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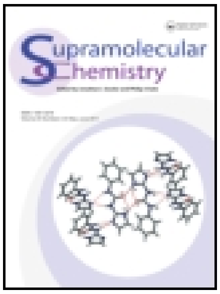

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Gelation of organic solvents by *N*-(*n*-tetradecylcarbamoyl)-L-amino acids

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A series of *N*-(*n*-alkylcarbamoyl)-L-amino acid amphiphiles with different amino acid head groups were designed and synthesised. The gelation abilities of these amphiphilic molecules were studied in toluene and *p*-xylene solvents. The hypothesis that steric crowding at the chiral head group destroys gelation ability of the amphiphile was examined. Indeed, beside L-alanine-based amphiphile, only L-serine and L-aspartic acid derivatives were found to gelate the organic liquids efficiently in the presence of a small quantity of water. The gels were characterised by a number of methods, including FT-IR, NMR and X-ray diffraction spectroscopy, scanning electron microscopy (SEM) and rheology. The SEM micrographs revealed three-dimensional networks of ribbon-like aggregates. The organogels were observed to be thermo-reversible in nature and have sufficient mechanical strength. The gels have gel-to-sol transition temperatures above the physiological temperature (310 K).

Keywords: amino acid; organogel; microscopy; rheology; X-ray diffraction

Introduction

A physical gel is a semi-solid material composed of low concentrations of low-molecular-weight gelator molecules that, in the presence of an appropriate solvent, self-assemble via physical interactions (e.g. dipole–dipole, van der Waals, hydrogen bonding and π–π stacking) (*1*) into an extensive three-dimensional (3D) network preventing solvent flow as a result of surface tension and capillary forces (*2*). In fact, gels have been described as being a meta-stable state between the solution and crystal (or precipitate) phases. Owing to the balance between gelator self-assembly forces and solubilising solvent–aggregate interactions, the macroscopic phase separation into crystalline and liquid layers is avoided in these systems. The overall thermodynamic and kinetic stability of the gel results from the interplay of the opposing forces related to the gelator's partial solubility in the continuous phase. These nano-structured soft materials have attracted tremendous attention in academics as well as in the industry because of their potential application in fields including drug delivery (*3*), tissue engineering (*4*), synthesis of nanomaterials and devices (*5*), sensing and soft lithography (*6*). Although a wide variety of gelators are reported, most have been discovered serendipitously (*7–12*). Only a few gelator molecules were developed by rational design. As physical gelation often involves one or more non-covalent weak forces, which are difficult to quantify, it is almost impossible to predict gelation ability of a molecule in a given solvent. However, it has been recognised that an effective gelator should possess functional groups that interact with each other via attractive interactions.

In the past three decades, gelation behaviour of a wide variety of molecules with diverse molecular structures including long-chain hydrocarbons (*13*), steroid derivatives (*14*), carbohydrate-derived systems (*15*), amino acid derivatives (*16*), dendrimers (*17*), metal complexes (*18*) and also two component systems (*19*) have been reported. Other types of amphiphilic molecules have also been used to achieve gelation of water and/or organic media (*20*). Bhattacharyya and co-workers have reported that fatty acid amides of L-alanine can gelate oil selectively from oil–water mixtures (*21*). They have also investigated gelation of a series of organic solvents by optically pure *N*-(alkanoyl)-L-amino acid (C_m-L-amino acid) amphiphiles. Among these, only L-Ala (C_m-L-Ala) and L-Phe (C_m-L-Phe) based gelators were found to be most efficient and versatile as they self-assembled into layered structures to form the gel network. It was observed that C_m-L-Phe gelates hydrocarbon solvents only, whereas C_m-L-Ala can gelate hydrocarbon as well as aromatic solvents. According to these authors (*21–23*), H-bonding interaction between amide groups as well as between carboxylic acid groups of two adjacent molecules is the driving force for the gelation. It was reported that steric crowding that hinders H-bonding interactions at the amino acid head group of the other C_m-L-amino acid amphiphiles is responsible for the failure to gel organic liquids. On the other hand, it is well known that H-bonding interaction of the amino acid side chain in L-Ser, L-Asn and L-Gln

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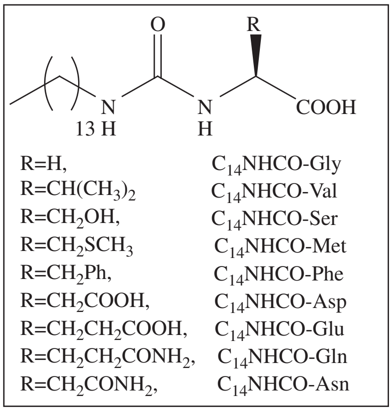
interferes with the amide (—HNCO—) or carboxylic acid (—COOH) groups prevents the formation of bilayer structure in water by the sodium salt of the corresponding amphiphiles (*24*). Recently, it has been shown by our group (*25*) that the incorporation of phenoxy group in the hydrocarbon chain enhances gelation ability of the C_m-L-Ala amphiphiles in organic solvents. Indeed, this type of molecules could also be ordered to form supramolecular aggregates through H-bonding interaction (*26, 27*). The fatty acid amides of amino acid system reported in the literature have one important advantage in that these molecules are totally biocompatible and hence biodegradable (*28*).

Like —HNCO— group, the urea linkage (—HNCONH—) has similar structure but with two H-bond donor sites and one H-bond acceptor site. Thus, urea derivatives form strong H-bonding network between a carbonyl group of one urea unit and two H-atoms of –HNCONH– of a neighbouring molecule (*29*). This results in a strong gelation ability of *N*,*N*′-dimethylurea (*30*), which is one of the lowest mass organogelators reported in the literature. Although amide and urea derivatives are normally H-bonding-type gelators, as the gel is often disrupted upon addition of a small amount of H-bonding substances, in a recent publication (*31*), we have shown that like C_m-L-Ala amphiphiles, the corresponding urido derivative also behaves as a good organogelator, but only upon addition of a small quantity of H-bonding additives such as H_2O, MeOH or urea. Nevertheless, in both types of gelators, intermolecular H-bonding interaction was shown to be the major driving force for gelation. Because substituted ureas are known to form strong H-bonds, it was thought that replacement of –HNCO– by –HNCONH– linkage might improve the gelation ability of other C_m-L-amino acid amphiphiles in organic solvents. Indeed, Wang and Hamilton (*32*) showed a remarkable self-assembling and gelation behaviour in H_2O by mono-urea L-Ser derivatives with low molecular weights. Efficient gelation of organic solvents by a series of L-Ser-based long-chain bis-urea derivatives was also reported by Polak and Lu (*33*). The presence of a hydroxyl group offers the potential for additional H-bonding interactions beyond those formed between the urea groups. Recently, we have reported (*34*) gelation behaviour of a series of L-cysteine-derived double hydrocarbon chain amphiphilic gelators L-(3-alkylcarbamoylsulfanyl)-2-(3-alkylurido)propionic acid with different hydrocarbon chain lengths (C_6–C_{16}). These gelators were observed to efficiently gelate, but only aromatic solvents.

In the present study, the –HNCO– group of the C_m-L-amino acid amphiphiles was replaced by a –HNCONH– group to produce C_nNHCO-amino acid amphiphiles in order to compensate for the steric crowding and/or H-bonding interactions of the amino acid side chain. In our previous publication (*31*), we have demonstrated good gelation abilities of C_nNHCO-Ala amphiphiles in a number of organic solvents. Earlier studies (*21, 22*) including ours (*31, 34*) have shown that the C_{14}-derivative of the L-Ala amphiphile has the highest gelation ability in comparison to those with shorter tail. The successful organogelation by C_nNHCO-Ala amphiphiles led to the present investigation of the gelation properties of *n*-tetradecylcarbamoyl derivative of the other optically active L-amino acids (C_{14}NHCO-amino acid). Thus in order to investigate head-group effect on organogelation, a series of C_{14}NHCO-amino acid amphiphiles (see Figure 1 for structures) containing –HNCONH– linkage in the hydrocarbon chain and L-Gly, L-Val, L-Phe, L-Met, L-Ser, L-Gln, L-Asn, L-Asp or L-Glu as head groups were synthesised. The gelation abilities were tested in two different organic solvents and compared. The gels were characterised by a number of techniques, including FT-IR, NMR and X-ray diffraction (XRD) spectroscopy, scanning electron microscopy (SEM) and rheology.



R=H,	C_{14}NHCO-Gly
R=CH(CH_3)$_2$	C_{14}NHCO-Val
R=CH_2OH,	C_{14}NHCO-Ser
R=CH_2SCH_3	C_{14}NHCO-Met
R=CH_2Ph,	C_{14}NHCO-Phe
R=CH_2COOH,	C_{14}NHCO-Asp
R=CH_2CH_2COOH,	C_{14}NHCO-Glu
R=$CH_2CH_2CONH_2$,	C_{14}NHCO-Gln
R=CH_2CONH_2,	C_{14}NHCO-Asn

Figure 1. The structures of the C_{14}NHCO-amino acid amphiphiles.

Experimental section

Materials

Mesitylene, tetradecyl isocyanate and the deuterated solvents, such as $CDCl_3$, D_2O and NaOD, were procured from Sigma-Aldrich (Bangalore, India). Glycine, L-valine, L-serine, L-aspartic acid, L-glutamic acid, L-phenylalanine, L-glutamine and L-asparagine were purchased from SRL (Mumbai, India) and were used without further purification. Analytical grade hydrochloric acid and triethylamine (TEA) were procured from SRL. These reagents were used directly from the bottle. The organic solvents, such as *n*-hexane, cyclohexane, benzene, toluene, *o*-xylene, *m*-xylene, *p*-xylene, chlorobenzene, notrobenzene, chloroform and tetrachloromethane were of highest purity commercially available and were dried and distilled fresh before use. All the solvents, ethanol, methanol, propanol, isopropanol, acetonitrile, acetone, dichloromethane, dimethyl foramide, dimethyl sulfoxide and pyridine, were commercially available with good quality and were dried and distilled fresh before use. The amphiphiles used in this study were synthesised according to Scheme 1 in the laboratory as described next.

Synthesis of N-(n*-alkylcarbamoyl)-*L*-amino acids*

The amphiphiles were synthesised following methods reported in the literature (*31*). Briefly, Gly, L-Val, L-Asp, L-Glu, L-Asn, L-Gln, L-Phe, and L-Ser (2.25 mmol) and tetradecyl isocyanate (1 equiv.) were reacted in 80:20 (v/v) ethanol/water mixture (10 mL) containing TEA (1.5 equiv.) in a round-bottomed flask at room temperature for 20 h (Scheme 1). The compound was precipitated from ethanol–water mixture upon acidification (pH 2) with 1 N HCl as white solid. The compound was recrystallised from ethanol–water mixture (1:1). Chemical structures were identified by elemental analysis, FT-IR and ^{1}H NMR spectra.

N-(n-tetradecylcarbamoyl)-glycine (C_{14}NHCO-Gly): Yield: 66%; m.p.: 94–96°C; FT-IR (KBr, cm^{-1}) 3340, 2858–2942, 1718, 1631, 1541; ^{1}H NMR: δ_H in ppm (200 MHz, D_2O) 0.81 (3H, t, *J* 6.3, CH_3), 1.20 (m, alkyl chain), 1.55 (2H, m, CH_2CH_2NH), 3.16 (2H, t, *J* 6.4, CH_2CH_2NH), 4.08 (1H, q, *J* 7.1, *C*H(NH)COOH). CHN analysis: calcd for $C_{17}H_{34}N_2O_3$ C: 64.93%, H: 10.90%, N: 8.91%; found C: 64.54%, H: 10.99%, N: 8.61%.

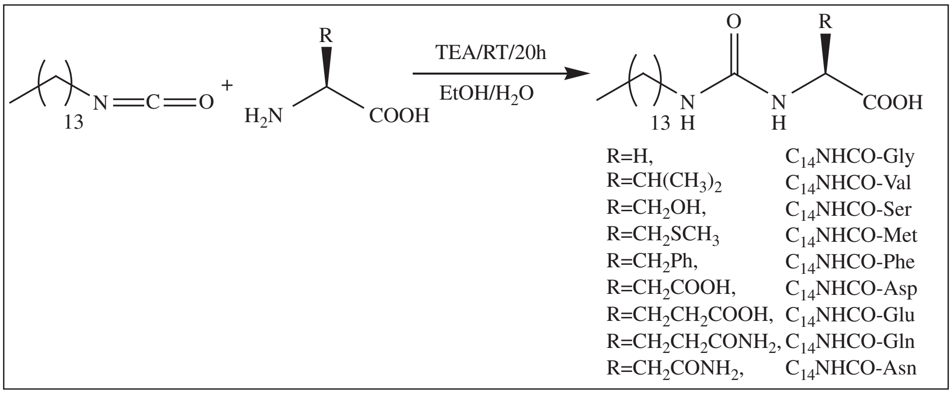
N-(ntTetradecylcarbamoyl)-L-serine (C_{14}NHCO-Ser): Yield: 68%; m.p.: 112–114°C, $[\alpha]_D^{25}$ (0.5%, MeOH) = +1.36° FT-IR (KBr, cm^{-1}) 3339, 2852–2956, 1716, 1629, 1562, 1214; ^{1}H NMR: δ_H in ppm (200 MHz, $CDCl_3$) 0.896 (3H, t, *J* 6.5, CH_3), 1.285 (24H, m, alkyl chain), 1.4(3H, d, *J* 6.4, $CH_3(CH)COOH$), 3.16 (2H, t, *J* 6.4, CH_2–NH), 4.02 (2H, m, CH_2–OH), 4.35 (1H, q, *J* 7.3, *C*H(NH)COOH); CHN analysis: calcd for $C_{18}H_{36}N_2O_4$ C: 62.76%, H: 10.53%, N: 8.13%; found C: 62.48%, H: 10.55%, N: 7.97%.

N-(n-tetradecylcarbamoyl)-L-valine (C_{14}NHCO-Val): Yield: 65%, m.p.: 94–96°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +1.45° FT-IR (KBr, cm^{-1}) 3379, 2852–2956, 1716, 1629, 1562, 1214; ^{1}H NMR: δ_H in ppm (200 MHz, $CDCl_3$): 0.875 (3H, t, *J* 6.2, CH_3), 0.93 (3H, d, *J* 6.8, CH—CH_3), 0.98 (3H, d, *J* 6.5, CH—CH_3) 1.25 (24H, m, alkyl chain), 2.70 (1H, m, *C*H—CH_3), 3.16 (2H, t, *J* 6.4, CH_2–NH), 4.45 (1H, q, *J* 7.6, *C*H(NH)COOH); CHN analysis: calcd for $C_{20}H_{40}N_2O_3$ C: 67.37%, H: 11.31%, N: 7.86%; found C: 67.18%, H: 11.58%, N: 7.70%.

N-(n-tetradecylcarbamoyl)-L-phenylalanine (C_{14}NHCO-Phe): Yield: 69%, m.p.: 90–92°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +3.26° FT-IR (KBr, cm^{-1}) 3349, 2852–2956, 1716, 1636, 1466 1562, 1214. ^{1}H NMR: δ_H in ppm (200 MHz, $CDCl_3$) 0.87 (3H, t, *J* 6.2, CH_3), 1.25 (24H, m, alkyl chain), 3.15 (2H, m, CH_2CH_2NH), 3.02 (2H, m, CH_2CH_2Ph), 4.57 (1H, NH—*C*H—COOH), 7.22 (m, Phenyl H); CHN analysis: calcd for $C_{24}H_{40}N_2O_3$ C: 71.25%, H: 9.97%, N: 6.92%; found C: 71.28%, H: 9.90%, N: 6.93%.

N-(n-tetradecylcarbamoyl)-L-aspartic acid (C_{14}NHCO-Asp): Yield: 62%, m.p.: 96–98°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +2.16° FT-IR (KBr, cm^{-1}) 3354, 2856–2936, 1773, 1727, 1643, 1471, 1226; ^{1}H NMR: δ_H in ppm (200 MHz, D_2O): 0.80 (3H, t, *J* 6.1, CH_3), 1.25 (24H, m, alkyl chain), 2.50 (2H, d, *J* 6.4, $CHCH_2COOH$), 3.04 (2H, m, CH_2–NH), 4.22 (1H, q, *J* 7.6, *C*H(NH)CH_2); CHN analysis: calcd for $C_{19}H_{36}N_2O_5$ C: 61.26%, H: 9.74%, N: 7.52%; found C: 62.53%, H: 9.96%, N: 7.86%.

N-(n-tetradecylcarbamoyl)-L-glutamic acid (C_{14}NHCO-Glu): Yield: 62%; m.p.: 116–118°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +2.95° FT-IR (KBr, cm^{-1}) 3395, 2852–2943, 1716, 1642, 1583, 1538, 1248; ^{1}H NMR: δ_H in ppm (200 MHz, D_2O) 0.79 (3H, t, *J* 6.05, CH_3), 1.19 (24H, m, alkyl chain), 1.87 (2H, q, *J* 7.4, $CHCH_2CH_2$), 2.10 (2H, t, *J* 6.3, CH_2CH_2COOH), 2.99 (2H, t, *J* 6.4, CH_2-NH), 3.90 (1H, t, *J* 7.6, *C*H(NH)CH_2); CHN analysis: calcd for $C_{20}H_{38}N_2O_5$ C: 62.15%, H: 9.91%, N: 7.25%; found C: 62.01%, H: 10.07%, N: 7.23%.



Scheme 1. Reaction scheme for the synthesis of *N*-(*n*-tetradecylcarbamoyl)-amino acids.

N-(n-tetradecylcarbamoyl)-L-methionine (C_{14}NHCO-Met): Yield: 61%; m.p.: 64–65°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +1.77° FT-IR (KBr, cm^{-1}) 3397, 2858–2942, 1720, 1657, 1541, 618 (weak); ^1H NMR: δ_H in ppm (200 MHz, D_2O) 0.79 (3H, t, *J* 6.1, CH_3), 1.19 (22H, m, alkyl chain), 1.55 (2H, m, CH_2CH_2NH), 2.09 (3H, s, SCH_3), 3.16 (2H, t, *J* 6.4, CH_2CH_2NH); 3.04 (2H, t, *J* 6.5, CH_2CH_2S); 4.74 (2H, t, *J* 6.6, C$H_2$$CH_2$S); CHN analysis: calcd for $C_{19}H_{38}N_2O_3S$ C: 61.81%, H: 10.37%, N: 7.21%; found C: 62.08%, H: 10.55%, N: 6.99%.

N-(n-tetradecylcarbamoyl)-L-asparagine (C_{14}NHCO-Asn): Yield: 67%; m.p.: 94–96°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +1.25° FT-IR (KBr, cm^{-1}) 3395, 2852–2943, 1716, 1642, 1583, 1538, 1248; ^1H NMR: δ_H in ppm (200 MHz, D_2O) 0.91 (3H, t, *J* 6.2, CH_3), 1.29 (24H, m, alkyl chain), 3.16 (2H, t, *J* 6.5, CH_2–NH), 2.80 (2H, m, CH_2CONH_2), 4.60 (1H, t, *J* 6.6, C*H*(NH)CH_2); CHN analysis: calcd for $C_{19}H_{37}N_3O_4$ C: 61.43%, H: 10.04%, N: 11.31%; found C: 61.78%, H: 11.57%, N: 11.23%.

N-(n-tetradecylcarbamoyl)-L-glutamine (C_{14}NHCO-Gln): Yield: 68%; m.p.: 128–130°C; $[\alpha]_D^{25}$ (0.5%, MeOH) = +1.66° FT-IR (KBr, cm^{-1}) 3395, 2851–2950, 1716, 1645, 1581, 1537; ^1H NMR: δ_H in ppm (200 MHz, D_2O) 0.91 (3H, t, *J* 6.1, CH_3), 1.29 (24H, m, alkyl chain), 3.16 (2H, t, *J* 6.4, CH_2–NH), 2.04 (2H, t, *J* 6.2, CH_2CH_2CO), 2.18 (2H, m, CH_2CONH_2), 4.46 (1H, t, *J* 7.1, C*H*(NH)CH_2); CHN analysis: calcd for $C_{20}H_{39}N_3O_4$ C: 62.41%, H: 10.20%, N: 10.90%; found C: 62.01%, H: 10.07%, N: 10.83%.

General instrumentation

A Perkin Elmer model 883 IR spectrometer was used for recording the FT-IR spectra. For solid samples, KBr pellet was used as a solvent. A Bruker SEM 200 or 400 instrument was used for recording ^1H and ^{13}C NMR spectra. Tetramethyl silane or acetonitrile was used as the internal standard. The elemental analysis was carried out with a Perkin Elmer 2400 Series II CHNS/O analyser (Perkin Elmer, USA). An Instind (Kolkata) melting point apparatus was used for determining the melting point using open capillaries. Optical rotations were measured on a digital polarimeter (Jasco P-1020, Jasco Corporation, Tokyo, Japan).

Field emission scanning electron microscopy

For Field emission scanning electron microscopy (FESEM) measurements, a thin layer of the sample was cast on a thoroughly cleaned copper or aluminium foil, allowed to cool at room temperature and then dried in air. The specimen was kept in desiccators until before use. A layer of gold was sputtered on the sample by vacuum spray to make conducting surface and finally transferred to the scanning electron microscope (Zeiss, Supra-40) operating at 5–10 kV.

Small-angle X-ray diffraction

Small-angle X-ray diffraction (SA-XRD) measurements were carried out using cast films of the gel. Spreading a few drops of the dispersion on a glass slide and slowly drying in atmosphere at room temperature prepared the films. The SA-XRD patterns of the cast films were measured on a PAN Analytical (PW 3040/60), X' pert PRO (the Netherland) diffractometer using Cu-Kα (154.05 pm) and Ni filter at a scanning rate of 0.001 s^{-1} operating at a voltage of 40 kV, with current 30 mA. The spectrum was recorded at room temperature between 2° and 12° in the 2θ scan mode in steps of 0.02° in 2θ. The interlayer distance (d) between the two successive planes was calculated using Bragg's equation:

$$n\lambda = 2d \sin\theta \tag{1}$$

where $n = 1$ for the first-order reflections and $\lambda = 1.54$ nm for Cu-Kα target.

Rheological measurements

All rheological measurements were carried out on a Bohlin RS D-100 rheometer (Malvern, UK) using parallel-plate (PP-20) geometry. The gap between the plates was fixed at 100–500 μm as per the stability of the gel by visual observation. The gel was placed on the rheometer and a stress-amplitude sweep experiment was carried out at a constant oscillation frequency of 1.0 Hz at 298 K. From this measurement, a liner viscoelastic region was identified and then a frequency sweep measurement was carried out over a wide frequency range of 0.01–100 Hz at a particular stress taken from the linear viscoelastic region at 298 K.

Results and discussion

Gelation behaviour

Gelation abilities of the amphiphiles were tested in different solvents, such as hexane, cyclohexane, benzene, toluene, *o*-xylene, *m*-xylene, *p*-xylene, mesitylene, chloroform, tetrachloromethane, chlorobenzene and nitrobenzene. However, except C_{14}NHCO-Asp, all other amphiphiles failed to gel any of the pure solvents used. Although C_{14}NHCO-Asp gelates toluene and *p*-xylene, the gelation ability increased in the presence of a small quantity of H_2O. Interestingly, C_{14}NHCO-Ser also gelated toluene and *p*-xylene, but in the presence of H_2O only. In other organic solvents, both these amphiphiles either remained insoluble or precipitated on cooling to room temperature even in the presence of water. It is important to note that in contrast to the corresponding amide derivative, C_{14}NHCO-Phe also failed to gel any of the solvents in the absence or presence of H_2O. Gelation

Table 1. Gelation behaviour and CGC values (±0.1% w/v) of the amphiphiles in the presence of H_2O, the numbers within the parentheses indicate corresponding CGC values in the absence of H_2O.

Gelator	PhMe	*p*-Xylene	T_{gs} (K)[a]
C_{14}NHCO-Gly	I	I	
C_{14}NHCO-Ala	0.9	1.0	338
C_{14}NHCO-Phe	S	S	
C_{14}NHCO-Ser	1.1	1.2	314
C_{14}NHCO-Met	Sw	DS	
C_{14}NHCO-Val	Cy	Cy	
C_{14}NHCO-Asp	1.2 (0.6)	1.6 (1.2)	310
C_{14}NHCO-Glu	S	S	
C_{14}NHCO-Asn	P	P	
C_{14}NHCO-Gln	P	P	

Note: I, insoluble; Cy, crystallisation; S, soluble; P, precipitation; Sw, swelling.

[a] T_{gs} values of the organogels were measured at a fixed gelator concentration of 0.06 M in *p*-xylene.

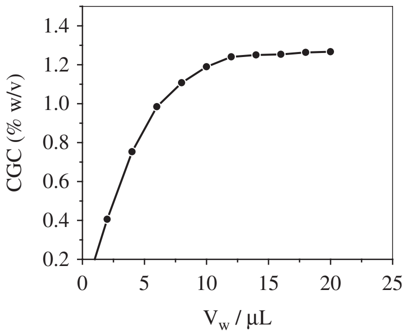


Figure 2. Variation of CGC of C_{14}NHCO-Ser in *p*-xylene with the added volume of H_2O (V_w).

properties of the amphiphiles in toluene and *p*-xylene are summarised in Table 1. The gelation abilities measured in terms of critical gelation concentration (CGC) are also summarised in the table.

The minimum amount of H_2O required for the gelation to get the maximum gelation ability for C_{14}NHCO-Ser was investigated by the same procedure as with C_{14}NHCO-Ala gelator reported earlier (*31*). Briefly, 5.5 mg of the gelator was weighed into 200 µL of solvent. The mixture was then heated, but the compound remained insoluble. Then, 2 µL of H_2O was added and heated again, the gelator started to become soluble and upon cooling transformed into a gel. More solvent was added to it until the organogel showed its maximum capacity of holding solvent. While reaching the limit, 2 µL of H_2O was added and the experiment was continued in the same manner. The plot in Figure 2 shows how CGC value varies with the H_2O content of the solvent. However, it should be noted that the addition of excess H_2O breaks the organogel. It was observed that the minimum amount of H_2O required for the gelation of C_{14}NHCO-Ser is ca. 12 µL/mL of solvent that is about 42 mol/mol of gelator. The required amount of H_2O is, however, slightly less than that in the case of C_{14}NHCO-Ala amphiphile. As solubility of water in the aromatic hydrocarbon solvents is in the range of 0.02–0.028 mM (*33*), most of the water molecules are used only in the self-assembly formation. We therefore determined CGC values in different solvents at a [water]/[gelator] mol ratio equal to 42. The CGC values of the amphiphiles in toluene and *p*-xylene solvents are included in Table 1. The corresponding values for C_{14}NHCO-Ala are also included for comparison purposes. The CGC value of C_{14}NHCO-Ala is the lowest, indicating its best gelling ability. However, with C_{14}NHCO-Asp, the CGC value is observed to increase upon addition of H_2O. Thus, when compared with C_{14}NHCO-Ala, the gelation abilities of both C_{14}NHCO-Ser and C_{14}NHCO-Asp are found to be less.

Morphology of the gels

Scanning electron microscopy

The FESEM images shown in Figure 3 were taken in order to visually observe the supramolecular structure of the gel aggregates. For comparison purposes, we have also included the FESEM image of C_{14}NHCO-Ala (Figure 3a) from our earlier publication (*31*). The images clearly show the existence of 3D networks of fibrous ribbon-like structures for all the gelators. The gel fibres of C_{14}NHCO-Ser and C_{14}NHCO-Asp organogels are slender and shorter in length. But the thickness of the gel fibres of C_{14}NHCO-Ala organogel is greater, indicating its better thermal and mechanical stability than the other two organogels.

X-ray diffraction

The XRD patterns (Figure 4) of the organogels (in *p*-xylene) of all the gelators exhibit periodic Bragg reflection peaks, suggesting that the gelator molecules are self-assembled into an ordered bilayer structure. The bilayer thickness (*d*) of the lamella is equal to the interlayer distance of 100 planes. The long d-spacing of the aggregates as obtained from XRD data is 3.80, 3.77 and 3.67 nm for C_{14}NHCO-Ser, C_{14}NHCO-Asp and C_{14}NHCO-Ala, respectively. These values are less than twice the hydrocarbon chain length (2.14 nm) of the gelator molecules. The hydrocarbon chain length of the amphiphiles was obtained from the energy-minimised (using MM2 force field of ChemDraw Ultra 7 software) structures of the amphiphiles; the distance between the β-carbon and the —CH_3 group was considered. This means that the gel fibres consist of repeating bilayer units in which the hydrocarbon chains are either interdigitated or tilted in the bilayer self-assembly. If the hydrocarbon

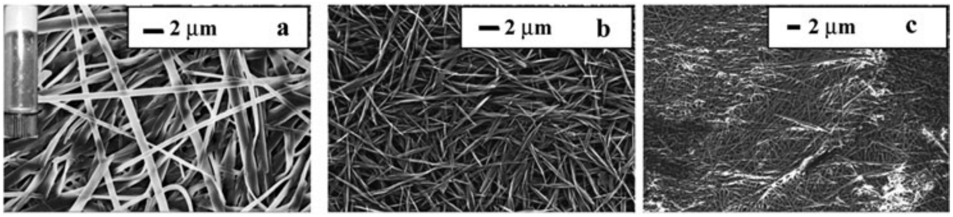


Figure 3. FESEM images of the *p*-xylene gels of (a) C_{14}NHCO-Ala, (b) C_{14}NHCO-Ser and (c) C_{14}NHCO-Asp gelators. Figure 3(a) is partially adapted with permission from Ref. [31]. Copyright © 2011 American Chemical Society.

chains were tilted in the bilayer, the *d*-spacing would have been similar in all the three amphiphiles having the same chain length. However, XRD data suggest that the *d*-value is less in the case of C_{14}NHCO-Ala gelator. Thus, it can be concluded that the hydrocarbon chains in the bilayer self-assembly are interdigitated.

Thermal stability

The thermal stability of the organogels was studied by measuring gel-to-sol transition temperature (T_{gs}). The T_{gs} values of the *p*-xylene organogels of C_{14}NHCO-Ala, C_{14}NHCO-Ser and C_{14}NHCO-Asp were measured at a fixed gelator concentration of 0.06 M. The T_{gs} values of the C_{14}NHCO-Ala and C_{14}NHCO-Ser organogels are 338 and 314 K, respectively. On the other hand, the T_{gs} values of C_{14}NHCO-Asp organogel formed with and without the addition of H_2O are, respectively, 310 and 307 K. The results show that the addition of H_2O increases thermal stability of the C_{14}NHCO-Asp organogel. Furthermore, the gel formed by C_{14}NHCO-Ala has greater thermal stability than those of the other two gelators.

Mechanical stability

As visually observed, the C_{14}NHCO-Ser organogels produced in pure solvents could not resist high mechanical force and broke upon even on slight shaking of the gel-containing vials. The C_{14}NHCO-Asp amphiphile, however, produced sufficiently stronger gels when appropriate volume of H_2O was added to the solvent. The mechanical strength of a gel which is measured by the storage modulus (G') and loss modulus (G'') was obtained for the organogels containing 0.15 M gelator in *p*-xylene solvent. The variations of G' and G'' with the frequency of the organogels are shown in Figure 5. The non-variance of both G' and G'' suggests gel structure. Furthermore, in the measured frequency range, the G' values are greater than G'' values, indicating solid-like behaviour of the gels. Rheology of C_{14}NHCO-Ala has been reported in our previous publications (*31*) and Figures 5a and 6a have been taken from the same reference.

The stress sweep plots in Figure 6 show that above a critical stress value, both G' and G'' abruptly fall to a very low value, indicating flow of the gel. This critical stress value is referred to as yield stress (σ_y) which is obtained from the stress sweep measurement of the organogels. The σ_y values of C_{14}NHCO-Ala, C_{14}NHCO-Asp and C_{14}NHCO-Ser are, respectively, 3912, 1109 and 312 Pa. That is, the organogel of C_{14}NHCO-Ala has the highest σ_y value, suggesting highest mechanical strength, while the C_{14}NHCO-Ser organogel has the lowest σ_y value and hence is weaker.

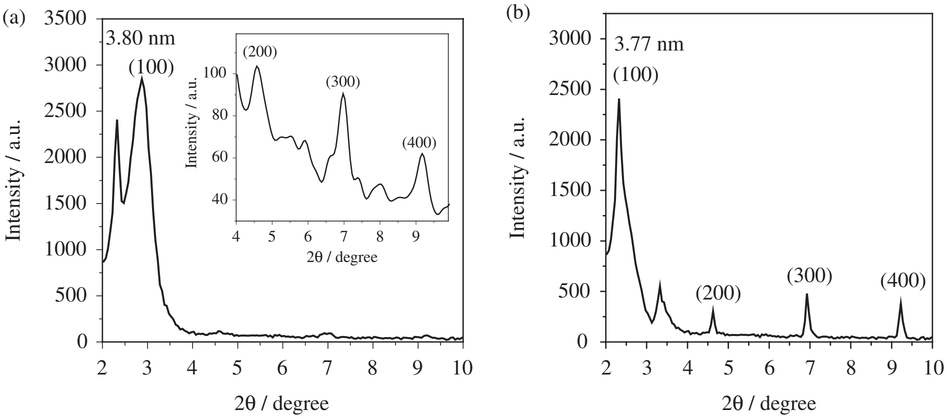


Figure 4. XRD patterns of the gel (*p*-xylene) cast films of (a) C_{14}NHCO-Ser and (b) C_{14}NHCO-Asp gelators.

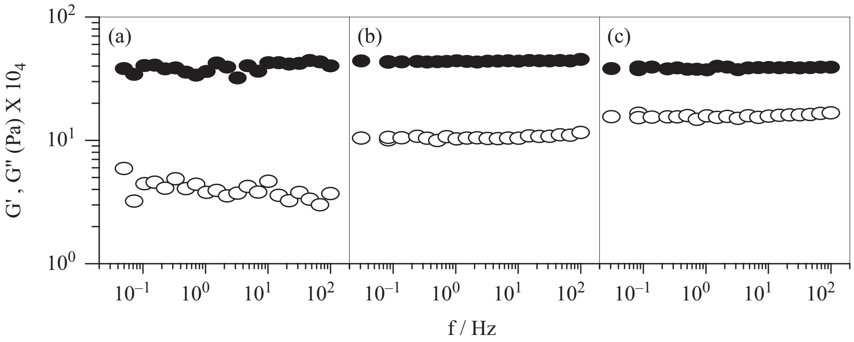


Figure 5. The variations of G' (●) and G'' (○) with the frequency of the organogels containing 0.15 M (a) C_{14}NHCO-Ala, (b) C_{14}NHCO-Asp and (c) C_{14}NHCO-Ser in *p*-xylene.

Driving force for gelation

Solubility of gelator molecules in solvents is an important parameter for the gelation as a subtle balance between the solubilisation and precipitation is required for the gel formation. Some recent studies (*35–37*) highlight the role played by solubility influencing gelation. In particular, the thermal stability (T_{gs}) and CGC values of gels formed by the gelators have been related in terms of different solubility parameters and self-assembly of gelator-building blocks. As discussed in our previous publication (*31*), the urea group present in the amphiphile causes a strong H-bonding in the molecules making it less soluble (or insoluble) in organic solvents. The extent of H-bonding can be qualitatively estimated by the solid-state m.p. and the stretching frequencies of vibrations of the NHCONH group (Table 2). Among all the amphiphiles, C_{14}NHCO-Ala has the highest m.p. indicating the presence of strongest H-bonding in the solid state. This is substantiated by lower values of stretching frequencies of amide A, amide I and C═O of —COOH groups. The solid-state m.p. of C_{14}NHCO-Asp is much lower than that of C_{14}NHCO-Ala. This is because the —COOH group of the amino acid side chain in C_{14}NHCO-Asp can either make intermolecular H-bond with the —NHCONH— group of another molecule or intramolecular H-bonding in the same molecule as shown in Figure 7, which disfavours the formation of intermolecular H-bonding between the urea groups. So the extent of intermolecular H-bonding in the solid state of C_{14}NHCO-Asp is lower which is also evident from its lower values of m.p. and stretching frequency. Thus, it becomes easily soluble in organic solvents on heating. The H-bond distance is ca. 0.26 nm which is below the maximum limit (0.26–0.30 nm) (*38*). Similar intramolecular H-bonding, however, is not possible with C_{14}NHCO-Glu, C_{14}NHCO-Asn and C_{14}NHCO-Gln amphiphiles. In these amphiphiles as shown by the respective structure in Figure 7, the H-bond distance (0.5–0.6 nm) is greater than the maximum limit. The m.p. of C_{14}NHCO-Met is the lowest, and consequently it becomes soluble in the organic solvent upon heating. Besides, the mp and the FT-IR values suggest that all the other amphiphiles have a strong H-bonding in their

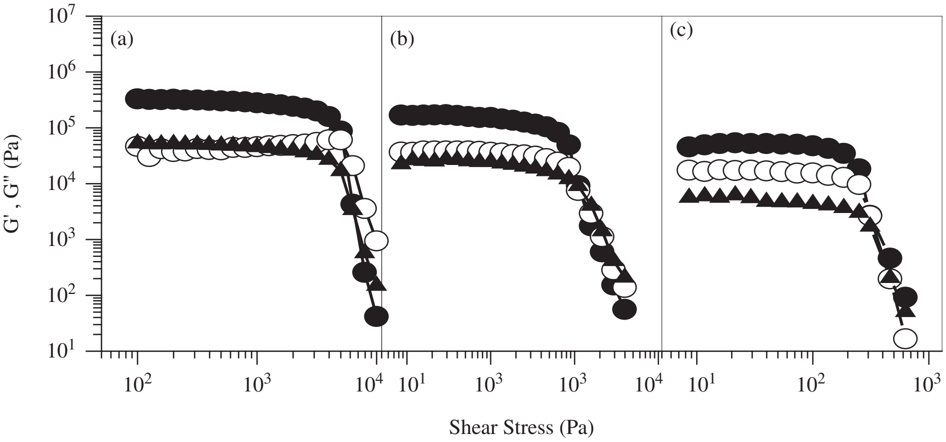


Figure 6. The variations of G' (●) and G'' (○) with the shear stress of the organogels of (a) C_{14}NHCO-Ala, (b) C_{14}NHCO-Asp and (c) C_{14}NHCO-Ser containing 0.15 M gelator in *p*-xylene. Figure 6(a) is partially adapted with permission from Ref. [31]. Copyright © 2011 American Chemical Society.

Table 2. Solid-state m.p. (K) and FT-IR spectral data of the amphiphiles.

	ν (cm^{-1})			
Amphiphiles	m.p. (K)	Amide A (CON—H)	Amide I (NHC=O)	C=O (COOH)
C_{14}NHCO-Gly	367–369	3340	1631	1718
C_{14}NHCO-Ala	403–405	3320	1629	1716
C_{14}NHCO-Phe	363–365	3349	1636	1716
C_{14}NHCO-Ser	385–387	3339	1629	1717
C_{14}NHCO-Met	337–339	3397	1657	1720
C_{14}NHCO-Val	367–369	3379	1629	1716
C_{14}NHCO-Asp	369–371	3354	1643	1727
C_{14}NHCO-Glu	389–391	3395	1642	1716

solid state. So H_2O is needed to weaken or break the H-bonds and thereby make them soluble in the organic solvents. For amphiphiles with large head groups, there is no intermolecular H-bonding because of either steric crowding or interference due to the intramolecular H-bonding interaction of the amino acid side chain and consequently fail to gel organic solvents. The amphiphiles which fulfil the criteria of subtle balance between the intermolecular H-bonding between urea groups and steric crowding or intramolecular H-bonding interaction by the amino acid side chain gelate organic solvents. Thus, gelation could be observed with C_{14}NHCO-Asp in pure organic solvents, but other amphiphiles require H_2O as additive. The role of steric crowding of the amino acid head group, which weakens H-bonding between urea groups of two adjacent molecules and causes packing of the hydrocarbon chains less tight in the bilayer self-assembly, is reflected by the XRD data (*d*-values), gel-to-sol transition temperature (T_{gs}) and yield stress (σ_y) of the gelators. Thus, the organogels of C_{14}NHCO-Ala were observed to have better gelation ability and have higher thermal as well as mechanical stabilities in comparison with C_{14}NHCO-Asp and C_{14}NHCO-Ser gelators.

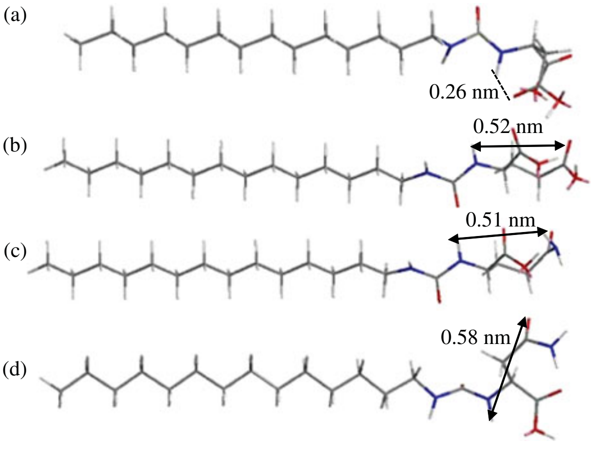


Figure 7. Structure of (a) C_{14}NHCO-Asp, (b) C_{14}NHCO-Glu, (c) C_{14}NHCO-Asn and (d) C_{14}NHCO-Gln showing possible intramolecular H-bonding between COOH and —NH—CO—NH— groups.

Conclusions

In summary, it has been found that L-Asp-derived urido amphiphile can gelate pure organic solvent, but the gelation ability increases in the presence of H_2O. On the other hand, the amphiphile with L-Ser as a head group requires H_2O to gelate aromatic solvents. However, their gelation abilities were observed to be lower than those of the corresponding L-Ala amphiphile, suggesting the importance of head-group structure. Bulky side chain attached to the chiral centre weakens or breaks the intermolecular H-bond, thus destroying gelation ability of the urido amphiphiles. As discussed in our earlier publication (*31*), strong intermolecular H-bonding is also responsible for not forming organogel. Weakening of the intermolecular H-bond between urea groups of adjacent C_{14}NHCO-Asp molecules due to the interference of the intramolecular H-bonding between the —COOH and –NHCONH– groups results in gelation even in the absence of H_2O. In other words, weak H-bonding between urea groups favours gelation and strong H-bonding favours crystallisation. The 3D network structure formed by C_{14}NHCO-Ala has greater aspect ratio than the organogels formed by C_{14}NHCO-Asp and C_{14}NHCO-Ser. The highest thermal and mechanical stability with the C_{14}NHCO-Ala gelator also indicates the formation of a stronger gel in the case of C_{14}NHCO-Ala.

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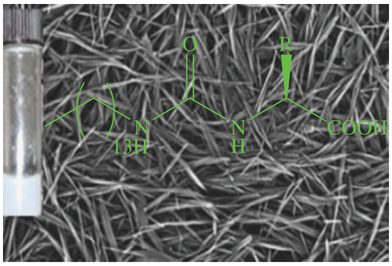

Amrita Pal and Joykrishna Dey

Gelation of organic solvents by *N*-(*n*-tetradecylcarbamoyl)-L-amino acids

1–10