



# Molecular and Crystal Engineering Approaches Towards the Design of Functional Supramolecular Gelators

Tapas Kumar Adalder, Uttam Kumar Das,  
Joydeb Majumder, Rajdip Roy and Parthasarathi Dastidar\*

**Abstract** | Supramolecular gelators are an important class of compounds capable of immobilizing various solvents resulting in gels. Not much is known about the gelation mechanism and consequently, designing gelator molecule is a daunting task. However, efforts are being made to decipher the mystery of gelation and various groups are engaged in designing new gelators. Both molecular- and crystal engineering are being applied to synthesize new gelator molecules. This review article describes briefly the developments including the recent ones in this area; it also covers interesting applications offered by these wonderful materials.

## 1 Introduction

When a small amount of a solid is dissolved in a solvent and subjected to various stimuli such as heat, change in pH, sound energy, photo-irradiation etc., the resultant solution may turn into a solid-like mass termed as gel.<sup>1</sup> Gels are ubiquitous in Nature and everyday modern life—starting from protoplasm to shaving cream. It is believed that a 3D network involving gelator molecules is responsible in gel formation by immobilizing the solvent molecules within the gel-network stabilized via surface tension. If the formation of such network is due to the self-assembly of the gelator molecules sustained by non-covalent interactions such as hydrogen bonding,  $\pi$ - $\pi$  stacking, van der Waals interactions etc., the resulting gel is known as *supramolecular* or *physical* gel.<sup>2</sup> On the other hand, if the gel network is formed due to polymerization involving covalent bond formation, it is termed as polymer or chemical gel. If the gelling solvent is organic, the corresponding gel is called organogel, whereas if pure water or aqueous solvent is used as gelling solvent, it is known as hydrogel. Usually, a given gelator molecule is either capable of making organo- or hydrogel. However, gelator molecules capable of gelling both organic and aqueous solvent are also known (ambidextrous gelators).<sup>3</sup> Supramolecular gels are usually thermoreversible over several cycles, indicating the

modular nature of the gel-network held together by non-covalent interactions. Although most of the gels are obtained at room temperature usually after cooling a hot gelator solution, reverse-thermal gelation, wherein gel formation takes place at higher temperatures, is also reported.<sup>4</sup> Because of the modular nature of the gel-network, amenability towards non-trivial synthetic modifications and various potential applications (such as in drug delivery and bio-medical applications,<sup>5</sup> sensors,<sup>6</sup> electrooptics/photonics,<sup>7</sup> cosmetics,<sup>8</sup> conservation of arts,<sup>9</sup> thermo-responsive materials<sup>10</sup> etc.), the study of supramolecular gels have become one of the most sought after research areas in material science and technology. In this review, we will focus our discussions on molecular- and crystal engineering approaches for designing supramolecular gelators. We will also touch upon briefly on the various applications that these wonderful soft materials offer.

## 2 Designing Supramolecular Gelators

Designing gelators remains a major challenge in supramolecular chemistry, mainly because of the fact that the molecular level understanding of the gel forming mechanism is still poorly understood. Various microscopic (optical-, scanning- and transmission-electron and atomic force microscopy—OM, SEM, TEM and AFM, respectively) data revealed

Department of Organic  
Chemistry, Indian  
Association for the  
Cultivation of Science  
(IACS), 2A & 2B Raja  
S. C. Mullick Road,  
Jadavpur, Kolkata 700032,  
West Bengal, India.

\*ocpd@iacs.res.in;  
parthod123@iacs.res.in

the existence of highly entangled 1D fibrous network in xerogels (dried gels). Small angle X-ray and neutron scattering also indicated the presence of 1D fibrous scatterer in the gel state. Thus, these findings clearly point towards the fact that the gelator molecules self-assembled into 1D network assisted by various non-covalent interactions, such as 1D fibers, then entangled either via junction zones or weak interactions resulting in a continuous 3D network structure known as self-assembled fibrillar networks (SAFINs)<sup>11</sup> within which the solvent molecules were immobilized resulting in gel. It may be noted that gel formation takes place only above a critical concentration of the gelator (minimum gelator concentration (MGC)). Thus, it is apparent that a molecule capable of self-assembling into a 1D network might be a potential gelator with a suitable solvent.

### 3 Molecular Engineering Approach

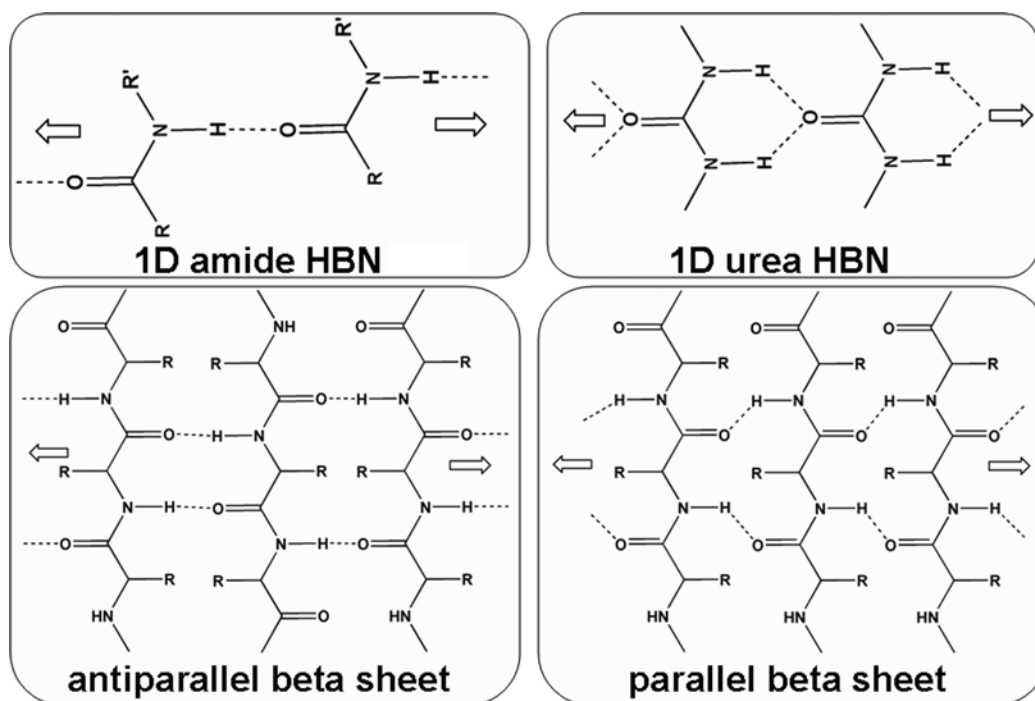
Serendipity and gelation are synonymous; most of the gels reported thus far have been found serendipitously. The second generation gels are then designed by modifying the parent gelator molecules. The foregoing discussions point out to the importance of 1D hydrogen bonding network in gelation. Various hydrogen bonding functionalities such as amide, urea, peptide, can give rise to 1D hydrogen bonded network (HBN); while amide can self-assemble via amide...amide hydrogen

bonding, leading to 1D polymeric catenated network; urea displays 1D network via N-H...O hydrogen bonding involving the urea >C=O and amide NH. Peptide, on the other hand, gives rise to 1D network sustained by complimentary peptide...peptide interactions displaying  $\beta$ -sheet tape architecture (Scheme 1). Thus, it is no wonder that innumerable examples of gelators having these hydrogen bonding functionalities are known.<sup>12</sup>

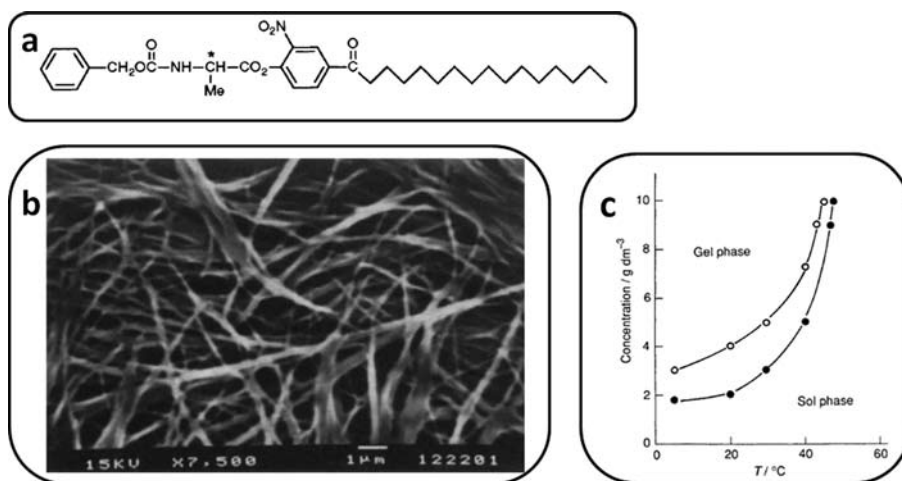
One of the early examples of amide based LMWG was N-Benzoyloxycarbonyl-L-alanine 4-hexadecanoyl-2-nitrophenyl ester which could gel methanol.<sup>13</sup> Microscopic observation revealed the existence of fibrillar network. The gel-sol dissociation temperature increased steadily with the increase in the concentration of the gelator, indicating the various supramolecular interactions such as hydrogen bonding responsible for gelation (Fig. 1).

The self-assembly of a series of geminal bis-urea compounds was studied. These bis-ureas displayed efficient gelation ability with a number of solvents.<sup>14</sup> Electron micrograph showed the presence of highly entangled network of fibers. Various analytical data including molecular modeling suggested the formation of 1D hydrogen bonding network of the these bis-ureas resulting in gel (Fig. 2).

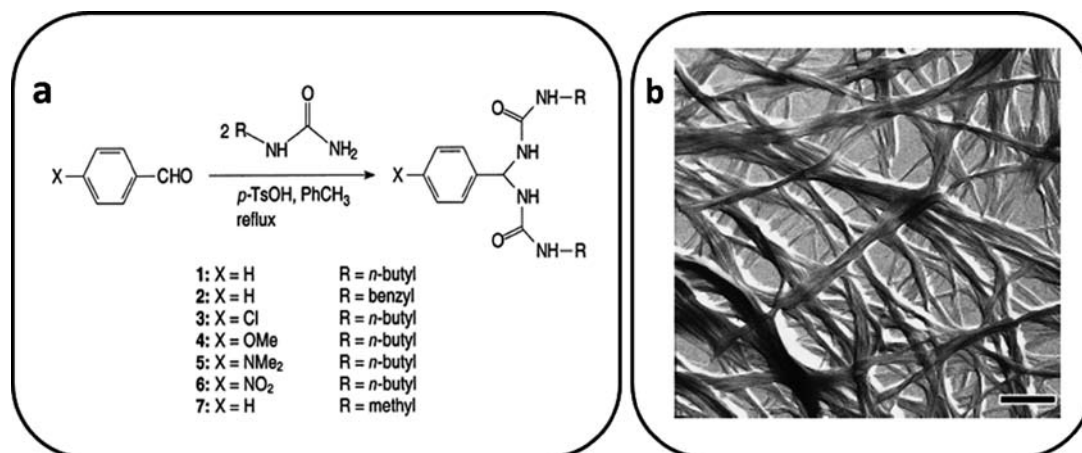
Hydrogen bonding and charge transfer interactions were exploited to generate one of the early examples of charge transfer based gelators.<sup>15</sup>



Scheme 1



**Figure 1:** a) Molecular structure of the L-alanine based gelator capable of gelling methanol; b) highly entangled network seen in SEM of the corresponding methanol gel; c) gelator vs gel-sol dissociation temperature ( $T/^\circ\text{C}$ ) plot. Reproduced from Ref. 13 with permission. Copyright 1992, Royal Society of Chemistry.



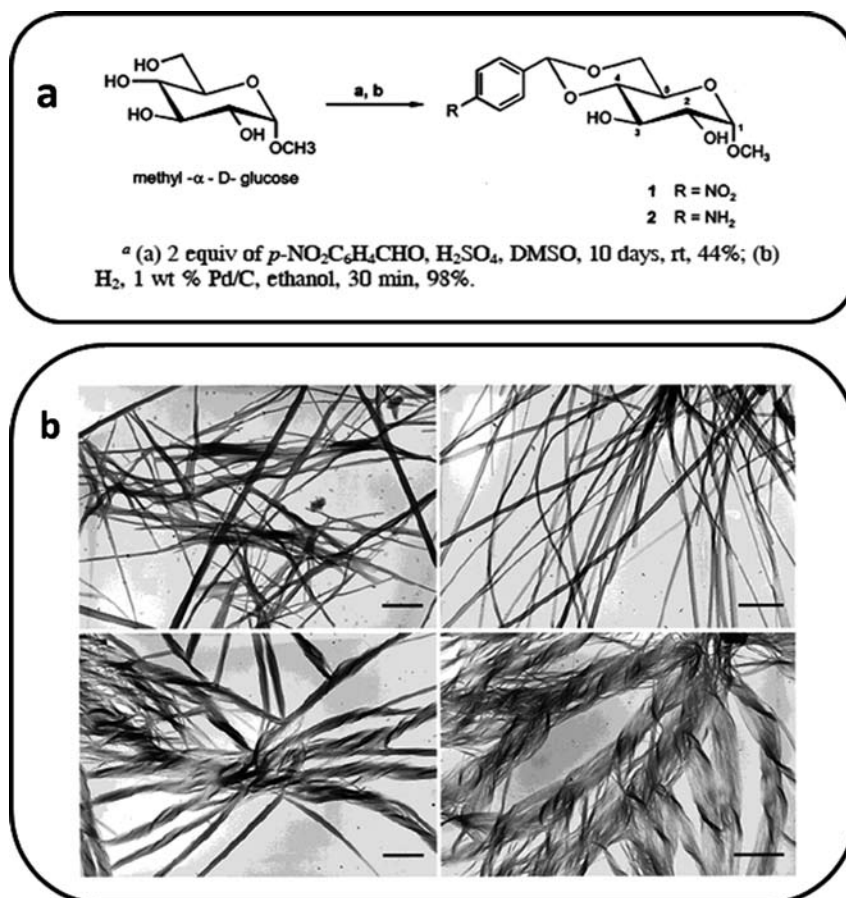
**Figure 2:** a) Synthesis of various geminal bis-urea gelators; b) electron micrograph of the gel network in tetralin gel. Reproduced from Ref. 14 with permission. Copyright 2013, Wiley-VCH Verlag GmbH & Co. KGaA.

Saccharide-based gelators having electron withdrawing ( $\text{NO}_2$ ) and donating ( $\text{NH}_2$ ) groups were synthesized. Both the compounds individually could gel a number of solvents. Mixture of these two compounds under various molar ratio could gel a few solvents with distinct colour change, indicating charge transfer (Fig. 3).

#### 4 Crystal Engineering Approach

Gels are soft-visco-elastic materials. Thus, in exactly what way could crystal engineering<sup>16a</sup> be linked up with the design of gelators? Powder X-ray diffraction (PXRD) experiments revealed that the dried gels (xerogels) were quite crystalline; even in some suitable cases, the gel itself was found to be quite ordered displaying well-resolved sharp PXRD pattern, indicating the crystalline nature of

the gel network. The success of any design depends on how well one knows the structure of the target subject. Thus, it is apparent that in order to develop a design strategy for LMWGs, the structure of the gel network must be understood. Since PXRD indicates the existence of a highly ordered structure of the gel network, deciphering its structure should be the key to successful design. However, due to the nano/micro size of the gel network, the possibility of utilizing single crystal X-ray diffraction (SXRD) is ruled out. Interestingly, more than a decade ago, Weiss et al. suggested an alternative method to solve the structure of gel network.<sup>16b</sup> They proposed to compare the PXRD patterns of bulk solid (i.e. as synthesized gelator molecule), simulated PXRD pattern (i.e. PXRD pattern obtained from SXRD data) in case the gelator's single crystal



**Figure 3:** a) Saccharide-based gelators; b) fibrous network seen in TEM of various xerogels produced by these gelators. Reproduced from Ref. 15 with permission. Copyright 2002, American Chemical Society.

structure is known and PXRD pattern of the xerogel or gel. Excellent match of these patterns would then mean that the gel network of the xerogel or gel represents the crystal structure of the gelator molecule. There are two major drawbacks of this approach; the first one is the requirement of the availability of single crystal of the gelator, which is often difficult, and the second one is the inherently weak PXRD of the gel sample due to scattering contribution of the gelling solvent and less amount of gelator in the gel. Thus, often one has to compromise by determining the structure of the gel network present in xerogel. It may be mentioned here that while going from gel to xerogel, during evaporation of the solvent, a new nucleation event or polymorphism of the gel network may happen leading to a different crystalline phase in xerogel. Nevertheless, it is found to be a good compromise, since such an event does not always happen, and synchrotron radiation—the only option to determine gel network structure by *ab initio* structure determination from PXRD data of gel—is not easily available and the method is not routine yet. Thus, after determining the structure

of the xerogel, it is possible to analyze the various noncovalent interactions responsible for making the gel network; installing such interaction-generating-functionality in the target molecule following supramolecular synthon approach,<sup>16c</sup> it is possible to design LMWGs. Based on several single crystal structures of sugar based gelators and nongelators, Shinkai et al. demonstrated that 1D HBN promoted gelation, whereas 2D or 3D HBN either produced weak gel or no gelation at all.<sup>17</sup> The hypothesis was based on the consideration that 1D HBN helped the molecule assemble in one direction resulting in 1D growth of the fibers, while 2D or 3D HBN promoted crystallization preventing 1D growth of the fibers.

One of the early examples pertaining to the structural studies of gel network was reported a decade ago.<sup>18</sup> In an attempt to crystallize a simple organic salt namely, imidazolium hydrogen cyclobutane-1,1-dicarboxylic acid (**ImHCBDA**), it gave excellent gels with nitrobenzene (MGC = 0.137 wt %, at RT), chlorobenzene (MGC = 1.396 wt %, at RT), and toluene (MGC = 34.64 wt % at 4 °C). Both optical and scanning electron microscopy

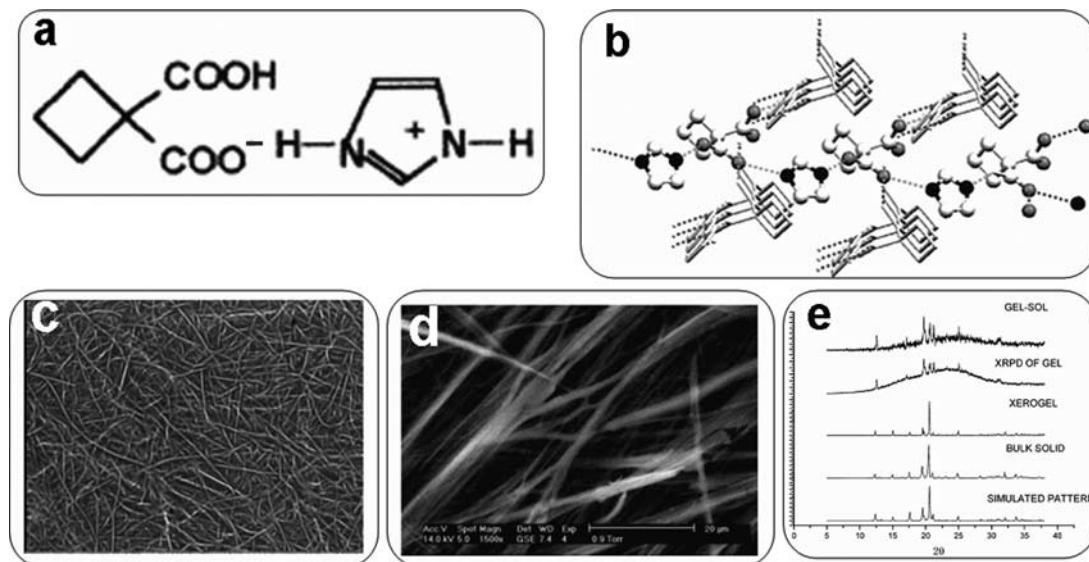
(OM and SEM) revealed the existence of highly entangled fibrous morphology of the gel network. SXRD of as synthesized **ImHCBDA** displayed a 3D HBN wherein a primary 1D network involving the imidazolium cation and monocarboxylate anion further propagates into 3D via  $\text{-COO}^-\cdots\text{HOOC-}$  hydrogen bonding. Detailed PXRD study revealed that the gel fibers present in the gel state underwent a phase transition resulting in the same crystalline phase as obtained in the thermodynamically more stable single crystal state (Fig. 4). It was thus apparent that the primary supramolecular 1D hydrogen bonded network involving imidazolium cation and hydrogen carboxylate mono-anion was responsible for fiber formation.

This serendipitous discovery revealed the advantages of salt based compounds as potential gelators: Salt formation is the easiest reaction to carry out resulting in quantitative or near quantitative yield thereby producing a large number of potential gelators within a relatively short period of time allowing rapid screening for gelation. Moreover, charge assisted hydrogen bond present in salt is strong and directional, thereby facilitating material formulation for real life applications. Analyzing various hydrogen bonding interactions present in organic salts, it is possible to identify 1D HBN forming supramolecular synthon that might be conducive for triggering SAFIN formation leading to gelation under suitable condition.

Consequent systematic investigations identified, four major synthons in various ammonium salts, namely primary ammonium monocarboxylate

(PAM),<sup>19</sup> primary ammonium dicarboxylate (PAD),<sup>20</sup> secondary ammonium monocarboxylate (SAM)<sup>21</sup> and secondary ammonium dicarboxylate (SAD).<sup>22</sup> It was observed that PAM salts usually resulted in two different types of columnar 1D synthon whereas PAD salts displayed 2D synthon. While both 1D polymeric and discrete 0D synthons were observed in SAM salt, SAD salts produced only 1D synthon by propagating 0D SAM synthon in 1D because of the bifunctional nature of the dicarboxylate (Scheme 2).

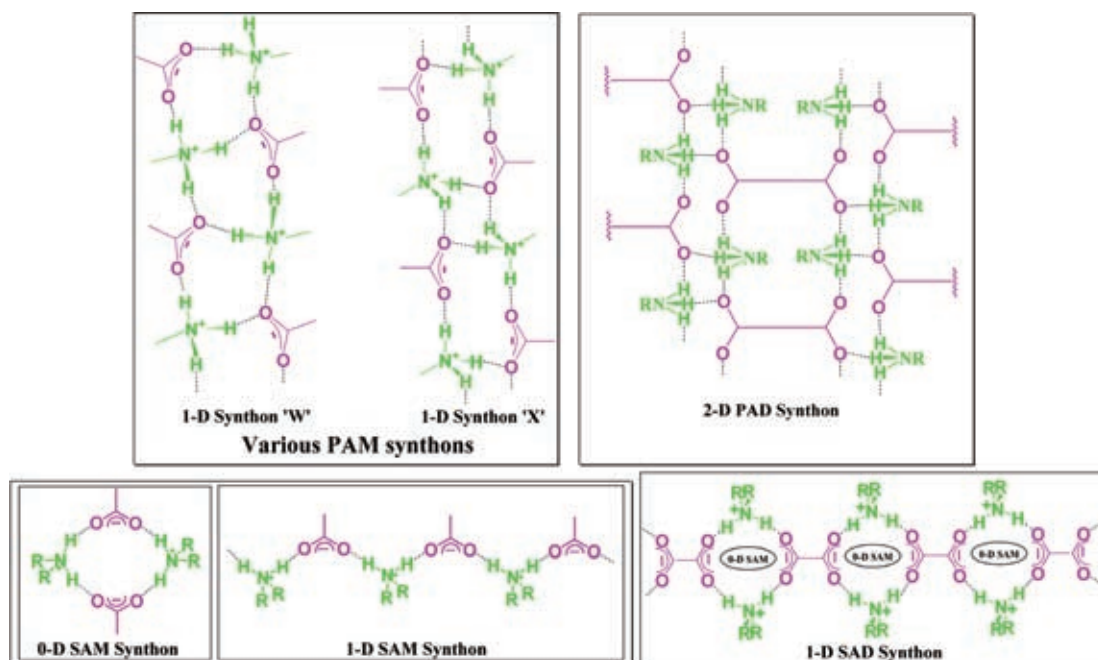
A series of benzylammonium cinnamate was reported as potential organo gelators capable of gelling a wide range of solvents including commercial fuel like petrol.<sup>23</sup> Structure-property correlation studies revealed the presence of various 1D columnar PAM synthons in these salts; while PAM synthon W was found to be present in majority of the salts, Synthon X and another 1D synthon never observed before were also seen. Since all the synthons were 1D, it was no wonder that 8 salts out of 13 could display gelation ability. One of the gelator salts namely benzylammonium cinnamate (**CIN**), displayed remarkable ability to gel various solvents including commercial fuel such as petrol instantaneously at room temperature. PXRD patterns of all the gelator salts recorded under various conditions (simulated, bulk solid, and xerogel) revealed excellent correspondence, meaning that the supramolecular synthon observed in the single crystals of these salts was also present in the corresponding xerogel. In the case of **CIN**, PXRD patterns of the



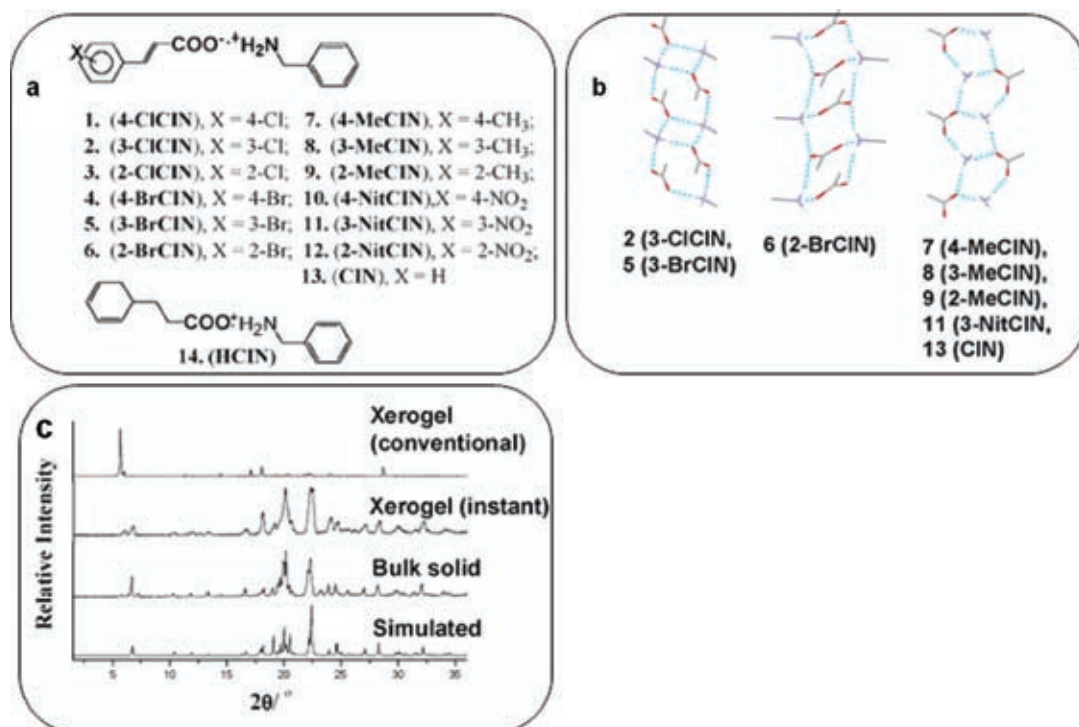
**Figure 4:** a) Molecular structure of the gelator salt **ImHCBDA**; b) single crystal structure of **ImHCBDA**; c) and d) optical and SEM micrographs of the gel network; e) PXRDs of **ImHCBDA** under various conditions. Reproduced from Ref. 18 with permission. Copyright 2003, American Chemical Society.

xerogel (prepared conventionally) did not match with that obtained from the xerogel (prepared in instant gelation), thereby pointing out to the possible phase transition (Fig. 5).

Recently, the robustness of PAM synthon was studied in a series of PAM salts derived from the free amine of L-phenylalanine-3-pyridyl amide and variously substituted benzoic acid.<sup>24</sup> Even



**Scheme 2**



**Figure 5:** a) Various PAM salts of cinnamic acid and benzyl amine as potential gelators; b) observed PAM synthon in the crystal structures; c) PXRD patterns of **CIN** under various conditions. Reproduced from Ref. 23 with permission. Copyright 2006, American Chemical Society.

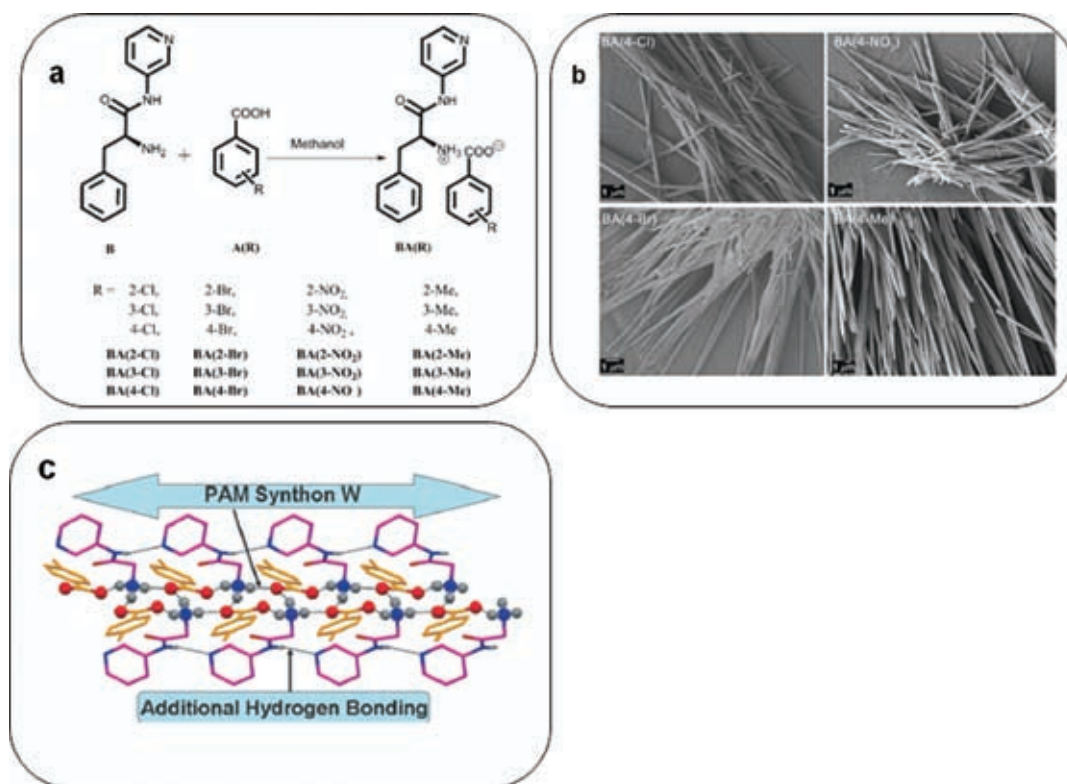
under the presence of additional hydrogen bonding functionalities like amide and pyridyl moieties in the primary amine, PAM synthon W was seen in the crystal structures of the salts. In most of the cases, the PXRD patterns under various conditions matched well establishing the existence of PAM synthon W in the gel network of the xerogel (Fig. 6).

In an interesting study, it was shown that long chain alkyl-alkyl interactions played a crucial role in triggering hydrogen bond isomerism resulting in nanotubular hydrogen bonding instead of the usually observed 2D network in PAD salts derived from 1,1-cyclobutane dicarboxylic acid and long chain amines having various alkyl chain length.<sup>25</sup> SXRD studies revealed that the PAD salts displayed the expected 2D synthon only when the alkyl chain was short ( $n = 5$ ), whereas hydrogen bond isomerism leading to 1D nanotubular network was observed with PAD salts having long alkyl chain length ( $n = 11, 12$ ). Remarkably, salts having  $n > 11$  showed gelation emphasizing the crucial role of 1D HBN on gelation (Fig. 7).

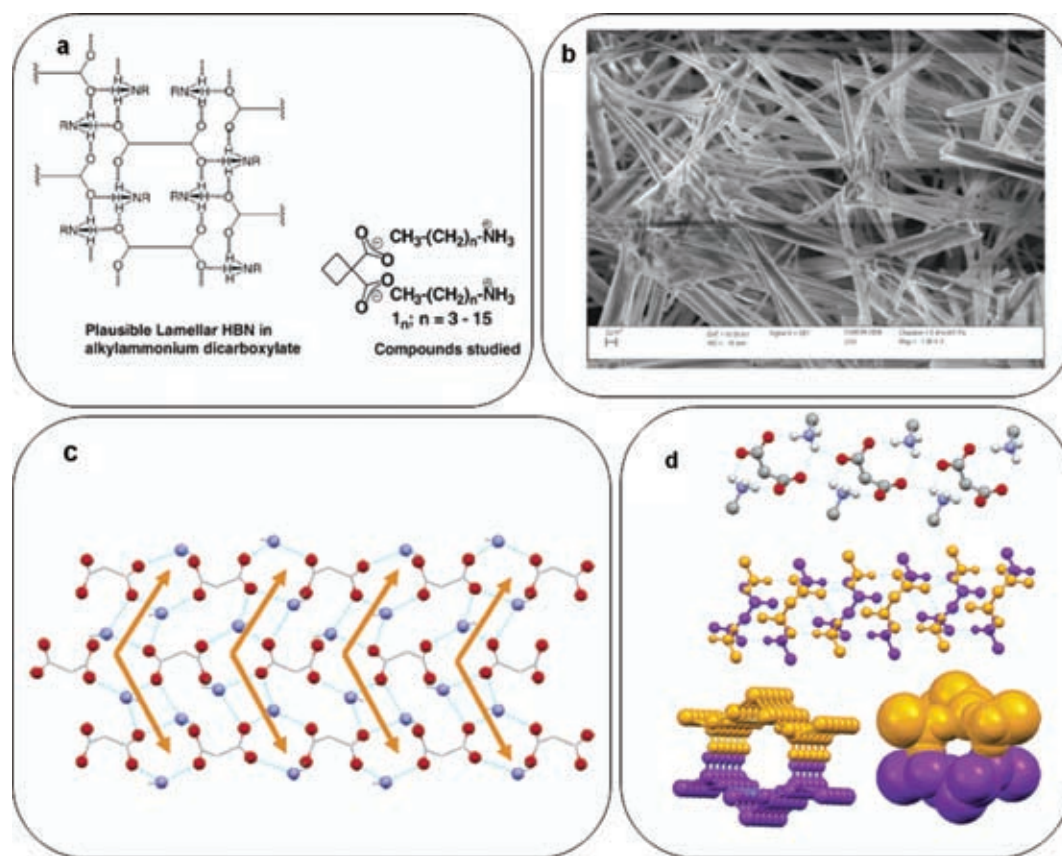
One of the early examples of supramolecular synthon approach in designing gelators was a series of SAM salts derived from variously substituted

cinnamic acid and dicyclohexyl amine.<sup>26</sup> With the help of a number of single crystal structures of gelator and nongelator salts, it was established that 1D HBN clearly played an important role in gelation. Excellent match of PXRD patterns of the gelator salts under various conditions proved the existence of 1D SAM synthon in the gel network of the corresponding xerogels. The most remarkable observation was that the salts that displayed 0D discrete SAM synthon never showed any gelation ability (Fig 8).

It was realized that the main disadvantage of SAM synthon was the possibility of producing discrete 0D non-gel forming synthon. To overcome this problem, SAD synthon was invoked wherein the discrete 0D hydrogen bonded network motif propagated into 1D by virtue of the bifunctionality of the anionic moiety, thereby increasing the possibility of inducing gelation ability in the resulting SAD salts. One of the elegant examples of SAD synthon in designing organo metallic based supramolecular gelator was the salt dicyclohexyl ammonium ferrocene-1,1'-dicarboxylate (**DCAFDC**)<sup>27</sup>. Single crystal structure of **DCAFDC** revealed the existence of SAD synthon and it was able to gel a wide range of solvents that included



**Figure 6:** a) A series of PAM salts having additional hydrogen bonding functionality; b) fibrous morphology observed in SEM of some of gels derived from these gelators; c) PAM synthon W in the crystal structures of the salts displaying robustness of the synthon. Reproduced from Ref. 24 with permission. Copyright 2013, Wiley-VCH Verlag GmbH & Co. KGaA.



**Figure 7:** a) Plausible lamellar synthon in PAD salts and various PAD salts derived from cyclobutane-1,1-dicarboxylic acid; b) highly entangled fibrous network observed under SEM in the xerogel of  $\mathbf{1}_{11}$ ; c) 2D HBN seen in the crystal structure of  $\mathbf{1}_5$ ; d) nanotubular 1D HBN observed in the crystal structure of  $\mathbf{1}_{11}$ . Reproduced from Ref. 25 with permission. Copyright 2006, American Chemical Society.

both polar and nonpolar solvents. The morphology of the gel network was found to be twisted fibers of both handedness (Fig. 9). This was the first example of crystal engineering based design of organometallic gelators which were otherwise quite tedious to synthesize.<sup>28</sup>

A few examples of salt based gelators are known in literature.<sup>29</sup> However, none of them were designed based on crystal engineering rationale. For example, salt formation was exploited to generate a series of bile acid based organic salts with various amines that showed interesting hydrogelation ability; the salt of lithocholic acid (LCA) gave hydrogels whereas the corresponding salt with deoxycholic acid (DCA) or cholic acid (CA) did not produce any hydrogel.<sup>30</sup> The flow behavior of the gel could be modulated by varying the acid : amine ratio as evident from rheological data.

## 5 Applications

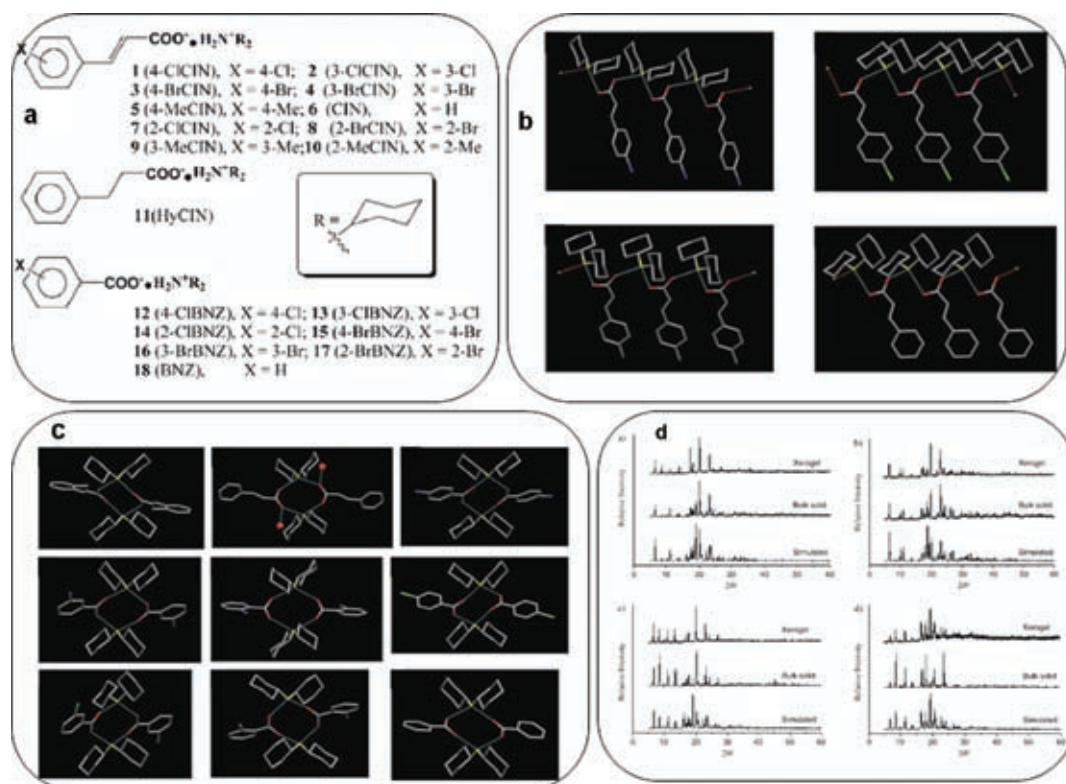
Supramolecular gels have been demonstrated to be useful in varied applications such as in oil spill,<sup>31–33</sup> catalysis,<sup>34</sup> light harvesting materials,<sup>35</sup>

pest control,<sup>36</sup> preserving ancient art,<sup>37</sup> various biomedical applications like drug delivery and tissue engineering.<sup>38</sup>

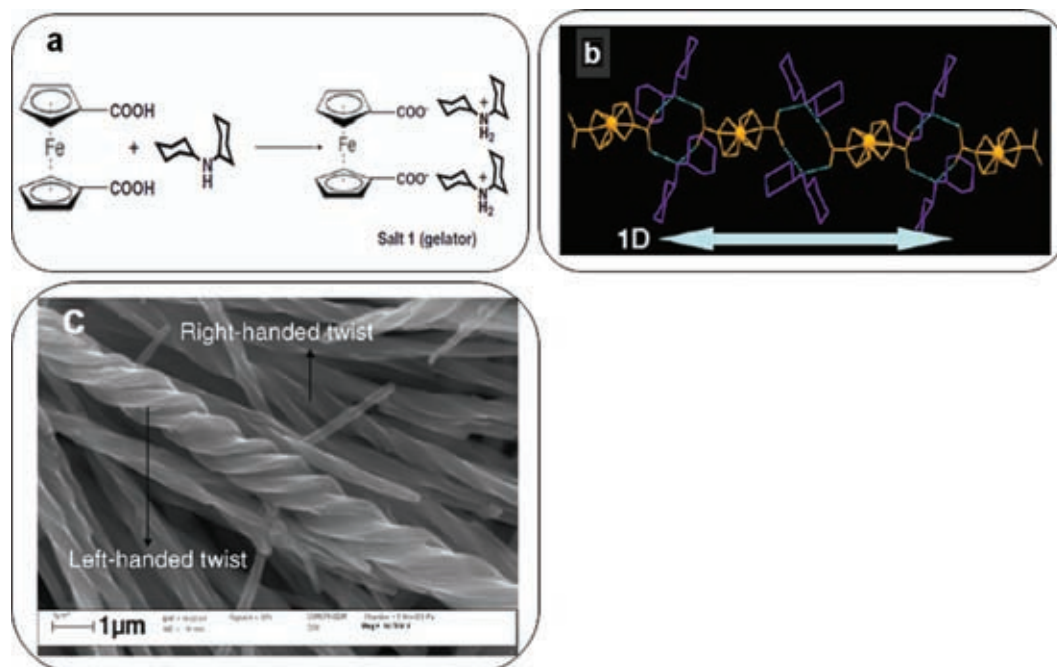
The first conceptual demonstration that supramolecular gels could be useful in containing oil spill was reported a decade ago.<sup>31</sup> A simple amino acid derivative, *N*-lauroyl-L-alanine was shown to gelate oil phase from a oil/water mixture. It was established that both amide and free COOH group were necessary in order to induce gelation (Fig. 10).

Two years later, a simple organic salt based gelators derived from variously substituted cinnamic acid and dicyclohexyl amine displayed the ability to gel commercial fuel like petrol or edible oil selectively from the corresponding oil/water mixture.<sup>32</sup> Single crystal structure of one of the derivatives (2-chlorocinnamate salt) displayed the presence of 1D SAM synthon. However, due to significant Cl...Cl non-bonded interactions, the overall network could be considered as 2D and probably, that could be the reason for this salt being a nongelator (Fig. 11).

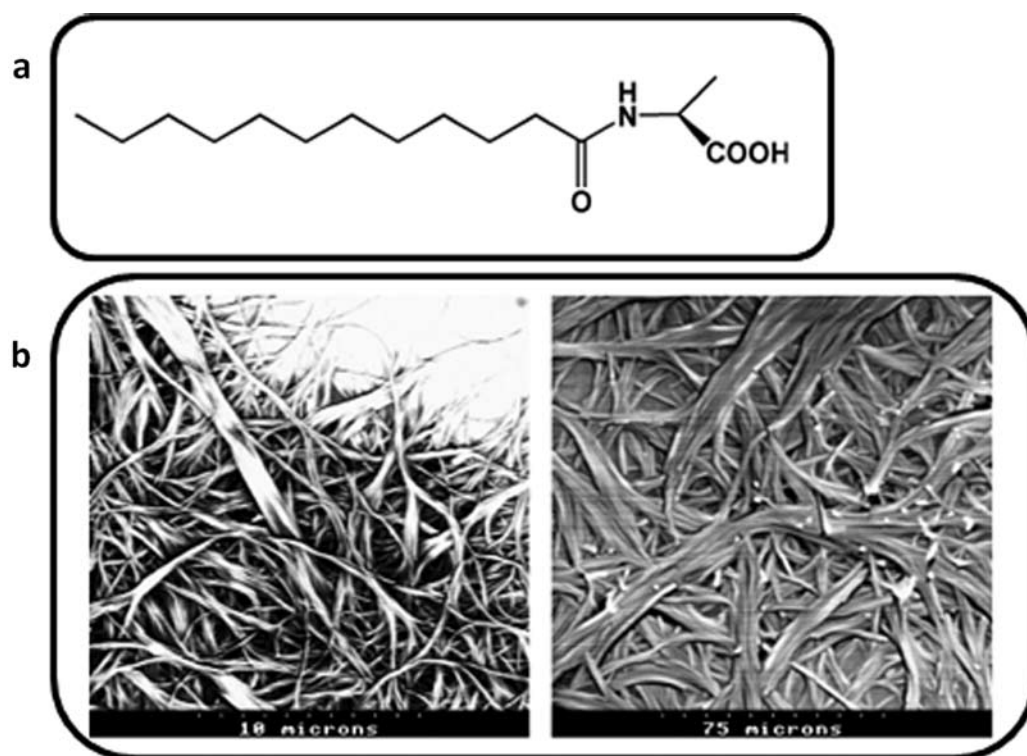




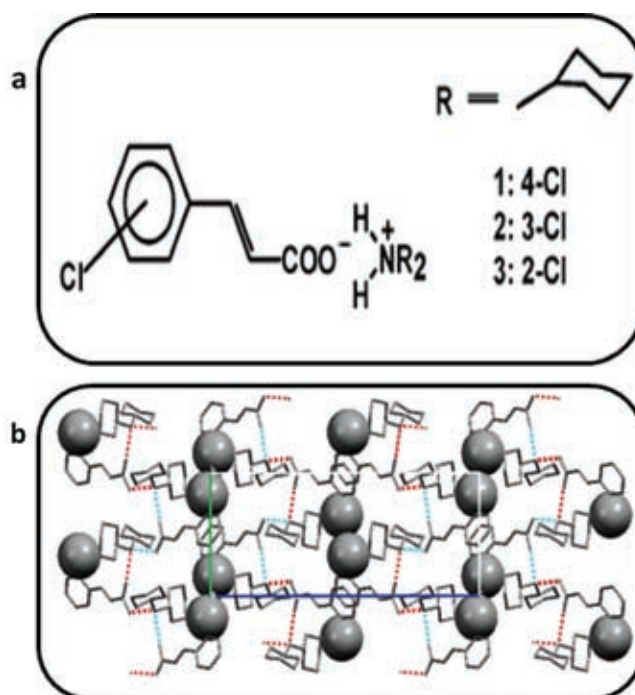
**Figure 8:** a) SAM salts derived from variously substituted cinnamic acid; b) 1D SAM synthon observed in the crystal structures of some gelator salts; c) discrete 0D SAM synthon observed in the nongelators; d) PXRDs of various gelator salt under different conditions. Reproduced from Ref. 26 with permission. Copyright 2004, Wiley-VCH Verlag GmbH & Co. KGaA.



**Figure 9:** a) SAD salt derived from ferrocene-1,1'-dicarboxylic acid as potential gelator; b) single crystal structure of the gelator salt DCAFDC displaying 1D SAD synthon; c) gel network morphology in SEM display severe twist of both handedness. Reproduced from Ref. 27 with permission. Copyright 2008, Elsevier.



**Figure 10:** a) L-alanine derivative capable of gelling oil from oil/water mixture; b) fibrous gel network seen in SEM. Reproduced from Ref. 31 with permission. Copyright 2001, Royal Society of Chemistry.



**Figure 11:** a) SAM salts derived from chlorocinnamic acids; 4-Cl salt displayed selective gelation of oil from oil/water mixture; b) single crystal structure of 2-Cl salt displaying both 1D SAM synthon and Cl...Cl interactions. Reproduced from Ref. 32 with permission. Copyright 2003, American Chemical Society.

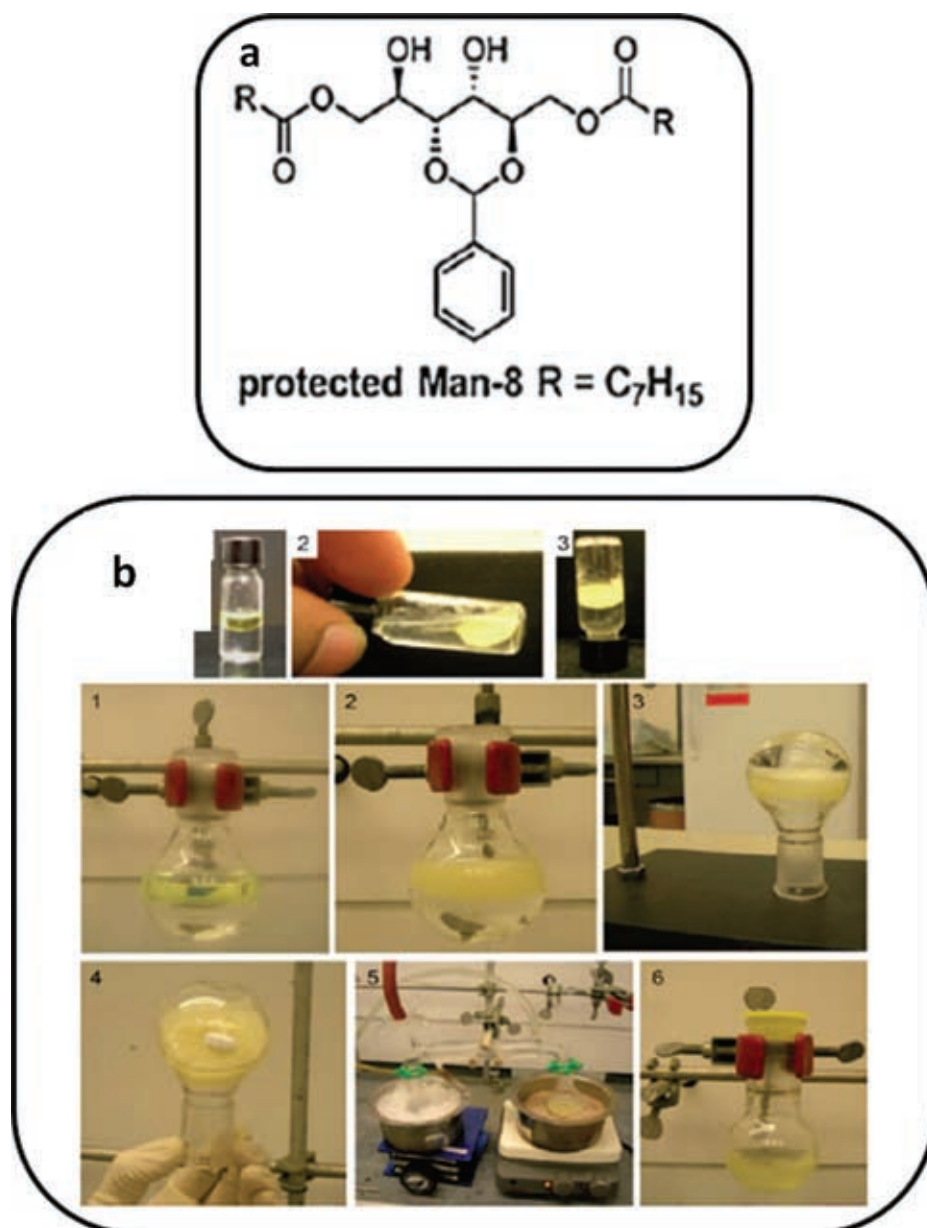
More recently, a sugar derivative synthesized from D-(+)-mannitol could successfully recover diesel from a biphasic mixture by gelling the oil phase selectively (Fig. 12).<sup>33</sup>

Research on supramolecular gels as reaction media and catalysis has been reviewed recently.<sup>34</sup>

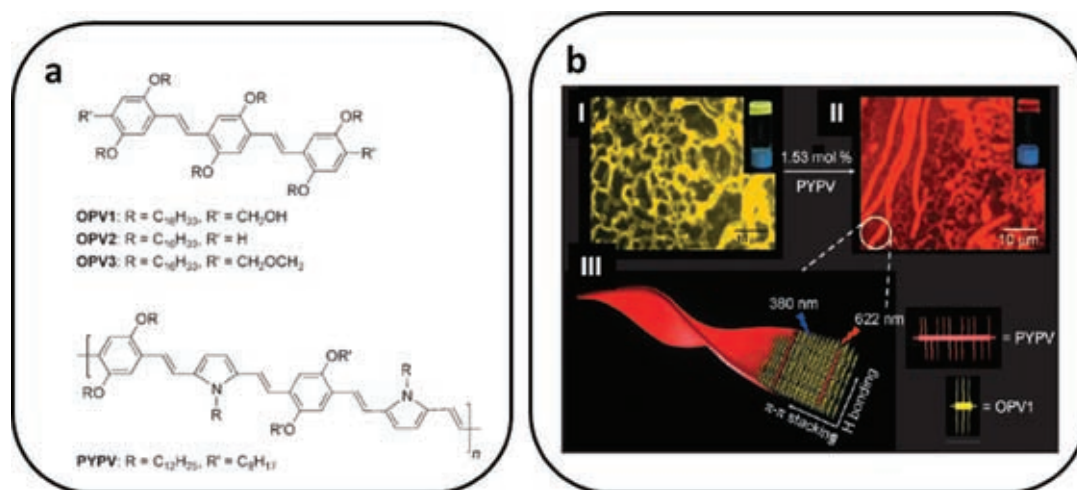
Artificial light harvesting assemblies were created by using oligo(p-phenylenevinylene)s or OPVs which have large  $\pi$  surface.<sup>35</sup> By carefully designing OPV donors and acceptors, it was possible to generate a novel organic supramolecular light-harvesting antenna by encapsulating an

energy-accepting molecular wire into an energy donating  $\pi$ -gel scaffold (Fig. 13).

Controlling inorganic nanostructure has been a challenge in modern materials chemistry. Supramolecular gels have been found quite useful in such endeavour. The gel networks have been used as template to generate interesting and useful inorganic nanostructures. For example, helical silica fibers, transition metal oxide nanotubes and helical CdS ribbons were generated using various supramolecular gels.<sup>39</sup> Since metal nanoparticles (MNPs) show different chemical



**Figure 12:** a) Sugar based gelator capable of gelling diesel from a biphasic mixture; b) various steps of recovering diesel from diesel/water mixture. Reproduced from Ref. 33 with permission. Copyright 2010, Wiley-VCH Verlag GmbH & Co. KGaA.



**Figure 13:** a) Molecular structure of OPV donors and acceptors; b) Fluorescence microscopy images of the drop-casted OPV1-cyclohexane gel (1.12 mm): I) in the absence and II) presence of PYPV (1.53 mol%), the insets show photographs of the gels under the respective conditions when illuminated at 365 nm. III) A schematic representation of a PYPV-encapsulated OPV1 tape. Reproduced from Ref. 35 with permission. Copyright 2007, Wiley-VCH Verlag GmbH & Co. KGaA.

properties as compared to the bulk metal due to enhanced surface area in the nanoscale, it has been a challenge to synthesize MNPs useful for catalysis or for other applications like bio-imaging.

One such early synthesis of Au nanoparticle was achieved from a supramolecular gel derived from dendritic peptide.<sup>40</sup> When  $\text{HAuCl}_4$  and tetraoctylammonium bromide were diffused into a gel derived from the dendritic peptide, AuNPs of 13 nm diameter were formed after UV irradiation. The gel network was shown to play an essential role in nanoparticle stabilization.

Rapid progress has been noticed in the area of biomedical applications involving supramolecular gels. One of the most interesting future applications is self-delivery of drug. In conventional drug delivery system, a carrier molecule is needed that ensures the safe-passage of the drug to the affected site. However, cytotoxicity of the carrier molecules, synthetic difficulty and drug-loading issue motivated scientists to look for an alternative such as self-delivery wherein a drug molecule is converted into a hydrogel which then deliver itself to the affected site.

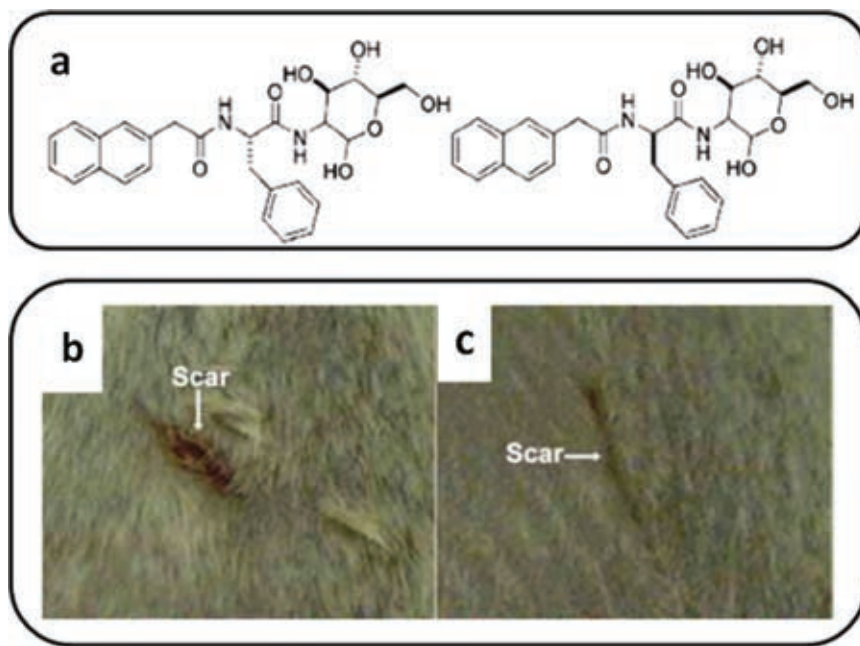
For example, a simple supramolecular hydrogel based on D-glucosamine, a naturally occurring aminosaccharide, was reported as new biomaterials for applications such as wound healing.<sup>41</sup> By synthetic modification, two hydrogelators namely Nap-L-Phe-D-glucosamine and Nap-D-Phe-D-glucosamine were prepared. Both the hydrogelator showed reasonable biocompatibility in MTT assay with HeLa cells. The hydrogels showed

excellent wound healing ability in mice wound model (Fig. 14).

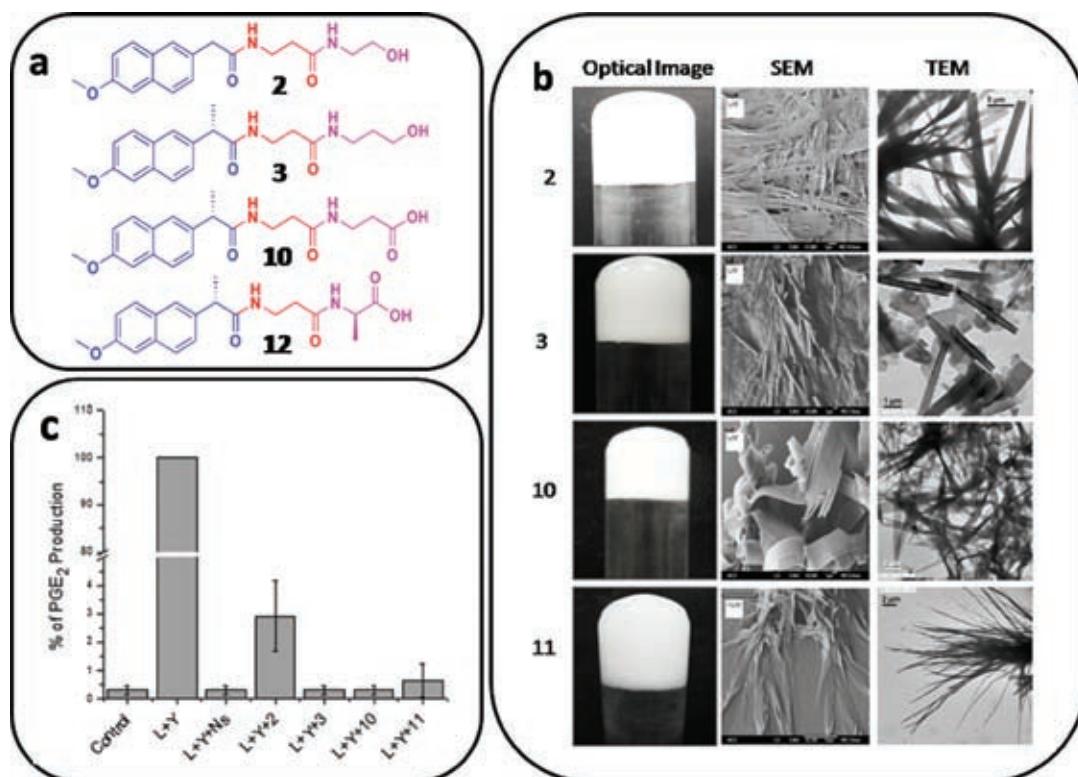
Recently a well known non-steroidal-anti-inflammatory-drug (NSAID)—naproxen was converted to hydrogelators by judicial design.<sup>42</sup> The hydrogelators were found to be stable at physiological conditions, displayed reasonable biocompatibility in MTT assay of RAW 264.7 cells, and showed comparable anti-inflammatory activity with the parent drug in  $\text{PGE}_2$  assay. Leaching experiments indicated that the hydrogel could be used for self-delivery applications (Fig. 15).

## 6 Future Perspective

Thus over the two decades of active research, supramolecular gels have already attracted much attention of materials community because of their various potential applications—from catalysis to biomedical applications—and many more applications, and real-life devices based on supramolecular gels appear to be not a distant reality. However, designing a gelator *a priori* still remains a major challenge despite significant progress made in molecular- and crystal engineering approaches as delineated in this review. The main problem in designing a gelator lies in the wide diversity of molecules known to impart gelation. While 1D hydrogen bonded network is important for gelation in most of the cases including the well documented salt based gelators, it is not an essential and sufficient condition. There were many examples wherein 1D hydrogen bonded network present in the crystalline form of the molecule did not ensure gelation—the reason being



**Figure 14:** a) Glucosamine based hydrogelators; gross appearance of scar before treatment; b) and after treatment; c) of the dorsal skins of Balb/C mice. Reproduced from Ref. 41. Copyright 2007, Royal Society of Chemistry.



**Figure 15:** a) Naproxen based hydrogelators; b) optical images of the hydrogels and their corresponding electron micrographs; c) PGE<sub>2</sub> assay of the hydrogelators. Reproduced from Ref. 42. Copyright 2013, American Chemical Society.

poor understanding of the nature of interactions involving the gel-network and gelling solvents. In order to step forward in gel science, it is of utmost importance that more and more efforts be dedicated to determine the structure of the gel network in the gel state. Theoreticians should closely collaborate with the experimentalists in order to improve the design aspect of gelators. Despite having such limitations, the field is growing rapidly and it is expected that real-life benefits will emerge from such endeavor.

### Acknowledgment

TKA, UKD, JM and RR thank CSIR, New Delhi for their research fellowship and all of them contributed equally. PD thanks DST and CSIR for financial support. Central Salt and Marine Chemicals Research Institute (CSMCR), Bhavnagar and Indian Association for the Cultivation of Science, Kolkata, for providing infrastructure and financial support are also thankfully acknowledged. Former group members of PD are also thankfully acknowledged for their contributions—without that this wonderful journey through the soft-world would not have been possible.

Received 24 October 2013.

### References

1. P. Terech and R. G. Weiss, Low Molecular Mass Gelators of Organic Liquids and the Properties of their Gels, *Chem. Rev.*, 97, 3133–3159 (1997).
2. R. G. Weiss and P. Terech, Eds. *Molecular Gels. Materials with Self-Assembled Fibrillar Networks*; Springer: Dordrecht, The Netherlands, (2005).
3. S. Nandi, H.-J. Altenbach, B. Jakob, K. Lange, R. Ihizane and M. P. Schneider, A Novel Class of Organo- (Hydro-) Gelators Based on Ascorbic Acid, *Org. Lett.*, 13, 1980–1983 (2011).
4. P. Sahoo, I. Chakraborty and P. Dastidar, Reverse Thermal Gelation of Aromatic Solvents by a Series of Easily Accessible Organic Salt Based Gelators, *Soft Matter*, 8, 2595–2598 (2012).
5. a) F. Zhao, M. L. Ma, B. Xu, Molecular Hydrogels of Therapeutic Agents, *Chem. Soc. Rev.*, 38, 883–891 (2009).  
b) K. Y. Lee and D. J. Mooney, Hydrogels for Tissue Engineering, *Chem. Rev.*, 101, 1869–1879 (2001).
6. I. Yoshimura, Y. Miyahara, N. Kasagi, H. Yamane, A. Ojida and I. Hamachi, Molecular Recognition in a Supramolecular Hydrogel to Afford a Semi-Wet Sensor Chip, *J. Am. Chem. Soc.*, 126, 12204–12205 (2004).
7. S. S. Babu, S. Prasanthkumar and A. Ajayaghosh, Self-Assembled Gelators for Organic Electronics, *Angew. Chem. Int. Ed.*, 51, 1766–1776 (2012).
8. A. Wynne, M. Whitefield, A. J. Dixon and S. Anderson, An Effective, Cosmetically Acceptable, Novel Hydro-Gel Emollient for the Management of Dry Skin Conditions, *J. Dermatol. Treat.*, 13, 61–66 (2002).
9. E. Carretti, M. Bonini, L. Dei, B. H. Berrie, L. V. Angelova, P. Baglioni and R. G. Weiss, New Frontiers in Materials Science for Art Conservation: Responsive Gels and Beyond, *Acc. Chem. Res.*, 43, 751–760 (2010).
10. K. Kuroiwa, T. Shibata, A. Takada, N. Nemoto and N. Kimizuka, Heat-Set Gel-Like Networks of Lipophilic Co(II) Triazole Complexes in Organic Media and their Thermochromic Structural Transitions, *J. Am. Chem. Soc.*, 126, 2016–2021 (2004).
11. M. George, and R. G. Weiss, Molecular Organogels. Soft Matter Comprised of Low-Molecular-Mass Organic Gelators and Organic Liquids, *Acc. Chem. Res.*, 39, 489–497 (2006).
12. a) Y. Jeong, K. Hanabusa, H. Masunaga, I. Akiba, K. Miyoshi, S. Sakurai and K. Sakurai, Solvent/Gelator Interactions and Supramolecular Structure of Gel Fibers in Cyclic Bis-Urea/Primary Alcohol Organogels, *Langmuir*, 21, 586–594 (2005).  
b) A. Pal, Y. K. Ghosh and S. Bhattacharya, Molecular mechanism of physical gelation of hydrocarbons by fatty acid amides of natural amino acids, *Tetrahedron*, 63, 7334–7348 (2007).  
c) M. Suzuki, Y. Nakajima, M. Yumoto, M. Kimura, H. Shirai, and K. Hanabusa, Effects of Hydrogen Bonding and van der Waals Interactions on Organogelation Using Designed Low-Molecular-Weight Gelators and Gel Formation at Room Temperature, *Langmuir*, 19, 8622–8624 (2003).
13. K. Hanabusa, K. Okui, K. Karaki, T. Koyama and H. Shirai, A Small Molecular Gelling Agent for Organic Liquids: N-Benzyloxycarbonyl-L-alanine 4-Hexadecanoyl-2-nitrophenyl Ester, *J. Chem. Soc., Chem. Commun.*, 1371–1373 (1992).
14. F. S. Schoonbeek, J. H. van Esch, R. Hulst, R. M. Kellogg, B. L. Feringa, Geminal Bis-ureas as gelators for organic solvents: Gelation properties and structural studies in solution and in the gel state, *Chem. Eur. J.*, 6, 2633–2643 (2006).
15. A. Friggeri, O. Gronwald, K. J. C. van Bommel, S. Shinkai and D. N. Reinhoudt, Charge-Transfer Phenomena in Novel, Dual-Component, Sugar-Based Organogels, *J. Am. Chem. Soc.*, 124, 10754–10758 (2002).
16. a) G. R. Desiraju, J. J. Vittal and A. Ramanan, *Crystal Engineering—A Textbook*, World Scientific, 2011.  
b) E. Ostuni, P. Kamaras, and R. G. Weiss, Novel X-ray Method for in Situ Determination of Gelator Strand Structure: Polymorphism of Cholesteryl Anthraquinone-2-carboxylate, *Angew. Chem. Int. Ed. Engl.* 35, 1324–1326 (1996).  
c) G. R. Desiraju, Supramolecular Synthons in Crystal Engineering—A New Organic Synthesis, *Angew. Chem., Int. Ed. Engl.*, 34, 2311–2327 (1995).
17. R. Luboradzki, O. Gronwald, M. Ikeda, S. Shinkai and D. N. Reinhoudt, An Attempt to Predict the Gelation Ability of Hydrogen-bond-based Gelators Utilizing a Glycoside Library, *Tetrahedron*, 56, 9595–9599 (2000).
18. A. Ballabh, D. R. Trivedi, and P. Dastidar, Structural Studies of a New Low Molecular Mass Organic Gelator for

- Organic Liquids Based on Simple Salt, *Chem. Mater.*, 15, 2136–2140 (2003).
19. a) D. R. Trivedi and P. Dastidar, Instant Gelation of Various Organic Fluids Including Petrol at Room Temperature by a New Class of Supramolecular Gelators, *Chem. Mater.* 18, 1470–1478 (2006).
- b) U. K. Das, D. R. Trivedi, N. N. Adarsh, and P. Dastidar, Supramolecular Synthons in Noncovalent Synthesis of a Class of Gelators Derived from Simple Organic Salts: Instant Gelation of Organic Fluids at Room Temperature via in situ Synthesis of the Gelators, *J. Org. Chem.*, 74, 7111–7121 (2009).
20. a) P. Sahoo, V. G. Puranik, A. K. Patra, P. U. Sastry and P. Dastidar Ferrocene Based Organometallic Gelators: A Supramolecular Synthon Approach, *Soft Matter*, 7, 3634–3641 (2011).
- b) P. Sahoo, N. N. Adarsh, G. E. Chacko, S. R. Raghavan, V. G. Puranik and P. Dastidar, Combinatorial Library of Primaryalkylammonium Dicarboxylate Gelators: A Supramolecular Synthon Approach, *Langmuir*, 25, 8742–8750 (2009).
21. a) D. R. Trivedi, A. Ballabh and P. Dastidar, Facile Preparation and Structure–property Correlation of Low Molecular Mass Organic Gelators Derived from Simple Organic Salts, *J. Mater. Chem.*, 15, 2606–2614 (2005).
- b) P. Sahoo, R. Sankolli, H.-Y. Lee, S. R. Raghavan, and P. Dastidar, Gel Sculpture: Moldable, Load-Bearing and Self-Healing Non-Polymeric Supramolecular Gel Derived from a Simple Organic Salt, *Chem. Eur. J.*, 18, 8057–8063 (2012).
22. a) D. R. Trivedi, A. Ballabh and P. Dastidar, Noncovalent Syntheses of Supramolecular Organo Gelators, *Crystal Growth & Design*, 6, 763–768 (2006).
- b) P. Sahoo and P. Dastidar, Secondary Ammonium Dicarboxylate (SAD): A Supramolecular Synthon in Designing Low Molecular Weight Gelators Derived from Azo-Dicarboxylates, *Cryst. Growth Des.*, 12, 5917–5924 (2012).
23. D. R. Trivedi and P. Dastidar, Instant Gelation of Various Organic Fluids Including Petrol at Room Temperature by a New Class of Supramolecular Gelators, *Chem. Mater.*, 18, 1470–1478 (2006).
24. U. K. Das, S. Banerjee and P. Dastidar, Primary Ammonium Monocarboxylate Synthon in Designing Supramolecular Gels: A New Series of Chiral Low-Molecular-Weight Gelators Derived from Simple Organic Salts that are Capable of Generating and Stabilizing Gold Nanoparticles, *Chem. Asian J.*, 8, 3022–3031 (2013).
25. A. Ballabh, D. R. Trivedi and P. Dastidar, From Nonfunctional Lamellae to Functional Nanotubes, *Org. Lett.*, 8, 1271–1274 (2006).
26. D. R. Trivedi, A. Ballabh, P. Dastidar and B. Ganguly, Structure-Property Correlation of a New Family of Organogelators Based on Organic Salts and their Selective Gelation of Oil from Oil/Water Mixtures, *Chem. Eur. J.*, 10, 5311–5322 (2004).
27. P. Sahoo, D. K. Kumar, D. R. Trivedi, and P. Dastidar, An Easy Access to an Organometallic Low Molecular Weight Gelator: A Crystal Engineering Approach, *Tetrahedron Lett.*, 49, 3052–3055 (2008).
28. a) A. Y-Y. Tam, K. M-C. Wong, G. Wang and V. W-W. Yam, Luminescent Metallogels of Platinum(II) Terpyridyl Complexes: Interplay of Metal...Metal,  $\pi$ - $\pi$  and Hydrophobic-Hydrophobic Interactions on Gel Formation, *Chem. Commun.*, 2028–2030 (2007).
- b) S-T. Lam, G. Wang and V. W-W. Yam, Luminescent Metallogels of Alkynylrhodium(I) Tricarbonyl Diimine Complexes, *Organometallics*, 27, 4545–4548 (2008).
- c) L. Yang, L. Luo, S. Zhang, X. Su, J. Lan, C-T. Chen and J. You, Self-assembly from Metal-Organic Vesicles to Globular Networks: Metallogel-Mediated Phenylation of Indole with Phenyl Boronic Acid, *Chem. Commun.*, 46, 3938–3940 (2010).
29. a) Y. Liu, T. Wang and M. Liu, Supramolecular Polymer Hydrogels from Bolaamphiphilic l-Histidine and Benzene Dicarboxylic Acids: Thixotropy and Significant Enhancement of Eu<sup>III</sup> Fluorescence, *Chem. Eur. J.*, 18, 14650–14659 (2012).
- b) K. Liu, N. Yan, J. Peng, J. Liu, Q. Zhang, and Y. Fang, Supramolecular gels based on organic diacid monoamides of cholesteryl glycinate, *Journal of Colloid and Interface Science*, 327, 233–242 (2008).
- c) S. H. Jung, H. Lee, S. Park and J. H. Jung, A cyanurate gel derived from two different hydrogen-bonding interactions in a binary system: evidence for the driving forces in gel formation, *New J. Chem.*, 36, 1957–1960 (2012).
- d) W. Edwards and D. K. Smith, Dynamic Evolving Two-Component Supramolecular Gels-Hierarchical Control over Component Selection in Complex Mixtures, *J. Am. Chem. Soc.*, 135, 5911–5920 (2013).
- e) M. Suzuki, H. Saito, H. Shirai and K. Hanabusa, Supramolecular organogel formation triggered by acid–base interaction in two-component system consisting of L-lysine derivative and aliphatic acids, *New J. Chem.*, 31, 1654–1660 (2007).
- f) T. Tani, K. Sada, M. Ayabe, Y. Iwashita, T. Kishida, M. Shirakawa, N. Fujita, and S. Shinkai, X-ray Crystallographic Study of Alkylammonium Anthracene-9-carboxylates as a Model for Fibrous Structure of Binary Anthracene Salt Gels, *Collect. Czech. Chem. Commun.*, 69, 1292–1300 (2004).
30. A. Pal, H. Basit, S. Sen, V. K. Aswal and S. Bhattacharya, Structure and Properties of Two Component Hydrogels Comprising Lithocholic Acid and Organic Amines, *J. Mater. Chem.*, 19, 4325–4334 (2009).
31. S. Bhattacharya and Y. Krishnan-Ghosh, First Report of Phase Selective Gelation of Oil from Oil/Water Mixtures. Possible Implications Toward Containing Oil Spills, *Chem. Commun.*, 185–186 (2001).
32. D. R. Trivedi, A. Ballabh and P. Dastidar, An Easy to Prepare Organic Salt as a Low Molecular Mass Organic

- Gelator Capable of Selective Gelation of Oil from Oil/Water Mixtures, *Chem. Mater.*, 15, 3971–3973 (2003).
33. S. R. Jadhav, P. K. Vemula, R. Kumar, S. R. Raghavan and G. John, Sugar-Derived Phase-Selective Molecular Gels as Model Solidifiers for Oil Spills, *Angew. Chem. Int. Ed.*, 49, 7695–7698 (2010).
  34. B. Escuder, F. Rodriguez-Llansola, J. F. Miravet, Supramolecular Gels as Active Media for Organic Reactions and Catalysis. *New J. Chem.*, 34, 1044–1054 (2010).
  35. A. Ajayaghosh, V. K. Praveen, C. Vijayakumar, and S. J. George, Molecular Wire Encapsulated into  $\pi$ -Organogels: Efficient Supramolecular Light-Harvesting Antennae with Color-Tunable Emission, *Angew. Chem. Int. Ed.*, 46, 6260–6265 (2007).
  36. a) P. Sahoo, D. K. Kumar, S. R. Raghavan and P. Dastidar, Supramolecular Synthons in Designing Low Molecular Mass Gelling Agents: L-Amino Acid Methyl Ester Cinnamate Salts and their Anti-Solvent-Induced Instant Gelation, *Chem. Asian J.*, 6, 1038–1047 (2011).  
b) D. Bhagat, S. K. Samanta and S. Bhattacharya, Efficient Management of Fruit Pests by Pheromone Nanogels, *Scientific Reports*, 3:1294 (2013).
  37. P. Baglioni, L. Dei, E. Carretti and R. Giorgi, Gels for the Conservation of Cultural Heritage, *Langmuir*, 25, 8373–8374 (2009).
  38. Z. Yang, G. Liang, L. Wang, and B. Xu, Using a Kinase/Phosphatase Switch to Regulate a Supramolecular Hydrogel and Forming the Supramolecular Hydrogel in Vivo, *J. Am. Chem. Soc.*, 128, 3038–3043 (2006).
  39. a) K. J. C. van Bommel, A. Friggeri and S. Shinkai, Organic Templates for the Generation of Inorganic Materials, *Angew. Chem. Int. Ed.*, 42, 980–999 (2003).  
b) S. Kobayashi, N. Hamasaki, M. Suzuki, M. Kimura, H. Shirai and K. Hanabusa, Preparation of Helical Transition-Metal Oxide Tubes Using Organogelators as Structure-Directing Agents, *J. Am. Chem. Soc.*, 124, 6550–6551 (2002).  
c) L. C. Palmer and S. I. Stupp, Molecular Self-Assembly into One-Dimensional Nanostructures, *Acc. Chem. Res.*, 41, 1674–1684 (2008).
  40. C. S. Love, V. Chechik, D. K. Smith, K. Wilson, I. Ashworth and C. Brennan, Synthesis of Gold Nanoparticles Within a Supramolecular Gel-phase Network, *Chem. Commun.*, 1971–1973 (2005).
  41. Z. Yang, G. Liang, M. Ma, A. S. Abbah, W. W. Luc and B. Xu, D-Glucosamine-based Supramolecular Hydrogels to Improve Wound Healing, *Chem. Commun.*, 843–845 (2007).
  42. J. Majumder, M. R. Das, J. Deb, S. S. Jana and P. Dastidar,  $\beta$ -Amino Acid and Amino-Alcohol Conjugation of a Nonsteroidal Anti-Inflammatory Drug (NSAID) Imparts Hydrogelation Displaying Remarkable Biostability, Biocompatibility, and Anti-Inflammatory Properties, *Langmuir*, 29, 10254–10263 (2013).



**Tapas Kumar Adalder** had completed both of his Undergraduate (In Chemistry Honours), 2005 and Postgraduate (In Organic Chemistry), 2007 studies from the Presidency College (currently known as Presidency University), Kolkata. He is presently working as a senior research fellow with Prof. P. Dastidar in the Department of Organic Chemistry, Indian Association for the Cultivation of Science (IACS), Kolkata, India, and has recently submitted his Ph.D. Thesis entitled “Supramolecular Synthons in Designing Organic materials”. His research interests include Crystal Engineering, Supramolecular Gel, Supramolecular Capsule, Pharmaceutical Cocrystal, Ultra-small metal Cluster etc.



**Uttam Kumar Das** completed his B.Sc. and M.Sc. degree in Chemistry from Kalyani University, West Bengal and IIT Bombay respectively. He is presently working as a senior research fellow with Prof. P. Dastidar in the Department of Organic Chemistry, Indian Association for the Cultivation of Science (IACS), Kolkata, India and has recently submitted his Ph.D. Thesis entitled “Designing and Synthesis of Organic and Metal-Organic Gelling agents: Crystal Engineering Approach”. His research interests include Crystal Engineering, Supramolecular Gel, Metal-Organic Framework (MOF) etc.



**Joydeb Majumder** was awarded National Scholarship, Govt. of India in 2003. In 2010, he received his M.Sc. degree in Chemistry from University of Kalyani, West Bengal. Currently, he is working with Professor Parthasarathi Dastidar at Department of Organic Chemistry, Indian Association for the Cultivation of Science (IACS), Kolkata for his Ph.D. degree investigating various drug based supramolecular gels for biomedical applications.



**Rajdip Roy** obtained his undergraduate and postgraduate degree in Chemistry from St. Xavier's College affiliated to Calcutta University in 2009 and IIT Kharagpur in 2011 respectively. He then moved to Indian Association for the Cultivation of Science (IACS) to pursue full time Ph.D. program with Prof. P. Dastidar in the same year. Currently, He is working on designing supramolecular gelators for drug delivery and biomedical applications.



**Parthasarathi Dastidar** received his Ph.D. degree from Indian Institute of Science, Bangalore in 1994. After a few postdoctoral stints in Tel-Aviv (Israel), UNAM (Mexico) and Wayne State University (USA), he joined CSMCRI, Bhavnagar, India in 1998 as a Scientist and recently moved to the Dept. of Organic Chemistry, IACS, Kolkata, India where he is currently a Professor. He was an invited JSPS fellow at Osaka University, Japan during 2004. His research interests include supramolecular gels, crystal engineering, LMWG, coordination polymers, pharmaceutical co-crystals etc.