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Organogel–Hydrogel Transformation by Simple Removal or Inclusion of *N*-Boc-Protection**

Tanmoy Kar, Subhra Kanti Mandal, and Prasanta Kumar Das*[a]

Abstract: Development of organo- and hydrogelators is on the rise because of their extensive applications, from advanced materials to biomedicine. However, designing both types of gelator from a common structural scaffold is challenging, and becomes more significant if transformation between them can be achieved by a simple method. The present work reports the design and synthesis of both organo- and hydrogelators from amino acid/peptide-based amphiphilic precursors with a naphthyl group at the N terminus and a primary amine-containing hydrophilic ethyleneoxy unit at the C terminus. In alkaline medium, *tert*-butyloxycarbonyl (Boc) protection at the primary amine of the amphiphiles resulted in efficient organogelators (minimum-gelation concentration (MGC) = 0.075–1.5 % *w*/*v*). Interestingly, removal of the Boc protection from the ethyleneoxy unit, under acidic conditions, yielded amphiphiles capable of gelating water (MGC = 0.9–3.0 % *w*/*v*). Simple protection and deprotection chemistry was used to achieve transformation between the organogel and hydrogel by alteration of the pH. Combinations of different aliphatic and aromatic amino acids were investigated to discover their cumulative effect on the gelation properties. Field-emission scanning electron microscopy (FESEM) and transmission electron microscopy (TEM) were employed to investigate the supramolecular morphology of the thermoreversible gels. Spectroscopic investigations (FTIR, photoluminescence, XRD) revealed that noncovalent interactions, such as hydrogen bonding, π–π stacking, and van der Waals interactions play a decisive role in self-assembled gelation.

Keywords: amino acids · amphiphiles · hydrogels · organogels · protecting groups

Introduction

The self-assembly of small functional molecules into a supramolecular arrangement is a prevailing approach toward the development of soft materials.[1] Supramolecular gels are a novel class of self-assembled materials that are receiving notable importance due to their impending applications in diverse fields, such as tissue engineering, drug delivery, template materials, enzyme-immobilization matrices, and many more.[2–7] This ever-expanding surge has amplified the need to design and synthesize low-molecular-weight gelators (LMWGs), preferably from abundant precursors by simple methods. Self organization of the LMWGs leads to the formation of three dimensional (3D) higher-order arrangements (e.g. fibrous, tubular) through combination of various noncovalent interactions, such as π–π stacking, hydrogen bonding, van der Waals forces, and electrostatic interactions.[6,7] Despite the known influence of noncovalent interactions in supramolecular gelation, it is difficult to rationally design and functionalize small gelator molecules for the development of desirable materials.

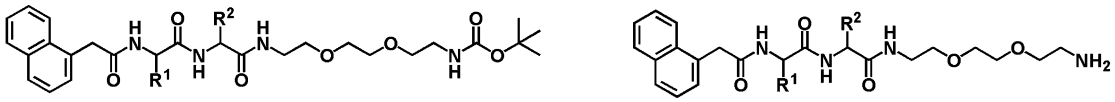
To this end, there are several reports (including ours) on the development of amino acid/dipeptide-based LMWGs capable of immobilizing different solvents: from water to organic solvents to ionic liquids.[8–10] In spite of these libraries of small-molecule gelators, there is still a demand for the design of simple precursors from which a variety of gelators can be synthesized with ease. However, reports on such common precursors are scarce. In earlier reports, we have shown that a hydrogen-bonding dipeptide moiety with a long hydrophobic chain at the C terminus and a free-amine group at the N terminus is an excellent gelator precursor. The quaternization of this amine with methyl iodide yielded a hydrogelator,[8a,b] and the same amine coupled with a fatty acid resulted in an efficient organogelator.[9b] However, transformation between these organo- and hydrogelators is not feasible because they are prepared by different synthetic methodology. Hence, investigation of a more simplistic approach to the development of both organo- and hydrogelators from the same scaffold is a worthy challenge. Additionally, transformation between an organogel and hydrogel by simple methodology would be of great importance for wider exploitation of these soft materials. At this point, we aim to develop organo- and hydrogelators by incorporating a stim-

[a] T. Kar, S. K. Mandal, Dr. P. K. Das
Department of Biological Chemistry
Indian Association for the Cultivation of Science
Jadavpur
Kolkata, 700032 (India)
Fax: (+91) 33-24732805
E-mail: bcpkd@iacs.res.in

[**] Boc = *tert*-butyloxycarbonyl.

Supporting information for this article (synthetic route to compounds **1**--**7** and **1a**–**7a**; characterization data; POM image of gelator **5**; FTIR spectra of **5**, **6**, **5a**, and **6a**) is available on the WWW under http://dx.doi.org/10.1002/chem.201101173.

R^1	Compound	
CH_3	1	1a
H_2C–Ph	2	2a
3-indolylmethyl	3	3a



R^1	R^2	Compound	
CH_3	CH_3	4	4a
H_2C–Ph	CH_3	5	5a
H_2C–Ph	H_2C–Ph	6	6a
H_2C–Ph	3-indolylmethyl	7	7a

Scheme 1. Structure of amphiphiles **1**–**7** and **1a**–**7a**.

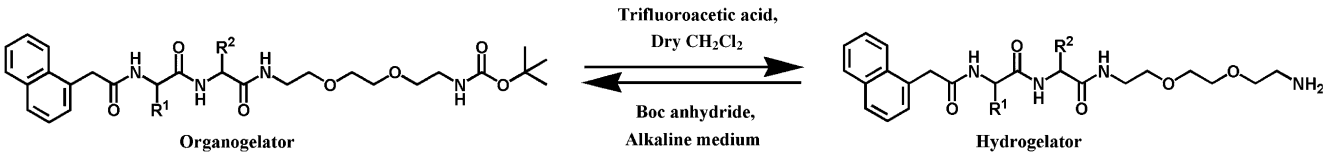
uli-sensitive functional moiety within the amino acid/dipeptide scaffold without compromising the hydrophilic–lipophilic balance (HLB) required for gelation. Ideally, the presence and absence of the stimuli-sensitive moiety should transform the solvent immobilizing ability of the gelator.

Here we report the development of amino acid/peptide-based amphiphilic gelators of both water (**1a**–**7a**) and organic solvents (**1**–**7**), synthesized from a common structural scaffold (Scheme 1). Gelation ability was transformed between organo- and hydrogelation by the presence or absence of the well-known *tert*-butyloxycarbonyl (Boc) protecting group at the primary amine of the hydrophilic ethyleneoxy unit at the C terminus (Scheme 2). *N*-Boc protection at the primary amine under alkaline conditions resulted in efficient organogelators (minimum-gelation concentration (MGC) = 0.075–1.5 % *w*/*v*, Table 1), whereas deprotection of the *N*-Boc moiety under acidic conditions yielded hydrogelators (MGC = 0.9–3.0 % *w*/*v*, Table 2). Influence of different amino acids with aliphatic/aromatic residues on the gelation efficiency and the corresponding changes in the supramolecular arrangements of the gels was investigated by spectroscopic and microscopic techniques.

Table 1. Minimum-gelation concentration (MGC) [% *w*/*v*] of **1**–**7** in organic solvents.[a]

Compound	Toluene	Tetralin	*o*-Xylene	*m*-Xylene	*p*-Xylene
1	S	S	S	S	S
2	S	S	S	S	S
3	S	S	S	S	S
4	1.5	1.5	1.45	1.5	1.4
5	0.5	0.55	0.5	0.45	0.45
6	0.08	0.08	0.075	0.08	0.09
7	0.2	0.25	0.2	0.25	0.2

[a] S = solution.



Scheme 2. Simple transformation between organogelators and hydrogelators.

Table 2. Minimum-gelation concentration (MGC) of **1a**–**7a** in water.[a]

Compound	MGC [% *w*/*v*]
1a	S
2a	1.7
3a	I
4a	S
5a	0.9
6a	3.0
7a	I

[a] S = solution; I = insoluble.

Results and Discussion

Designing organo- and hydrogelators from a common structural scaffold instead of from a variety of structural frameworks is of importance in the arena of soft materials. Moreover, the easier the method of transformation between these gelators, the wider the application of such self-assembled gels.[2–7] We wanted to develop amino acid/dipeptide-based common precursors of gelators with appropriate stimuli-responsive functional moieties to assist subtle and simple transformation between organo- and hydrogelation. Accordingly, we synthesized a series of amphiphilic molecules from different aliphatic and aromatic amino acids with a naphthyl moiety at the N terminus and an ethyleneoxy unit with a free or Boc-protected amine (NH_2/NHBoc) at the C terminus (Schemes 1 and 2). Amino acids were chosen as the basic structural scaffold for the gelators because of potential compatibility with biological systems. The ethyleneoxy unit containing a primary amine was integrated mainly to provide the necessary hydrophilicity in the structure. The naphthalene unit provides a hydrophobic segment to attain the optimum HLB, which plays a crucial role in the gelation efficiency of the compounds in solvents of different polarities. Also, the planar naphthalene aromatic ring is expected to facilitate self-assembled gelation through well-known π–π-stacking interactions.[4a,11,12]

N-Boc-protected L-alanine-based amphiphile **1**, with the smallest side-chain residue, was found to be soluble in different organic solvents (Table 1) and insoluble in water. Surprisingly, replacement of the aliphatic L-alanine residue with an aromatic L-phenylalanine or L-tryptophan residue (compounds **2** and **3**, respectively) in the amphiphilic structure failed to induce any solvent-immobilization ability, despite additional π–π interactions of the aromatic side chain. In this context, it is widely reported that hydrogen bonding is a major driving force for gelation in organic solvents.[13] Therefore, we thought that the presence of a dipeptide unit instead of a single amino acid may influence gelation because the additional amide linkage would facilitate the hydrogen bonding. Thus, we synthesized dipeptide-based amphiphilic compounds **4–7** from combinations of aliphatic (L-alanine) and aromatic (L-phenylalanine and L-tryptophan) amino acids. Encouragingly, amphiphiles **4–7** exhibited excellent organogelation efficacy in different aromatic solvents (Table 1). Gelation ability was studied by the "stable-to-inversion of the container" method. Compound **4**, comprised of two L-alanine residues, formed a stable gel in toluene and other aromatic solvents with a MGC = 1.4–1.5 % *w*/*v* (Table 1). The formation of an organogel in the absence of any aromatic amino acid indicates the important influence of the additional hydrogen-bonding unit of the dipeptide in self-assembled gelation. Interestingly, the amphiphilic compound **5**, in which the N-terminal alanine residue was replaced by L-phenylalanine, showed a three-fold enhancement in gelation efficiency in toluene (MGC = 0.5 % *w*/*v*, Table 1) relative to **4**. Improvement in the gelation efficiency promoted by the synergistic effect of the peptide bond and aromatic moiety provided the rationale for the synthesis of dipeptide amphiphiles with two aromatic residues; compound **6** (two L-phenylalanine residues) and **7** (L-phenylalanine and L-tryptophan residues). Indeed, both **6** and **7** showed a two- to six-fold improvement in gelation efficiency relative to **5** (one aromatic amino acid). Interestingly, compound **6** was a super organogelator with a MGC as low as 0.075–0.09 % *w*/*v* (Table 1), which is almost 20-times lower than the equivalent aliphatic dipeptide-based gelator **4**. Thus, the concurrent presence of a hydrogen-bonding dipeptide unit and an aromatic moiety dramatically promotes self-aggregation of the amphiphiles, which leads to superior gelation in organic solvents.

However, *N*-Boc-protected amphiphiles **1–7** did not exhibit any hydrogelation ability; rather they were insoluble in water. The Boc protection was removed (Scheme 2) by treatment with trifluoroacetic acid (TFA) to induce more hydrophilicity within the structures (**1a**–**7a**, Scheme 1). A more-polar environment at the N terminus might be favorable for solubilization, as well as for self-assembled gelation in water of amphiphiles containing a free-amine group (NH_2). The gelation ability of these newly synthesized compounds **1a**–**7a** in water was studied by the "stable-to-inversion of the container" method (Table 2).

Although L-alanine-containing amphiphile **1a** was found to be soluble in water, encouragingly, L-phenylalanine-based amphiphile **2a** exhibited efficient hydrogelation ability with a MGC = 1.7 % *w*/*v* (Table 2). The presence of a π–π-stacking unit (phenyl ring) in addition to the naphthalene moiety seems to be important to induce hydrogelation for single amino acid based amphiphiles. However, compound **3a**, which contained a different aromatic amino acid residue (L-tryptophan), was found to be insoluble in water. The extended aromaticity of the indole ring in **3a** might have perturbed the optimum HLB required for gelation. We were keen to know the water-gelation ability of primary amine *N*-Boc-deprotected hydrophilic dipeptides **4a**–**7a**. Amphiphile **4a** was found to be a non-gelator of water, although its corresponding *N*-Boc-protected analogue **4** was an organogelator. The absence of any aromaticity within the central dipeptide scaffold of **4a** possibly enhanced its hydrophilic character and assisted solubilization in water rather than gelation. Interestingly, compound **5a**, composed of a dipeptide with one aromatic and one aliphatic amino acid, showed excellent hydrogelation ability with an MGC = 0.9 % *w*/*v*. This observation reiterates the important influence of planar aro-

matic rings in gelation. However, replacement of the aliphatic amino acid (L-alanine) with an aromatic residue (L-phenylalanine) resulted in a decline of the water-gelation efficiency (MGC for **6a** = 3.0 % *w*/*v*). Following this trend, the gelation ability was eventually lost for **7a**, in which the C-terminal L-phenylalanine residue of the dipeptide was replaced with L-tryptophan (a residue with an extended aromatic ring system). The increase in aromaticity clearly disturbed the HLB due to the augmentation of the overall hydrophobicity of the amphiphiles.[12a] Thus, it can be inferred that a dipeptide comprised of one aromatic and one aliphatic amino acid was the ideal central scaffold for hydrogelation of amphiphiles that contained a primary amine group. Interestingly, hydrogelators **1a**–**7a** reverted to efficient organogelators **1**–**7** by *N*-Boc protection in alkaline medium (Scheme 2). In summary, transformation between organo- and hydrogelation ability from a common structural scaffold was achieved by simple pH-responsive removal or inclusion of a Boc moiety.

All of the hydro- and organogels were thermoreversible in nature; they melted upon slow heating and returned to gel form upon cooling. The gel-melting temperature (T_{gel}) is the temperature at which the gel-to-sol transition occurs. The T_{gel} values of the gelators were comparable at their MGCs (37–42 °C) and increased with increasing gelator concentration (Figure 1).[14] All of the gels were stable at room temperature for several months.

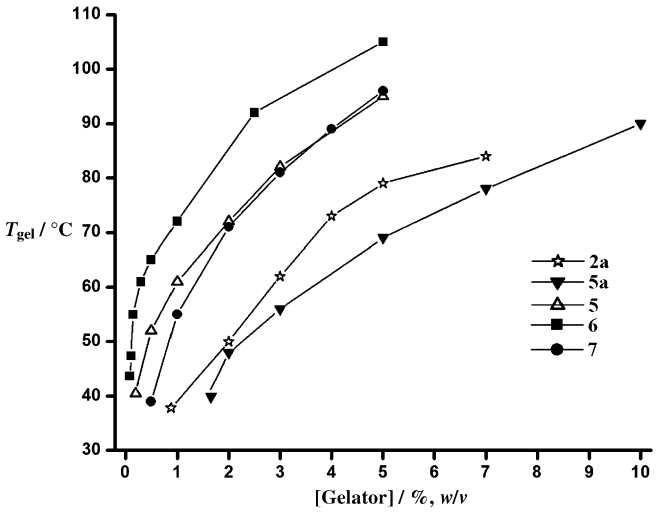


Figure 1. Variation of T_{gel} with gelator concentration.

Microscopic studies: Field-emission scanning electron microscopy (FESEM) was employed to gain visual insight into the supramolecular arrangement of both the hydro- and organogels. All the xerogels, prepared either from water or toluene, showed the presence of a 3D fibrillar network at their MGC (Figure 2), although the nature and size of the fiber was dissimilar and dependent on the structure of the LMWG. The xerogel of **4** (comprised of two aliphatic amino acid residues) showed fibrous morphology with an average fiber thickness of 350–400 nm and fiber length up to several micrometers (Figure 2a). The xerogel of **5** (one aliphatic and one aromatic residue) prepared from toluene showed an interconnected fibrillar network with an individual fiber diameter of approximately 120–150 nm. Some of the fibers were associated with each other to form thicker fibers of approximately 250 nm diameter (Figure 2b). Upon incorporation of an L-phenylalanine residue in the gelator structure, a three-fold improvement in gelation efficiency was observed for **5**, relative to **4**, attributed to this variation in nature and size of the fiber. This reiterates the pronounced effect of an aromatic residue in modulating the gelation efficacy. In the case of the dried gel of **6** (two aromatic L-phenylalanine residues), a considerable change in the nature of the fiber was observed. The network was formed by intertwined fibrils approximately 40–50 nm thick. The length of the fibers was found to be several micrometers, with uniform diameter (Figure 2c). Presumably, the molecular structure played an important role in the determination of the morphology of the network. This densely packed, intertwined fibrous network entraps more solvent molecules within its supramolecular assembly and is the most efficient organogel (MGC = 0.08 % *w*/*v*, Table 1) among all the gelators as a result. The supramolecular arrangement of gelator **7** (an L-phenylalanine and L-tryptophan dipeptide core) also showed an entangled network of fibrils with a thickness of approximately 50–60 nm. Some of the fibers were curled together to form thicker fibers of approximately 150–200 nm diameter (Figure 2d).

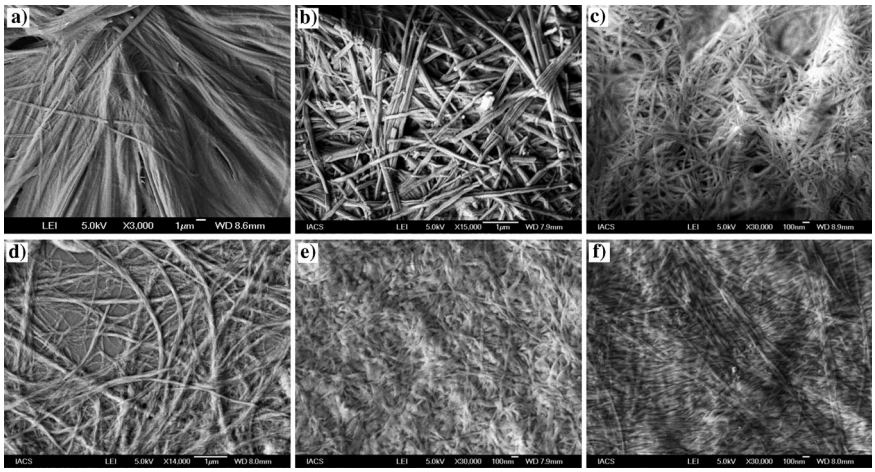


Figure 2. FESEM images of dried samples of a) **4**, b) **5**, c) **6**, and d) **7** in toluene; FESEM images of dried samples of e) **5a** and f) **6a** in water at the MGC.

Similar entangled fibril networks were observed for the hydrogels. In the case of **5a**, densely populated, interconnected fibrils with uniform thickness (≈40–50 nm) (Figure 2e) notably improved the water-immobilization ability in the self-assembled state. The hydrogel of **6a** showed the presence of lamellar, as well as intertwined fibril structure of comparable diameter but with a length of a few micrometers (Figure 2f). The similarity in the fibril network of both the organo- and hydrogels indicates that transformation between the gelators does not affect the supramolecular arrangement in self-assembled gelation. This could be due to the common structural scaffold for both the organo- and hydrogelators, the only difference is the presence or absence of a Boc moiety. Hence, simply by pH-sensitive removal or inclusion of a protecting group, a switch in the gelation behavior to extreme opposite polarity solvents can be easily achieved without compromising the self-aggregation behavior of the amphiphiles.

The presence of fibrous morphology within the organogel of **6** (the best organogelator) and hydrogels of **5a** and **6a** was further confirmed by transmission electron microscopy (TEM) images of their respective xerogels (Figure 3). The TEM images at five-times lower concentration than the MGC showed similar intertwined fibers of approximately 30–40 nm thickness for **6** (Figure 3a), and **5a** and **6a** exhibited fibers of several micrometers in length and approximately 40 nm diameter (Figure 3b,c), which supports the corresponding FESEM images (Figure 2e,f). A birefringence character (Figure S1 in the Supporting Information) within the entangled fibrous network was also observed in the polarizing optical microscopic (POM) image of **5** (xerogel prepared from toluene). The observed birefringence in the POM image indicates the high degree of molecular ordering in the gel state.[15]

Circular dichroism (CD) study: The expression of supramolecular chirality that originates from the highly ordered arrangement of hydrogelators **2a**, **5a**, and **6a** was investigated by recording their CD spectra in water at different concentrations (Figure 4).[16] The aqueous solutions of all of the hydrogelators had a negative peak at 228–233 nm and a positive peak at 218 nm in the spectra. The observed Cotton effect at the amide absorption region (228–233 nm) is due to the π–π* transition of the amide bond. These transitions are extremely sensitive to coupling with neighboring amide groups.[16b,c] In all cases, the pattern of the peaks in the spectra is analogous to that generally observed for the β-sheet (but not by the position of the peaks) protein structure (positive peak at 197 nm and negative peak at 218 nm).[17] Moreover, the sharp increase in the molar ellipticity with increasing gelator concentration also suggested a highly ordered arrangement of chiral planes at the supramolecular level.

FTIR study: Participation of noncovalent interactions, such as hydrogen bonding, during the self-assembly of the gelators was studied by FTIR spectroscopy. FTIR spectra were recorded for toluene xerogels, D_2O gels, and the non-self-assembled state of the gelators in chloroform. The FTIR spectra of gelators **5**, **6**, **5a**, and **6a** in chloroform showed transmission bands at $\tilde{\nu}$ = 3415–3420, 1665–1671, and 1512–1525 cm^{-1}, which are characteristic of non-hydrogen-bonded N–H (amide A), C=O (amide I), and N–H (amide II) frequencies, respectively (Figure 5, Figure S2 in the Supporting Information).[13c,14a,18] However, the transmission bands of the corresponding toluene xerogels of **5** and **6** appeared at $\tilde{\nu}$ = 3280, 1639–1642, and 1542–1545 cm^{-1}, respectively (Figure 5a, Figure S2a in the Supporting Information). This lowering of the stretching bands for N–H (amide A) and C=O (amide I), and increase in the bending band for N–H (amide II) indicates the presence of intermolecular hydrogen bonding between the carbonyl group and amide NH group in the gel state.[14a,18] Existence of intermolecular hydrogen bonding was also observed for **5a** and **6a**; the C=O (amide I) band at $\tilde{\nu}$ = 1668 cm^{-1} in chloroform shifted to $\tilde{\nu}$ = 1627 and 1631 cm^{-1}, respectively, in the gel state in D_2O (Figure 5b, Figure S2B in the Supporting Information). Thus, intermolecular hydrogen bonding plays an important role in the self-assembled gelation of both organo- and hydrogelators.

Luminescence study: In addition to hydrogen bonding, hydrophobic interactions are also known to play a crucial role in supramolecular gelation. To understand the participation of hydrophobic interactions during gelation, we examined the intrinsic fluorescence of the aromatic rings of the gelators rather than utilizing an external fluorescence probe. The luminescence spectra of gelators **6** (Figure 6a) and **5a** (Figure 6b) were recorded with varying concentrations in toluene and water, respectively, upon excitation of the molecules at 280 nm. Initially, at very low concentration, the emission intensity at 340 nm with a shoulder at 330 nm was found to gradually increase with concentration up to 0.01 % *w*/*v*, which is far below the MGC for both gelators. However, with further increase in the gelator concentration a sharp decrease in emission intensity was observed, along with broadening of the emission peak up to the MGC and above. The emission intensity increased until the gelators were in a non-self-assembled

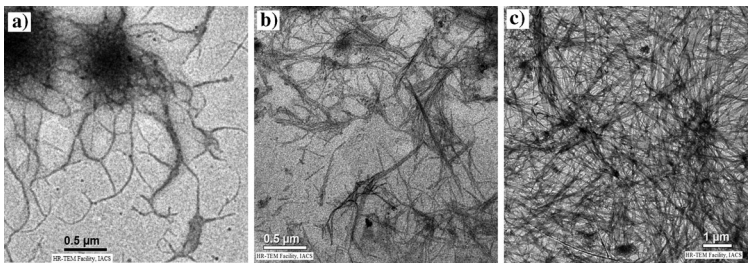


Figure 3. TEM images of dried samples of a) **6** (in toluene), b) **5a**, and c) **6a** (in water).

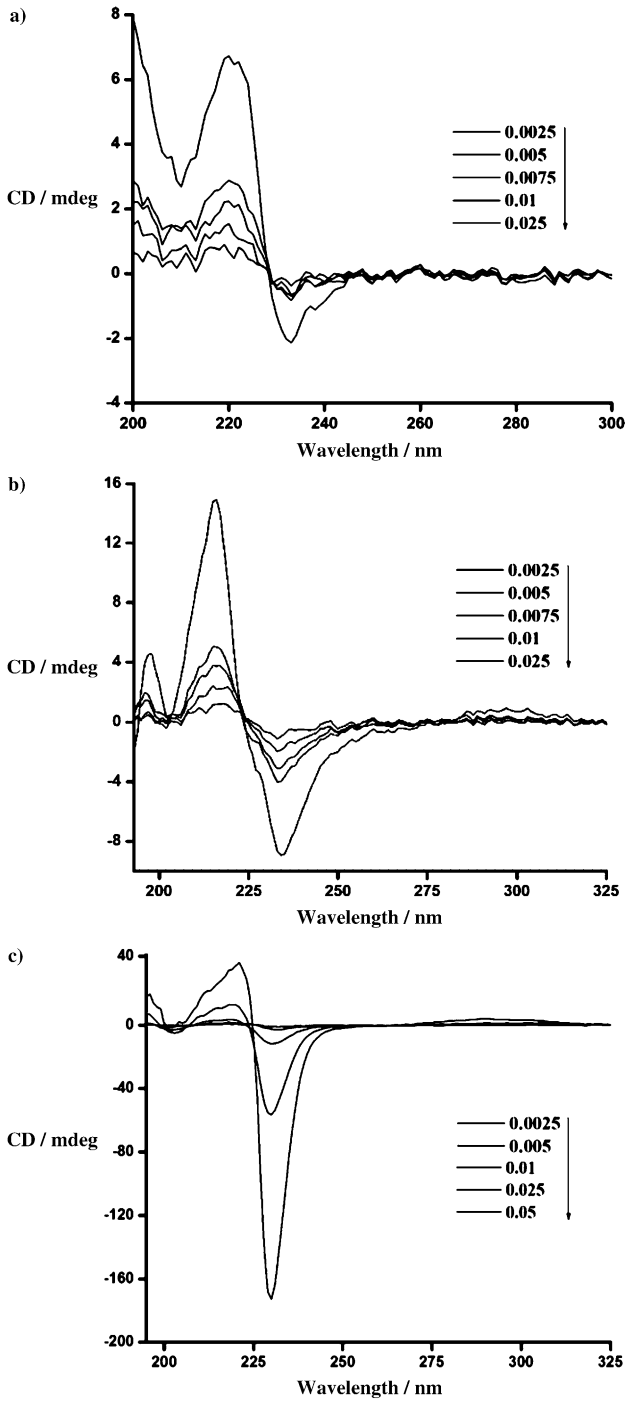


Figure 4. CD spectra of a) **2a**, b) **5a**, and c) **6a**, with varying concentrations [% *w*/*v*] in water at RT.

state. At higher concentrations (>0.01 % *w*/*v*), the amphiphilic molecules began to self-assemble for gelation. In this process of self-organization, the planar aromatic rings got closer to each other, which gradually quenched the fluorescence ability of the naphthalene unit, as well as the phenyl rings of the amino acid residues.[19]

XRD study: In addition to the preceding microscopic and spectroscopic studies, we measured the XRD spectra of

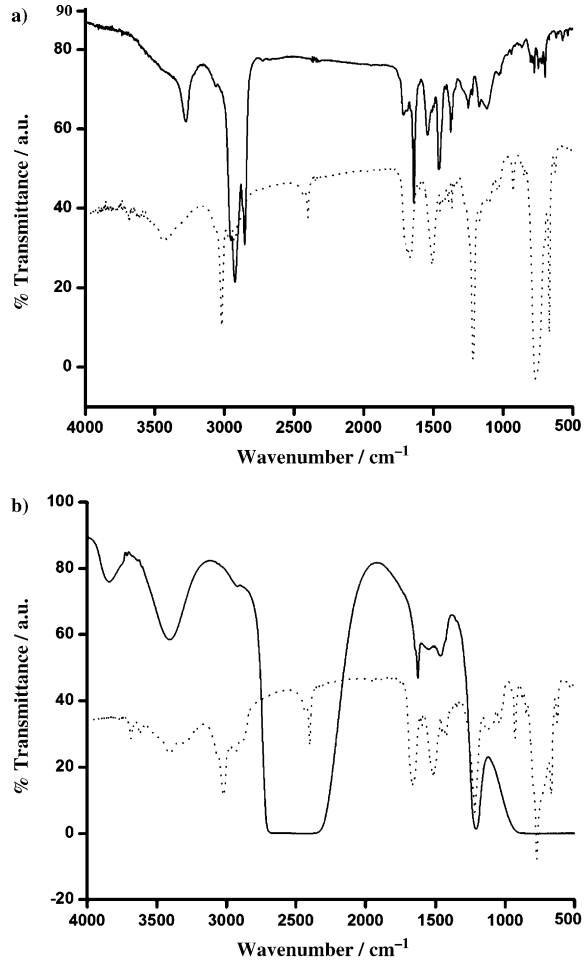


Figure 5. a) FTIR spectra of the xerogel of **6** in toluene (——) and in chloroform (·····). b) FTIR spectra of **5a** in D_2O in the gel state (——) and in chloroform (·····).

both the organogels and hydrogels to investigate the molecular packing and orientation of the gelators in the supramolecular gel state. Xerogels of **5** and **6** (taken as representative) obtained from toluene gave a peak at $2\theta = 19.40°$ (d spacing = 4.57 Å), accompanied by another peak at $2\theta = 9.6°$ with a d spacing of 9.4 Å (Figure 7a). These two peaks usually indicate the presence of antiparallel ordering, in which each molecule aligns (via cross) with two other molecules and forms hydrogen bonds.[4a] Similarly, hydrogel **2a** showed peaks at $2\theta = 9.5$ and 18.3° (d spacing = 9.6 and 4.33 Å, respectively) and hydrogel **5a** showed peaks at $2\theta = 10.6$ and 20.93° (d spacing = 8.34 and 4.23 Å, respectively; Figure 7b). This periodicity arises from spacing between the peptide chains and two stacked layers. Another peak at $2\theta = 23.7°$ (d spacing = 3.75 Å) further indicates the presence of the π–π-stacking interaction between the planar aromatic rings in the self-assembled structure.[20] These aromatic–aromatic interactions not only facilitate the long-range ordering of the molecules but also provide the hydrophobic environment that greatly increases the propensity for self-assembled gelation. The observed spectroscopic and microscopic studies suggest the involvement of hydrogen bonding, π–π stack-

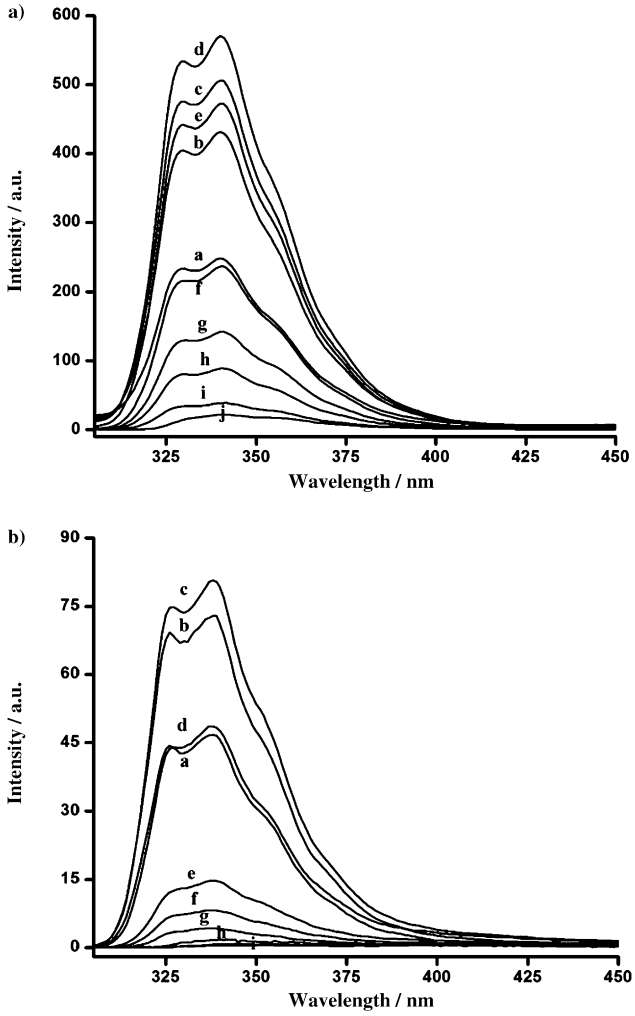


Figure 6. a) Luminescence spectra of gelator **6** at varying concentrations in toluene at RT. $\lambda_{ex}=280$ nm; [**6**]: a = 0.0025, b = 0.005, c = 0.0075, d = 0.01, e = 0.025, f = 0.05, g = 0.075, h = 0.1, i = 0.2, j = 0.3 % *w/v*. b) Luminescence spectra of gelator **5a** at varying concentrations in water at RT. $\lambda_{ex}=280$ nm; [**5a**]: a = 0.0025, b = 0.005, c = 0.01, d = 0.025, e = 0.05, f = 0.075, g = 0.1, h = 0.5, i = 1.5 % *w/v*.

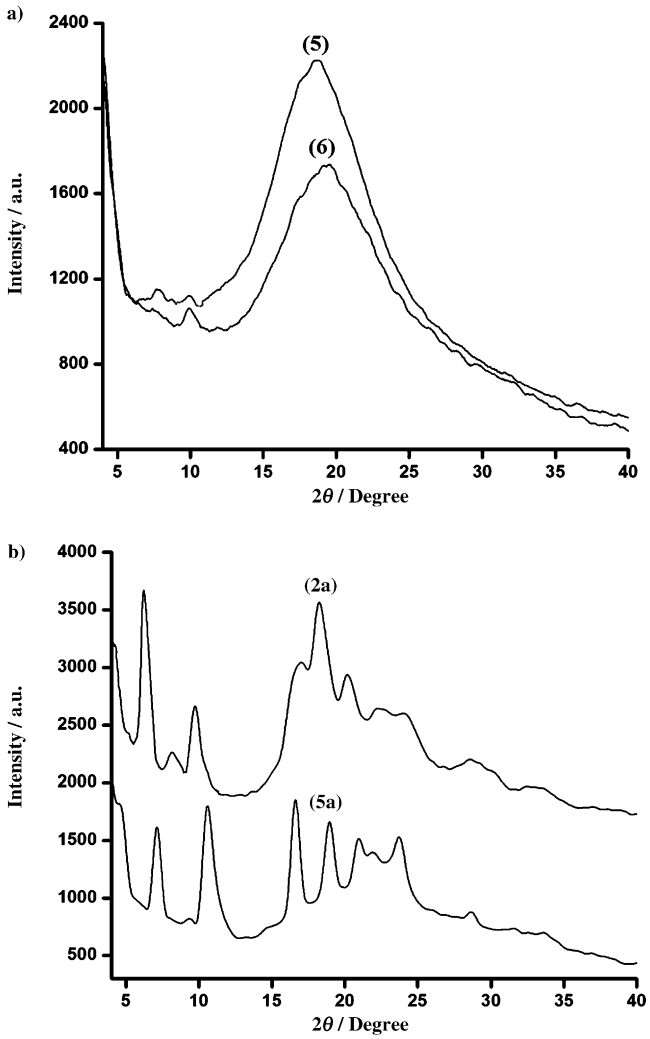


Figure 7. XRD spectra of a) dried organogels of **5** and **6**; b) dried hydrogels of **2a** and **5a**.

ing, and hydrophobic interactions in the self-assembled gelation through an ordered arrangement of the amphiphiles. This is schematically shown in Figure 8 for representative gelator, **6**.

Rheology: The mechanical strengths of representative organo- and hydrogels were characterized by rheological experiments. Rheological studies give an indication of the flow behavior and rigidity of the gel. The two main parameters are the storage modulus (G'), which represents the ability of the deformed material to store energy, and the loss modulus (G''), which corresponds to the flow behavior of the material under stress. In the gel state $G' > G''$ (G' and $G'' \approx \omega^0$) and in the sol state $G'' > G'$ ($G' \approx \omega^2$ and $G'' \approx \omega$; $\omega =$ angular frequency). The crossover point between G' and G'' (known as yield stress) indicates the transition point from elastic solid to viscous liquid. This is determined by measurement of the stress value at which G'' becomes higher than G' (stress-amplitude sweep experiment).[21] We carried out rheological experiments with the organogels of **5** and **6** and hydrogel **5a**. Initially, for all of the gels, G' was higher than G'' and with a gradual increase in applied stress both G' and G'' remained invariant, but deviated from linearity beyond a certain stress (Figure 9). In the case of the organogel of **5**, yield stress at the crossover point was 27.2 Pa (Figure 9a), whereas for **6** yield stress was higher than 100 Pa (Figure 9b). This implies superior mechanical strength of the organogel of **6** relative to that of **5**, which is in agreement with the better gelation efficiency of **6**. This considerable difference in the viscoelastic properties of the organogels can be attributed to the variation in the size and dimension of fibers within the intertwined supramolecular 3D network of the gels.[21b] However, the yield stress for hydrogel **5a** was found to be much lower (9.5 Pa) than that of either of the organogels studied (Figure 9c). The organogelator **5** and hydrogelator **5a** are comprised of a common structural motif, distinguished by the presence or absence of an *N*-Boc moiety. This subtle varia-

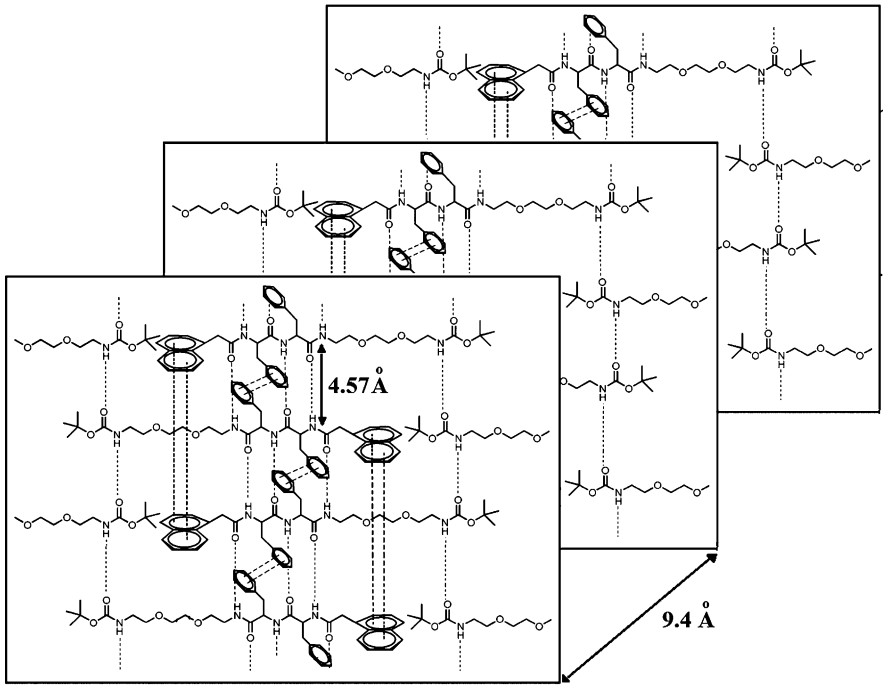


Figure 8. Schematic representation of the possible arrangement of **6** in the gel state.

tion in their structure provides an additional hydrogen-bonding site for organogel **5** due to the extra amide linkage, which might be the possible cause for its higher elasticity relative to hydrogel **5a**.[21b] The observed rheological behavior of the gels is in accordance with the viscoelastic behavior of soft materials reported in literature.[21]

Conclusion

We have successfully demonstrated an easy approach to develop efficient organo- and hydrogelators from a common amino acid/dipeptide-based precursor scaffold. Transformation was possible by simple pH-responsive inclusion or removal of an *N*-Boc moiety. A detailed structure–property investigation was carried out by judicious alterations of the amino acid residues to determine a rationale behind the development of efficient gelators. Involvement of different noncovalent interactions in the self-assembled gelation was established by spectroscopic and microscopic techniques. The supramolecular assembly of these amphiphiles could be utilized for the development of soft nanocomposites by in situ synthesis of metal nanoparticles within the gel matrix. Further, these gel-nanoparticle soft composites have potential applications in diverse fields, from materials science to biotechnology.

Experimental Section

Materials: All amino acids, Boc anhydride, dicyclohexylcarbodiimide (DCC), 4-*N*,*N*-dimethylaminopyridine (DMAP), 1-hydroxybenzotriazole (HOBT), and solvents were purchased from SRL, India. Trifluoroacetic acid (TFA), α-naphthyl acetic acid, 1,1'-carbonyl diimidazole (CDI), thionyl chloride, and sodium hydroxide were procured from Spectrochem, India. All deuterated solvents for NMR and FTIR spectroscopy studies and 2,2'-(ethylenedioxy)bis(ethylamine) were obtained from Aldrich Chemical Co. TLC was performed on Merck precoated silica gel 60-F_{254} plates. ^{1}H NMR spectra were recorded on an AVANCE 500 MHz (Bruker) spectrometer. Mass spectra were acquired by electron-spray ionization (ESI) on a Q-TOF-micro quadrupole mass spectrometer (Micromass). Elemental analyses were performed on Perkin–Elmer 2400 CHN analyzer.

Synthetic procedure: All amphiphilic gelators were synthesized by well-established peptide chemistry (see the Supporting Information, Scheme S1).

Synthesis of 1–3: The carboxylic acid group of the L-amino acid was protected by conversion to a methyl ester. The ester-protected amino acid was coupled with α-naphthyl acetic acid in dry CH_2Cl_2 with CDI (1 equiv) as the coupling agent. The ester-protected amide was purified by column chromatography on 60–120 mesh silica gel (ethyl acetate/hexane). The product was then hydrolyzed by treatment with 1 N NaOH solution (1.1 equiv) in MeOH for 6 h with stirring at RT. The reaction mixture was concentrated on a rotary evaporator, then diluted with water. The aqueous mixture was washed with ether, subsequently acidified with a 1 N aqueous solution of HCl, and the carboxylic acid was extracted into ethyl acetate. This acid was coupled with mono-Boc-protected 2,2'-(ethylenedioxy)bis(ethylamine) by treatment with DCC (1 equiv), DMAP (cat.), and HOBt (1 equiv) in dry CH_2Cl_2. The product was purified by column chromatography on 100–200 mesh silica gel (methanol/chloroform).

Synthesis of compounds 4–7: For the synthesis of amphiphiles **4**--**7**, the methyl ester of the appropriate L-amino acid was coupled with α-naphthyl acetic acid, then hydrolysis by treatment with NaOH gave the desired carboxylic acid, as described above. This acid was further coupled with a second methyl ester-protected amino acid by reaction with DCC (1 equiv), DMAP (cat.), and HOBt (1 equiv) in dry CH_2Cl_2. This methyl ester was hydrolyzed with NaOH, as described above, to afford the acid. The free acid at the C terminus of the dipeptide was coupled with mono-Boc-protected 2,2'-(ethylenedioxy)bis(ethylamine) by treatment with DCC (1 equiv), DMAP (cat.), and HOBt (1 equiv) in dry CH_2Cl_2. The product was purified by column chromatography on 100–200 mesh silica gel (methanol/chloroform).

Synthesis of compounds 1a–7a: The pure *N*-Boc-protected compounds **1–7** were Boc-deprotected by treatment with TFA (2 equiv) in dry CH_2Cl_2 under magnetic stirring for approximately 2 h. The volatile compounds were removed on a rotary evaporator and CH_2Cl_2 was added. The CH_2Cl_2 layer was washed with a 10% aqueous solution of Na_2CO_3 and then brine, to neutrality. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the desired amine. The product was purified by column chromatography on 100–200 mesh silica gel (methanol/chloroform). All compounds were characterized by NMR spectroscopy, elemental analysis, and mass spectrometry; the data are provided in the Supporting Information.

Preparation of gels: The required amount of compound was added to a screw-capped vial with an internal diameter (i.d.) of 10 mm, then slowly heated to dissolve, either in organic solvent or water. The solution was al-

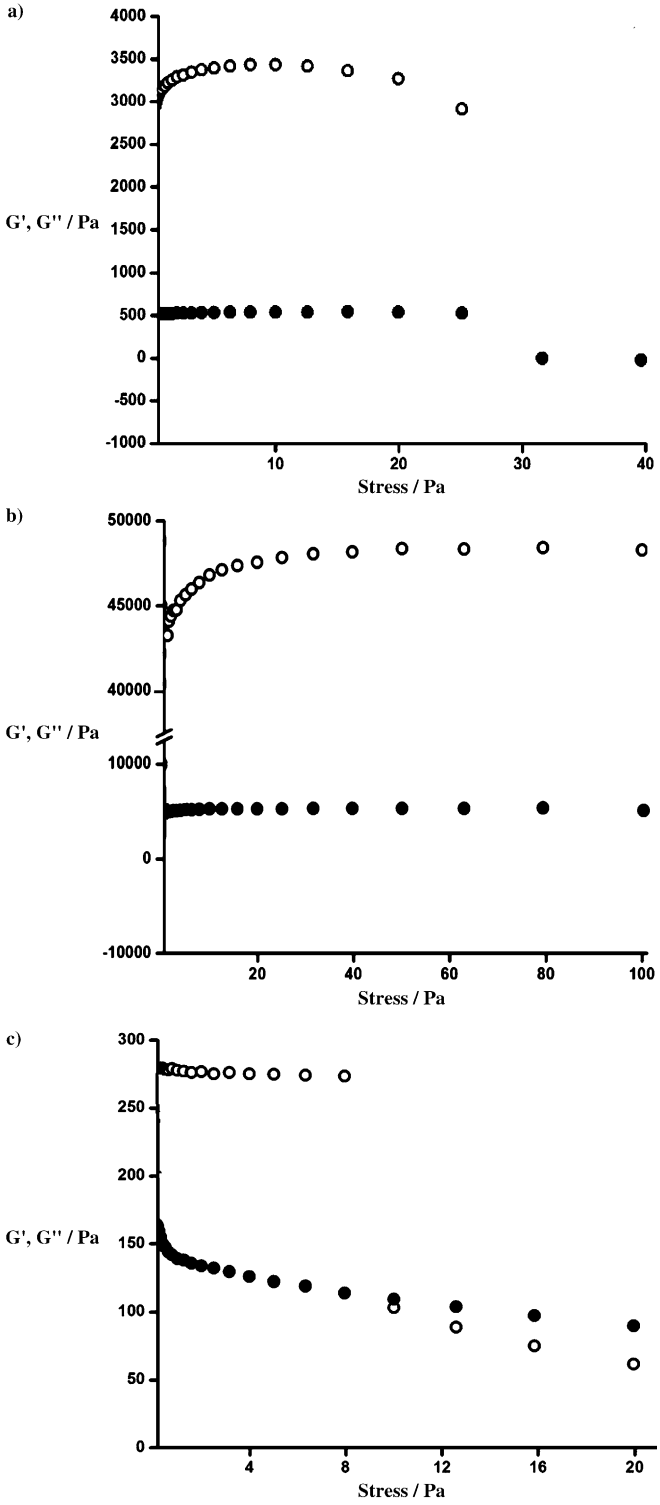


Figure 9. Plots of storage modulus (G', ○) and loss modulus (G'', ●) versus stress for organogels a) **5** and b) **6** (in toluene) and c) hydrogel **5a** at a concentration of 2% *w*/*v*.

lowed to cool slowly (undisturbed) to RT. The gelation of the aggregated material was assessed by the "stable-to-inversion of the vial" method.

Determination of the gel-to-sol transition temperature (T_{gel}): The gel-to-sol transition temperature (T_{gel}) was determined by placing the glass vial (i.d. 10 mm) containing the gel in a thermostated oil bath and slowly raising the temperature at a rate of 2°C/min. The T_{gel} was defined as the temperature (±0.5°C) at which the gel melted and started to flow.

Microscopic study: FESEM images were obtained on a JEOL-6700F microscope. A drop of gel (at the MGC) was placed on a cover slip and dried for few hours under vacuum before imaging. TEM experiments were performed on a JEOL JEM 2010 high-resolution microscope operated at an accelerating voltage 200 kV. Dilute solutions of gel were placed on a 300-mesh carbon-coated Cu grid and dried for few hours under vacuum before imaging. The hydrogelators were negatively stained with uranyl acetate (2% *w*/*v*). POM images were taken on Olympus U-TV1X-2 microscope.

FTIR measurements: FTIR measurements of the gelators in $CHCl_3$ solution (KBr cell), D_2O (CaF_2 cell; for hydrogels), and dried gels from toluene (KBr pellets) were performed on a Perkin–Elmer Spectrum 100 FTIR spectrometer.

Circular dichroism (CD) spectra: CD spectra of aqueous solutions of gelators **2a**, **5a**, and **6a** with varying concentrations were recorded in a quartz cuvette (1 mm path length) on a JASCO J-815 spectrometer.

XRD spectra: XRD measurements of the xerogels were obtained on a Bruker D8 Advance diffractometer fitted with a $Cu_{K\alpha}$ radiation source ($\alpha = 0.15406$ nm) with a voltage and current of 40 kV and 30 mA, respectively. All xerogels were scanned from 1 to 40°.

Fluorescence spectroscopy: The emission spectra of the amphiphiles were recorded on a Varian Cary Eclipse luminescence spectrometer at varying concentration from 0.0025% *w*/*v*–>MGC. A stock solution of the amphiphiles was prepared, which was subsequently diluted in water or toluene to obtain the spectra. Solutions were excited at $\lambda_{ex} = 280$ nm. The excitation and emission slit width were both 5 nm.

Rheological experiments: The rheological experiments were performed by cone-and-plate geometry (diameter was 40 mm) on the rheometer plate with an Advanced Rheometer AR 2000 (TA Instruments, USA). The organogels of **5** and **6** and hydrogel of **5a** were prepared at 2% *w*/*v* and kept overnight at RT. The gel was scooped on the rheometer plate so that there was no air gap with the cone. Stress-amplitude sweep experiments were performed at a constant oscillation frequency of 1 Hz for the strain range 0.01–100 Pa at 25°C and the storage modulus (G') and the loss modulus (G'') were plotted against oscillatory stress.

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