

Water-Induced Physical Gelation of Organic Solvents by *N*-(*n*-Alkylcarbamoyl)-L-alanine Amphiphiles

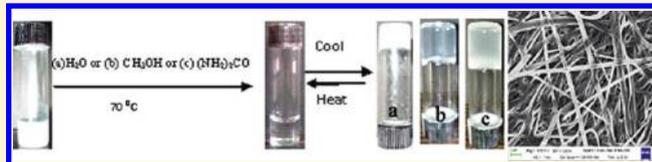
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Supporting Information

ABSTRACT: A series of amino acid-based gelators *N*-(*n*-alkylcarbamoyl)-L-alanine were synthesized, and their gelation abilities in a series of organic solvents were tested. No gelation was observed in pure solvents employed. All the amphiphilic molecules were found to form stable organogels in the solvents in the presence of a small amount of water, methanol, or urea.

The volume of solvent gelled by a given amount of the gelator was observed to depend upon the volume of added water. The gelation behavior of the amphiphiles in a given solvent containing a known volume of water was compared. The effects of chirality and substitution on the acid group on the gelation ability were examined. Although the corresponding *N*-(*n*-tetradecylcarbamoyl)-DL-alanine was found to form only weak organogel in pure solvents, the achiral amphiphilic compound *N*-(*n*-tetradecylcarbamoyl)- β -alanine, however, did not form gel in the absence of water. The methyl ester of *N*-(*n*-tetradecylcarbamoyl)-L-alanine was also observed to form gels in the same solvents, but only in the presence of water. The organogels were characterized by several techniques, including ^1H NMR, Fourier transform IR, X-ray diffraction, and field emission scanning electron microscopy. The thermal and rheological properties of the organogels were studied. The mechanical strength of the organogel formed by *N*-(*n*-tetradecylcarbamoyl)-DL-alanine was observed to increase upon the addition of water. It was concluded that water-mediated intermolecular hydrogen-bonding interaction between amphiphiles caused formation of supramolecular self-assemblies.



INTRODUCTION

Low-molecular-weight organogelators (LMOGs) have received considerable attention over recent decades^{1–10} because they exhibit interesting self-assembly phenomena, forming three-dimensional (3-D) networks. The interest in this area is driven by their unique supramolecular architectures and wide-ranging applications in industrial fields including drug delivery,¹¹ tissue engineering,¹² synthesis of nanomaterials and devices,¹³ sensing and soft lithography.¹⁴ The self-assembly of LMOGs is often driven by one or more noncovalent forces, such as dipolar interaction, van der Waals forces, hydrogen-bonding (H-bonding), and metal-coordination bonds.¹⁵ The self-assembly leads spontaneously to formation of one-dimensional (1-D) aggregates, which either by physical cross-linking or by entanglement produce 3-D network structures that entrap and immobilize a large volume of solvent in the compartments of self-assembled fibrillar networks (SAFINs) having a large solid–liquid interface area by surface tension and capillary forces.¹⁶ Thus gel formation requires a suitable organogelator that can form aggregates with high aspect ratio (i.e., 1-D) at a very low concentration.

About a decade ago, Bhattacharya and co-workers reported gelation of a series of organic solvents by optically pure *N*-alkanoyl-L-alanine amphiphiles.¹⁷ It was shown that amide hydrogen-bonding (H-bonding) between two adjacent molecules is the driving force for gelation process. Recently, we have also shown that incorporation of a phenoxy group in the hydrocarbon chain enhances gelation ability of the *N*-alkanoyl-

L-alanine amphiphile in organic solvents.¹⁸ Indeed molecules can be ordered through H-bonding.¹⁹ The SAFIN structures, when depending solely on the H-bonding networks, are destroyed by the addition of a small amount of H-bonding additives, such as water, methanol, urea, thiourea, etc. The geometry and strength of H-bonding can be used to control the shape of the molecular arrangement. In fact, nature is known to use H-bonding to form catalytic pockets in enzymes. Hydrogen bonds enhance the attractive forces in crystals, which is manifested by the increase of melting point.

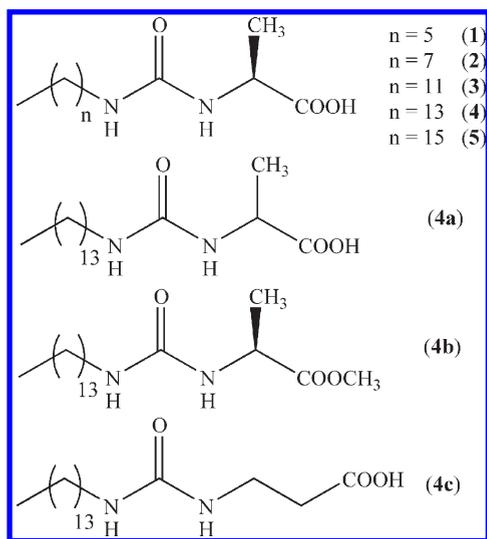
The urea linkage is simple in structure with two hydrogen bond donor sites and one hydrogen bond acceptor site and therefore can be used as a very useful hydrogen bond building block for supramolecular organization.^{20–22} Indeed one of the lowest-mass organogelators reported in the literature is *N,N'*-dimethylurea.²³ Urea derivatives form a H-bonding network between a carbonyl group of one urea unit and two hydrogen atoms of a neighboring molecule. This type of H-bonding is termed as 'bifurcated hydrogen bonding'^{24,25} and has been shown to be responsible for the higher stability of the monolayer of the urea derivatives compared to the corresponding amide derivatives.²⁶ Due to their characteristic structure-forming abilities derived from this H-bonding, long chain urea derivatives have attracted attention in the recent past.²³ Hamilton and

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Chart 1. Chemical Structure of the Amphiphiles



co-workers²⁷ have reported that methyl and ethyl esters of *N*-(*n*-alkylcarbamoyl)-*L*-serine amphiphiles gel water above a critical concentration. Since substituted ureas are known to form strong hydrogen bonds,²⁸ we thought replacement of the amide group (NHCO) by a urea group (NHCONH) might improve the gelation ability of *N*-(*n*-alkanoyl)-*L*-alanine in organic solvents. Therefore, in this work, we have synthesized a series of urea amphiphiles *N*-(*n*-alkylcarbamoyl)-*L*-alanine (see Chart 1 for structures) and investigated their gelation behavior in different organic solvents. The amides and ureas are normally H-bonding type gelators, as the gel is often disrupted upon addition of a small amount of H-bonding substances. However, in this paper, we show that addition of H-bonding substances, such as water, methanol, or urea, induces gelation of organic solvents by the amphiphiles. The gelation ability of the amphiphiles has been compared with corresponding *N*-(*n*-alkanoyl)-*L*-alanine reported in the literature.^{17b} The effect of hydrocarbon chain length on gelation behavior was investigated. The effects of optical purity, chirality, and substitution on the acid group on the gelation ability of *N*-(*n*-tetradecylcarbamoyl)-*L*-alanine were also examined. The thermal and rheological properties of the organogels formed by these amphiphiles have been discussed.

EXPERIMENTAL SECTION

Materials. *L*-Alanine, *DL*-alanine, sodium bicarbonate, *o*-xylene, *m*-xylene, *p*-xylene, benzene, toluene, chlorobenzene, and nitrobenzene were purchased from SRL, Mumbai, India, and were used without further purification. *L*-Alanine methyl ester, β -alanine, mesitylene, hexyl isocyanate, octyl isocyanate, dodecyl isocyanate, tetradecyl isocyanate, and hexadecyl isocyanate were obtained from Aldrich. All other organic solvents were of highest purity commercially available and were dried and distilled fresh before use. The amphiphiles employed in this study were synthesized in the laboratory as described below.

Synthesis of Amphiphiles. The amphiphiles 1–5, 4a, 4b, 4c (Chart 1) were synthesized following literature reported methods.²⁹ The synthetic scheme and the chemical identification of the amphiphiles have been included in the Supporting Information.

Methods and Instrumentation. The melting point of solid compounds was measured using an Instind (Kolkata) melting point

apparatus with open capillaries. The measurements of optical rotations were performed with a JASCO (Model P-1020) digital polarimeter. The FT-IR spectra were measured with a Perkin-Elmer (Model Spectrum Rx I) spectrometer. The ¹H NMR spectra were recorded on an AVANCE DAX-400 (Bruker, Sweden) 400 MHz NMR spectrometer in CD₃OD or CDCl₃ solvent.

The melting temperature of the organogels was determined by an inverted-tube experiment in which the screw-capped vial containing the gel was put in a temperature-controlled water bath (Julabo, Model F12). The temperature of the bath was gradually increased at a rate of 1°/min, and the temperature was noted where the gelled mass started to flow upon tilting of the vial. The melting temperature did not vary more than ± 1 °C.

For electron micrographs, the hot sample solution was placed on the aluminum foil, allowed to cool and air-dry at room temperature. The gel cast films were further dried in desiccators for 24 h. A layer of gold was sputtered on top to make a conducting surface, and finally the specimen was transferred into the field emission scanning electron microscope (FESEM, Zeiss, Supra-40) operating at 5–10 kV to obtain the micrograph.

The XRD spectra were taken at room temperature for all air-dried organogel samples prepared on a glass slide. The experiment was performed on a Panalytica X'Pert pro X-ray diffractometer using a Cu target (Cu K α) and Ni filter at a scanning rate of 0.001 s⁻¹ between 2° to 12° or 10°, operating at a voltage of 40 kV and current 30 mA.

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 μ m. The rheometer is fitted with a solvent trap and a peltier device that controls temperature within 298 \pm 0.1 K. An equilibration time of 30 min was allowed before measurements were taken for each sample. All measurements were taken on matured gels after 10 h of cooling. Oscillatory stress sweeps from 100 to 10 000 Pa (or 100 to 1000 Pa) were measured at a constant frequency of 1 Hz to obtain storage modulus (G') and loss modulus (G''). The frequency sweep measurements were performed in the frequency range from 0.01 to 100 Hz in a constant stress of 100 Pa.

RESULTS AND DISCUSSION

Gelation Behavior. To begin, the gelation test was first performed using amphiphile 4 as gelator. To our surprise the compound was found to be poorly soluble even when heated at 70 °C in most of the solvents employed in this investigation. In fact, the amphiphiles 1–5, 4a, 4b, 4c remained insoluble also in aliphatic hydrocarbon solvents under the same condition. Although the solubility of amphiphile 1 having the shortest hydrocarbon chain could be improved by heating, excess compound precipitated from saturated solution when cooled to room temperature. However, when the suspension of the amphiphiles 1–5, 4a, 4b, 4c in chlorinated hydrocarbons or in aromatic solvents was heated in the presence of a small amount of water, a clear solution was obtained, which upon cooling to room temperature gelled the solvent within 10–15 min. However, this was not observed in aliphatic hydrocarbon solvents. The gelation in the presence of water was confirmed by the flow to “inversion test” method (Figure 1). It is important to note that organogels were produced also in the presence of a small volume of methanol or urea (Figure 1). Organogel formation (not shown) was also observed in the presence of tetrahydrofuran (THF) and acetonitrile. The solubility behavior of the amphiphiles, except 4a, was observed to be very similar, and they did not form gel in the pure solvents employed. It was interesting to observe that the racemic compound 4a produced weak gels in the

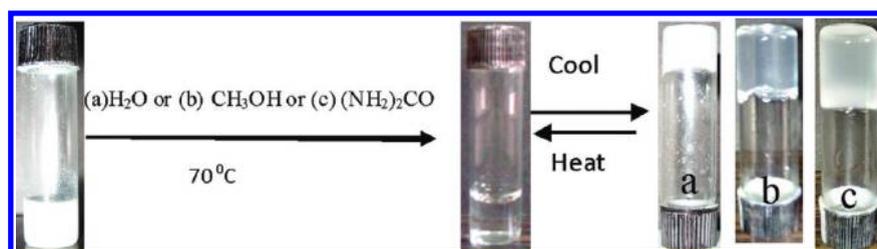


Figure 1. Photographs of vials showing gelation in the presence of (a) H₂O, (b) CH₃OH, and (c) (NH₂)₂CO.

Table 1. Critical Gelation Concentration (CGC, mg/mL) of the Amphiphiles in the Presence of Water (50 mol/mol of gelator) in Various Organic Solvents at 25 °C

solvent	CGC (mg/mL)								
	1 ^a	2	3	4	4a	4a ^b	4b	4c	5
tetrachloromethane	18.1	13.5	12.0	8.2	—	—	25.7	12.2	14.8
benzene	19.3	13.6	11.5	7.5	6.2	10.5	13.2	6.5	14.9
<i>p</i> -xylene	12.5	12.5	11.6	10.2	11.1	12.6	23.5	5.5	16.4
<i>m</i> -xylene	13.8	13.2	12.4	11.5	12.8	13.2	24.1	7.6	18.9
toluene	19.9	14.0	11.9	9.1	7.2	11.3	14.0	7.8	18.2
mesitylene	26.9	18.0	11.4	10.1	12.5	13.6	17.8	9.3	21.0
<i>o</i> -xylene	17.7	17.3	14.1	14.3	15.1	15.9	25.5	8.7	23.0
chloroform	15.3	10.5	8.6	7.1	—	—	24.2	9.1	12.8
chlorobenzene	11.6	11.2	10.3	8.9	11.9	12.9	26.2	7.9	16.8
nitrobenzene	10.0	10.2	10.0	8.2	13.4	16.5	25.3	7.0	14.9

^a Measured at 20 °C. ^b Measured in the absence of water.

pure solvents employed. However, when water was added to the suspension, the organogels of **4a** became stronger (visual observation). The gelation behavior of all the amphiphiles were systematically studied in various solvents at a concentration of 1% (w/v), and the results are summarized in Table 1. The organogels were opaque in aromatic hydrocarbon as well as in chlorinated hydrocarbon solvents. In nitrobenzene solvent, however, the organogel became transparent after a few days. Organogels in the presence of methanol and THF, however, were found to be transparent. This may be either due to increased solubility of the gelators or due to reduction of sizes of the self-assembled aggregates. On the other hand, translucent organogels were obtained when urea or acetonitrile was added instead of water. The gelation was found to be reversible for many heating cycles, suggesting that the organogels are thermoreversible. It should be noted that addition of excess methanol or urea or THF destroys the gel structure showing gel–sol transition, whereas phase-selective gelation was observed in the presence of excess water. This can be attributed to the increased solubility of the gelators in excess methanol or THF solvents. However, the gelators being poorly soluble in water the gel phase remains separated from water. The phase-sensitive gelation of corresponding amide derivatives has also been reported by others.^{17a}

It was observed that the volume of solvent gelled by a given amount of gelator depends upon the volume of added water (or methanol or urea). The gelling ability of the amphiphile **4** as measured by the critical gelation concentration, CGC (amount of gelator required to gel unit volume of a liquid), or gelation number (number of moles of solvent gelled per mole of gelator) was determined in the presence of different volumes of water (pH 6.5) in *p*-xylene and nitrobenzene solvents. The plots in

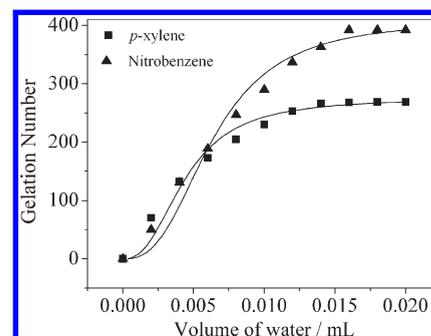


Figure 2. Variation of gelation number of **4** in *p*-xylene and nitrobenzene solvents with the added volume of water.

Figure 2 show how gelation number changes as a function of water content of the solvent. It is observed that for 5.5 mg of **4**, the volume of solvent gelled increased with the increase of volume of water added reaching maximum at ca. 15 μ L. This means that it requires about 50 mol of water per mole of **4**. Since solubility of water in the aromatic hydrocarbon solvents is in the range of 0.02 to 0.028 mM,³⁰ the maximum number of water molecules is used in self-assembly formation. We therefore determined CGC values of all the amphiphiles in different solvents at a [water]/[gelator] mole ratio equal to 50. Since organogels of amphiphile **1** were found unstable at room temperature (25 °C), the CGC values were determined at 20 °C.

Table 1 lists the CGC values of all the gelators in different solvents arranged in an increasing order of dielectric constant. It is observed that for any gelator, the CGC value depends upon the chemical structure of the solvent. However, within a series of structurally similar solvent, for example *p*-, *m*-, and *o*-xylene, the CGC value increases linearly (Figure S1 of Supporting Information) with the dielectric constant. The data in the table show that the CGC value of **4** is $\leq 1.5\%$ (w/v). It should be noted that the corresponding amide derivative *N*-(*n*-hexadecanoyl)-*L*-alanine bearing the same number of atoms as **4**, but a NH group that is substituted by a CH₂ group, as reported elsewhere, has a CGC value ca. 1.0% (w/v) and forms only a weak gel in toluene.^{17b}

The results in Table 1 show that in any given solvent, the amphiphile **4** has the lowest CGC value (i.e., highest gelation number) among amphiphiles **1**–**5**. The CGC value decreases with increasing hydrocarbon chain length (C_n) in going from amphiphile **1** to **4**. Figure S2 of Supporting Information shows the histograms of CGC value of the amphiphiles in benzene as a function of C_n . It is seen that amphiphile **5** despite having higher chain length (C_{16}) has a higher CGC value compared to **4**. Similar behavior has been reported previously by us¹⁸ as well as by others.¹⁷ The lower gelation number of **5** compared to **4** may be attributed to a bent hydrocarbon chain. It is well-known that

Table 2. Gel Melting Temperatures (T_{gel}/K) of the Organogels Containing 20 mg/mL Gelator and 50 Mol Water/Mol of Gelator

solvent	4 ^a	4a ^a	4b ^b
tetrachloromethane	343	—	300
benzene	323	319	303
<i>p</i> -xylene	338	328	307
<i>m</i> -xylene	330	323	311
toluene	325	321	305
mesitylene	326	324	305
<i>o</i> -xylene	333	321	313
chloroform	330	—	304
chlorobenzene	356	315	309
nitrobenzene	351	307	301

^a T_{gel} values were measured at a gelator concentration of 0.06 M. ^b T_{gel} values were measured at a gelator concentration of 0.08 M.

normally up to C₁₄ chain length the hydrocarbon tail remains straight and then starts to bend with further increase of the number of methylene groups. The bent hydrocarbon tail in **5** may inhibit tight packing in the self-assembled structure thus inhibiting growth of the aggregates.

The role played by chirality in controlling and mediating the self-assembly of gelators is very important since many of the commonly employed LMOGs include chiral centers.³¹ The gelling ability of compound **4a** in the absence of water suggests that stronger homochiral and H-bonding interactions in **4** results in precipitation instead of forming gel. The CGC value of **4a** in pure solvents was observed to be slightly higher than that in the presence of water. This proves that water facilitates the gelation process. This means that in contrast to literature reports,¹⁷ chirality is not mandatory for the gelation to occur. Interestingly, in the present case, it disfavors gelation. This is substantiated by the better gelation ability of the amphiphile **4c**, which has no chiral center but has a CGC value lower than that of **4** (in aromatic solvents). A higher CGC value (i.e., lower gelation ability) of **4** compared to **4c** must be due to weaker H-bonding interaction due to steric crowding at the headgroup. Also, the data in Table 1 show that the amphiphile **4a** has a CGC value much higher than that of **4**. Thus, it can be concluded that although enantiomeric purity or the presence of chirality is not mandatory for gelation, the same stereochemistry of the headgroups of neighboring gelator molecules facilitates intermolecular hydrogen bond formation between urea moieties thus favoring gelation process. The presence of both D- and L-isomers, on the other hand, hinders hydrogen bond formation near the headgroup region of the amphiphiles. This is also indicated by the lower melting point of **4a** (369–371 K) compared to **4** (403–405 K).

The ability to produce gel by the gelator **4b** which is the methyl ester of **4** demonstrates that the acidic hydrogen of the COOH is also not essential for gelation. This contrasts reports of Bhattacharyya and co-workers on the organogels of corresponding amide derivatives.¹⁷ However, the data in Table 1 show that in any solvent, the CGC value of **4b** is higher than that of **4**. This means that although the carboxylic hydrogen is not required for gelation, it enhances the gelation ability of the latter obviously through intermolecular H-bonding interactions.

Thermal Stability. The organogels of **4** were found to be very stable at room temperature (25 °C), and no significant changes

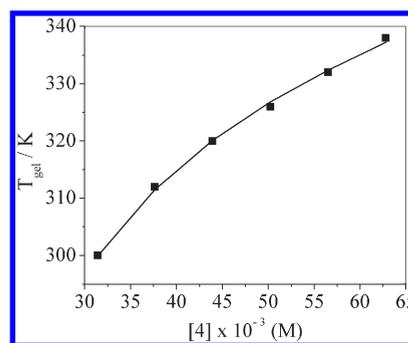


Figure 3. Plot of T_{gel} (K) with varying concentrations of **4** in *p*-xylene.

were observed after 6 months of storage in a sealed tube. When the temperature was increased above a certain value, the gel collapsed to produce a solution/dispersion. The process could be reversed to produce organogel by cooling to room temperature. The gelation ability was not affected when the heating–cooling cycle was repeated many times, suggesting thermoreversibility of the organogels. The thermal stability of the organogels can be expressed in terms of the gel-to-sol transition temperature (T_{gel}). The T_{gel} values of the organogels of **4**, **4a**, and **4b** have been listed in Table 2. The variation of T_{gel} value with the hydrocarbon chain length has been shown in Figure S3 of Supporting Information. It is observed that the organogels of **4** have highest T_{gel} values, indicating higher thermal stability compared with those of other gelators. Both increase and decrease of chain length from C₁₄ decreases T_{gel} value. This is consistent with the change of CGC value with the change of chain length. The T_{gel} value also depends on concentration of the gelator as shown by the plot in Figure 3. It is observed that T_{gel} value of the organogels of **4** increases nonlinearly with its concentration. The higher thermal stability at a higher concentration of the gelator can be attributed to 1-D growth of the aggregates, causing more entanglement or physical branching of the fibers. Since the hydrocarbon chain length is same for both gelators **4** and **4a**, the lower T_{gel} value for the organogels of the latter gelator can be attributed to less entanglement of the fibers.

Viscoelastic Behavior. Visual observation showed that the organogels formed by gelator **4a** in pure solvents could not resist high mechanical force and break upon shaking of the gel-containing vials. In contrast, all the other amphiphiles produced sufficiently stronger gels when an appropriate volume of water was added to the solvent. The mechanical strength of a gel which is measured by the storage modulus (G') and loss modulus (G'') is dependent on gelator concentration. Therefore, rheological properties of the organogels of all the amphiphiles were studied at 0.15 M concentration in *p*-xylene solvent. Figure 4 shows the variation of G' and G'' with frequency. It is observed that in every case, both G' and G'' are almost independent of frequency which is characteristic of gel structure. Also at any given frequency, the G' is higher than G'' , as indicated by the G'/G'' values in Table 3. The G'/G'' values are in the range 3–12, suggesting more elastic nature of the gels, like solids.

Figure 5 shows the plots of G' and G'' versus applied stress (σ) at a constant frequency of 1 Hz. It can be observed that above a critical stress value, both G' and G'' abruptly fall to a very low value, indicating flow of the hydrogel. This critical stress value is referred to as yield stress (σ_y). The σ_y values are collected in Table 3. The organogel of **4** has the highest σ_y value, indicating highest mechanical strength, whereas the organogel of **4a** has the

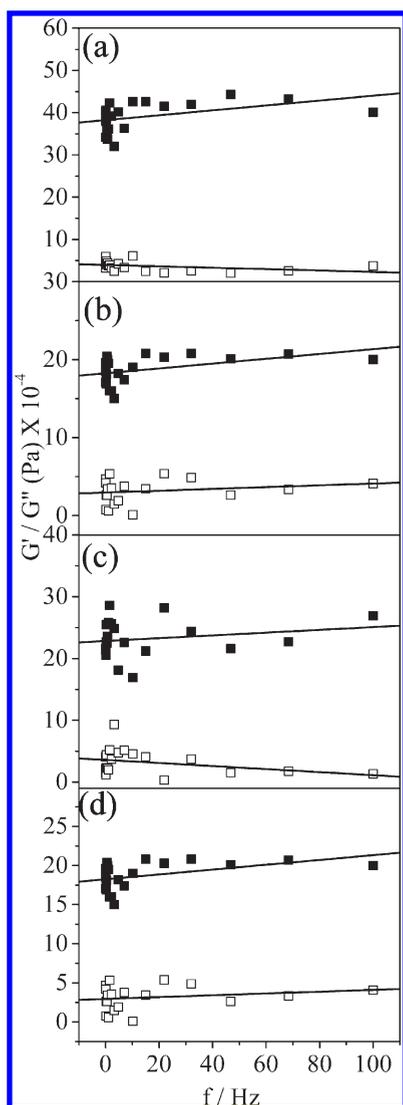


Figure 4. Variation of storage modulus (G')/loss modulus (G'') with frequency (f) of organogel in *p*-xylene of (a) **4**, (b) **4a**, (c) **4b**, and (d) **4c** at 298 K.

lowest σ_y value and hence is weaker. The data in Table 3 also suggest that the mechanical strength of the organogel of **4** is higher than that of **4b** and **4c**. The increased mechanical stability of the organogels of **4a** in the presence of water can be attributed to growth of 1-D aggregates as a result of water-mediated intermolecular H-bonding interactions.

Morphology of the Organogels. It is well established that the nature of self-assembled structures depends on the type of gelator, its alkyl chain length, and the cooling rate. On the basis of the intermolecular H-bonding energies, it has been shown that elongated aggregates are favored by urea derivatives.³² For urea derivatives, it has also been found that lengths of the aggregated structures are reduced considerably when the alkyl chain length is increased.²³ In order to get visual insight into the aggregation mode of the gelators and microscopic morphology of their organogels, FESEM measurements were performed. Figure 6 exhibits FESEM images of the air-dried organogels in *p*-xylene solvent. The examination of the images reveals that the morphology of the organogels of all the amphiphiles, except **4a**, can be characterized by thick ribbon-like fibrous aggregates of high

Table 3. Rheological Properties of the Organogels of the Amphiphiles (0.15 M) in *p*-Xylene Solvent

amphiphile	amplitude sweep		frequency sweep
	σ_y (Pa)	G'/G''	G'/G''
4	3912	2.72	11.9
4a	346	2.66	5.9
4b	1165	2.72	8.1
4c	2209	4.06	4.0

aspect ratio, forming three-dimensional (3-D) networks. The FESEM image (Figure S4 of Supporting Information) of the transparent organogel prepared in the presence of methanol also showed similar fibrous aggregates. The denser intertwined fibrous structure of the organogels reflects greater intermolecular cohesiveness and hence higher thermal stability (which means higher T_{gel} value) and mechanical strength (i.e., greater yield stress). For the organogel of **4a**, however, the length of the aggregated objects is reduced which is consistent with the lower T_{gel} value. The homochiral interaction also facilitates one-dimensional (1-D) growth of the fibrous aggregates, the physical entanglement of which leads to the 3-D network structures. In the case of gelator **4a**, because such interaction is absent and the intermolecular H-bonding is hindered, the 1-D growth is limited, causing less entanglement of the fibers and hence lower yield stress value. The homochiral effect is also manifested by the difference between melting points of the solid compounds.

X-ray Diffraction Studies. The nature of the microstructure of the aggregates was further studied by XRD spectra (see Figure S5 in the Supporting Information) of the dry gels. The XRD spectrum of the organogel of the amphiphile **1** could not be measured because of its instability at room temperature. The XRD spectra of all other gels exhibit sharp periodic peaks in the range $2\theta = 2^\circ$ to 10° or 12° . The XRD data have been collected in Table 4. For gelators **2**, **4a**, and **4c** the periodic peaks suggest existence of 1-D lamellar structures. On the other hand, the XRD data for gelators **3** suggest formation of 1-D cylindrical aggregates. It is interesting to note that organogel of **4** exhibits both cylindrical and lamellar aggregates. The XRD spectrum of the air-dried transparent organogel produced in *p*-xylene in the presence of methanol also exhibits periodic peaks corresponding to lamellar structures. Thus, it is concluded that the transparent nature of the organogel is not due to change in morphology, but as mentioned earlier it is due to increased solubility of the gelator in the presence of methanol (or THF). The powder XRD spectrum (Figure S5) of gelator **4** also exhibits sharp peaks, which suggests its crystalline character. The bilayer thickness of the lamella which is equal to the interlayer distance (d) of the 100 plane and the calculated length³³ of the fully extended alkyl chain are collected in Table 4. The bilayer thickness in the case of **2**, **4**, and **4c** is slightly smaller than twice the extended chain length of the hydrophobic tail of the gelator molecule, but larger than the length of hydrophobic tail. This implies that the aggregate has interdigitated hydrocarbon tails. However, it is interesting to note that despite the same alkyl chain length the d -spacing in the case of **4a** is much less than that of **4**. This might be either due to large interdigitation of the hydrocarbon tail in **4a** or is possibly due to tilt of the long axis of the molecule with respect to the layer planes. Perhaps due to the difference in headgroup stereochemistry of the D and L isomers in the racemic compound **4a**, the hydrocarbon chains within the monolayer are disordered,

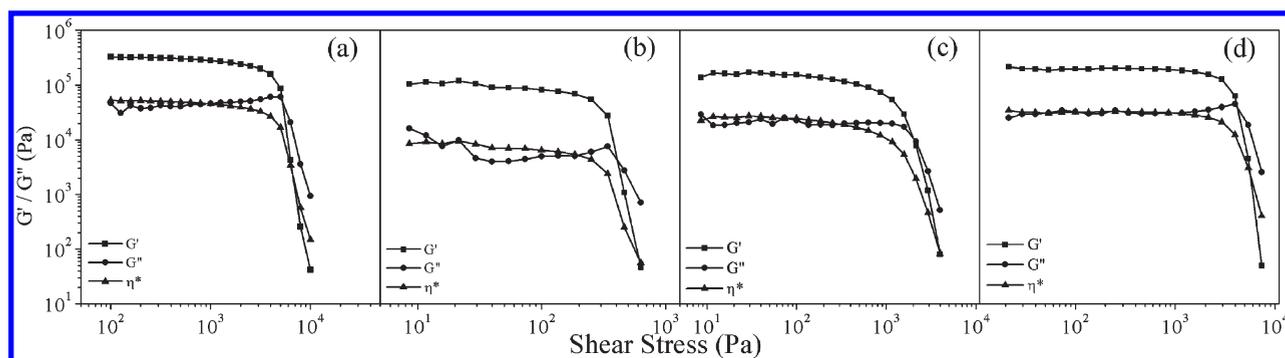


Figure 5. Variation of storage modulus (G')/loss modulus (G'') with frequency shear stress of organogel of (a) 4, (b) 4a, (c) 4b, and (d) 4c in *p*-xylene at 298 K.

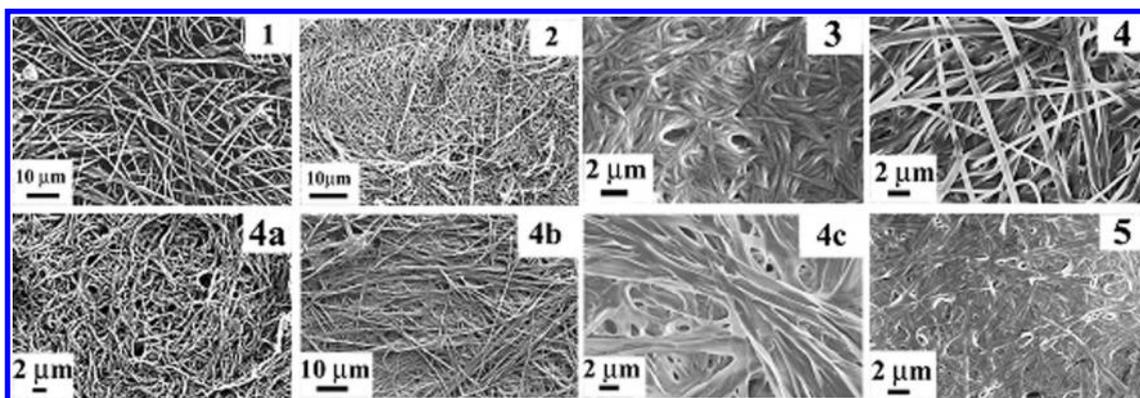


Figure 6. FESEM images of the air-dried gels of the amphiphiles in *p*-xylene.

Table 4. XRD Data of Gels in *p*-Xylene Solvent

gelator	l_c (nm)	2θ (deg)	d (nm)	plane
2	1.81	3.35, 6.59	2.63	100, 200
3	2.10	2.47, 4.29, 6.62	3.56	100, 110, 210
4	2.14	2.33, 3.89, 6.63, 7.72, 9.28, 11.60	3.67	100, 110, 210, 310, 400, 500
4a	2.14	3.00, 5.91, 8.90	2.94	100, 200, 300
4c	2.14	2.19, 6.52, 8.70	4.01	100, 200, 300

causing more penetration into the other monolayers of the bilayer assembly.

Role of Water. The subtle self-assembly process of the urea amphiphiles as described above is influenced by different factors, including concentration, solvent, temperature, and especially additive. The inability to gel a particular solvent by the urea gelators can be understood by studying their interaction in the solid state. The gelator 4 is crystalline and has a melting point 403–405 K, which is much higher than that of 4a (369–371 K) and the corresponding amide derivative (364–366 K). This must be due to stronger H-bonding interaction between urea groups, which is supported by the FT-IR spectra of the solid compounds. It is observed that the amide-I stretching frequency of the urea group (1628 cm^{-1}) is far more red-shifted compared to the amide (1646 cm^{-1}).^{17b} On the other hand, the amide-II stretching frequency of 4 (1569 cm^{-1}) is blue-shifted relative to that of corresponding amide group (1528 cm^{-1}).^{17b} The strong intermolecular H-bonding and homochiral interactions make the enantiomerically pure urea gelators insoluble in hydrocarbon solvents. The melting point and bond frequency data suggest that

the intermolecular H-bonding interaction in 4a is weaker than in 4, making it more soluble. In fact, the H-bonding interaction, as reported by many authors is weaker in the case of racemic compounds.³⁴ Consequently, amphiphile 4a forms gel even in the absence of water. The addition of H-bonding solvents, such as methanol, urea, or water, breaks or weakens this hydrogen bond and thus enhances solubility in the solvent.

The fact that the amphiphiles fail to gelate a particular solvent in the absence of water clearly suggests that water plays a major role in the gelation process. The gelation behavior of the amphiphiles is very similar to that of lecithin, a phospholipid, which has been observed to form organogels in 50 different organic solvents upon addition of a small but a critical amount of water as demonstrated by extensive studies.³⁵ Several studies have shown that in the case of lecithin, the gelation of organic solvents is due to formation of hollow cylindrical reversed micelles of high aspect ratio.³⁶ Like that for lecithin, gelation of organic solvents by a polymer in the presence of thiourea, a strong H-bonding agent, has also been reported previously and has been shown to be a consequence of breaking of H-bonds

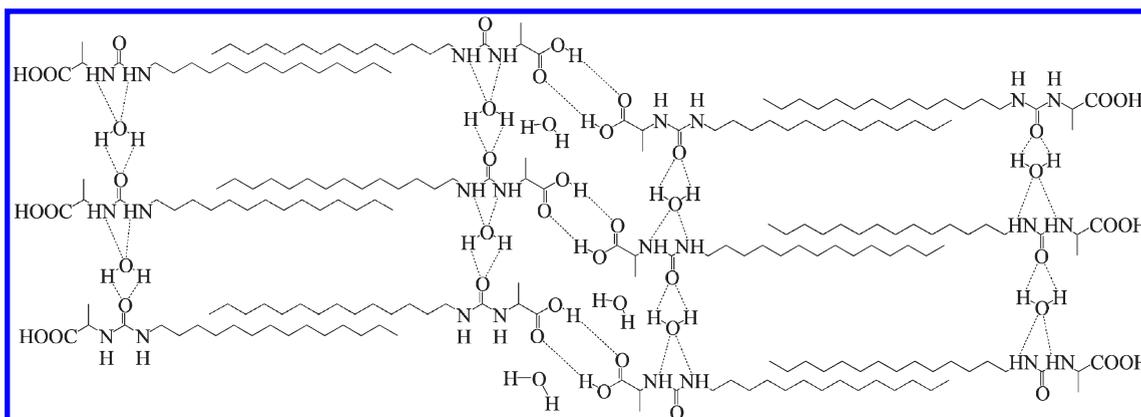


Figure 7. Bilayer structure of organogels in the presence of water.

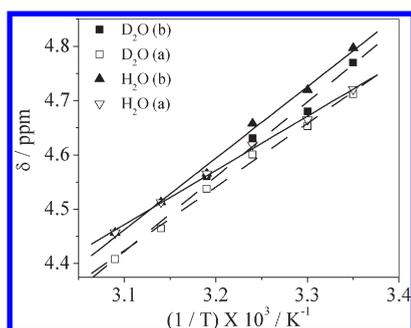


Figure 8. Variation of chemical shift of H₂O and HDO with temperature in ¹H NMR spectra of the organogel of 4 in CDCl₃ solvent.

among polymer chains which enhances solubility of the polymer chain in the solvent.³⁷ In fact, it is now well accepted that gelation occurs as a result of subtle balance between a tendency of the gelator molecules to dissolve and a tendency to aggregate leading to precipitation or crystallization. As discussed previously, water molecules weaken or break intermolecular hydrogen bonds between urea groups and thus prevent crystallization.

In order to investigate how the intermolecular interactions of water with the gelator regulate such supramolecular arrangements of individual gelators in the 3-D framework, ¹H NMR analysis was performed. The solvent CDCl₃ was found to be tightly hardened by 4 as an opaque gel at 1.5 w/v% at 298 K and returned to solution at 328 K. The ¹H NMR spectra at these two states are shown in Figure S6 of Supporting Information. In the gel state (298 K), two chemical shift (δ) positions corresponding to H₂O molecules entrapped (a) between bilayers and those bound (b) to urea groups can be observed. At higher temperatures (≥ 328 K), however, they merge into one peak. The chemical shift positions of both types of H₂O protons exhibit a significant downfield shift from δ 4.4 at 328 K to δ 4.7 and 4.8 ppm at 298 K, clearly indicating formation of hydrogen bonds between the H₂O molecule and the urea group (see Figure 7) of the alkyl chain during the sol–gel transition. A similar experiment was also carried out with D₂O which contains HDO as impurity. The change of δ values of H₂O and HDO with temperature is shown in Figure 8. As discussed above, the gelator molecules in the presence of water reorganize to form lamellar liquid crystal (LC) structures, which upon growth at higher gelator concentrations transform the constituent solvent to a gel. The water molecules thus stabilize the lamellar aggregates. The molecules arrange themselves in lamella in which the molecules

are parallel. Therefore, the LC phase of the urea amphiphiles is expected to be much more stable than that of the corresponding amide amphiphiles. The different behavior of the urea and amide derivatives is thus shown to be caused by the hydrogen bonds. The above discussion shows how gelation can be tuned by tuning the H-bonding interaction and chirality of the molecule.

CONCLUSIONS

We have presented rare examples of gelators that produce organogels in the presence of critical amounts of water. In fact, we have shown that upon addition of H-bonding additives, such as methanol, water, and urea, the gelators 1–5 gelled aromatic organic solvents at a relatively low concentration. However, phase-selective gelation of organic solvents was observed in the presence of large excesses of water. The organogels were found to be thermostable and thermoreversible. The gelators, in the presence of water, self-assembled to form long ribbon-like bilayer structures, forming 3-D network structures. It has been shown that strong intermolecular H-bonding between urea groups is responsible for the inability of the gelators to produce organogels, and water-mediated intermolecular H-bonding interaction between amphiphiles caused formation of the supramolecular self-assemblies. All the organogels, except those of 4a, have reasonably high yield stress values, indicating their higher mechanical strength. The D,L-derivative (4a) forms a very weak organogel in the absence of water. The mechanical strength of the organogel of 4a increased upon addition of water. The results have suggested that a gelator in the racemic form produces weaker gels compared to those of the enantiomerically pure compound. This work has demonstrated that gelation can be tuned by tuning the intermolecular H-bonding interaction and chirality of the molecule. It should be noted that although the organogels of the gelators 1–5, and lecithin, on a macroscopic scale appear jelly-like, on a microscopic scale, the latter is actually a 3-D network of giant cylindrical reverse micelles. Finally, the coexistence of aqueous and organic phases separated by a large interface and the possibility to entrap therapeutic agents within the gel matrix can result in improved organogel-based topical drug delivery systems. Work in this direction is currently being carried out in this laboratory.

ASSOCIATED CONTENT

S Supporting Information. Synthesis and chemical identification of the amphiphiles, plots of CGC and gel melting

temperature versus number of carbon atoms (C_n) in the hydrocarbon chain of the amphiphiles, XRD patterns of xerogels and powder, and ^1H NMR spectra of the organogel in CDCl_3 solvent at two different temperatures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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