogels could be produced in the presence of drug additives such as ibuprofen, they can find potential applications in drug delivery. For example, the CF organogel can be used as injectable biodegradable and biocompatible in-situ-forming drug delivery system, since the presence of alcohol partially disrupts the interactions between gelator molecules, which maintains the formulation in a sol state and allows injection of the formulations at room temperature.<sup>47</sup> Upon parenteral injection, ethanol will gradually diffuse into the surrounding aqueous environment and the gelator molecules will self-assemble to create 3D network at the body temperature, thus causing the gelling of chloroform again. With time, the implant formed in situ will slowly degrade in vivo and will release their payload. Therefore, the organogels have the potential for applications as parenteral implants for the systemic, sustained delivery of low-molecular-weight hydrophobic drugs, or lubricants between bone junctions for curing rheumatism. Further research work will focus on gelation behavior of PEG<sub>360</sub>-Cys and mPEG<sub>300</sub>-Cys in biocompatible solvents and also on the effect of solvent on the morphology of the supramolecular aggregates forming the organogels.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

Details regarding the IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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