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Hybrid Covalent and Non-Covalent Routes toward the Rational Design and Synthesis of an Organogel

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Abstract: A urea derived compound based on L-phenylalanine was synthesized and subsequently converted into an organic salt through a time-efficient procedure. The resulting salt exhibited effective gelation in chlorobenzene. Comprehensive rheological analysis, including table top as well as dynamic measurements further confirmed the mechanical robustness of the gel, while HR-TEM imaging revealed an entangled fibrous network characteristic of supramolecular self-assembly. The successful design of this bioconjugate, originating from a naturally occurring amino acid, underscores an effective strategy for converting simple bio-derived building blocks into functional supramolecular gelators with broad potential in materials science and soft-matter applications.

Keywords: SAFiNs; Supramolecular gels; 1D HBN

Introduction

Over the past few decades, supramolecular gelators; particularly low-molecular-weight gelators (LMWGs) [1–6] have attracted impetus attentions due to their diverse and promising applications in fields such as electro-optics, [7] photonics, sensors, [8] cosmetics, [9] structure-directing agents, [10] catalytic reaction media, [11] art conservation, [12] biomaterials [13–16] and so on. LMWGs are typically small organic molecules (MW < 3000) capable of immobilizing solvent molecules to form gels. However, the rational design of gelators remains a significant challenge because the molecular-level mechanism of gelation is not yet fully understood. A wide range of molecular systems have been reported as effective gelators, spanning structures as small as simple urea derivatives to large and complex phthalocyanine-based molecules. Both hydrogen-bonding-functional molecules (e.g. ureas, amides, peptides) and those lacking classical hydrogen-bonding motifs (e.g. steroid derivatives) have been shown to induce gelation. Consequently, the ab initio design of gelator molecules remains highly challenging, therefore most of the gelators described in the literature have been discovered serendipitously. Current insights suggest that gelator molecules initially assemble into one-dimensional (1D) fibrous structures through various non-covalent interactions such as hydrogen bonding, π–π stacking, van der Waals forces, hydrophobic interactions, halogen bonding, and charge-transfer interactions etc. These primary fibers subsequently entangle into complex three-dimensional self-assembled fibrillar networks (SAFiNs), [17]

within which solvent molecules become immobilized; resulting in a gel formation. Shinkai and co-workers [18] demonstrated that the presence of a continuous one-dimensional hydrogen-bonded network (HBN) is crucial for effective gelation, whereas predominantly two- or three-dimensional HBNs typically result in weak gels or no gelation at all. In this context it should be mentioned that Urea-based low-molecular-weight gelators are well known to self-assemble into supramolecular architectures through directional hydrogen-bonding interactions. Esch, Feringa, and co-workers reported a series of geminal bisurea derivatives that act as efficient gelators.[19] Suzuki and co-workers demonstrated the possibility of in situ gelation by generating urea derivatives directly in the corresponding gelling solvents at room temperature. In their study, a new series of bis- and tris-urea-based gelators was synthesized through the reaction of amines with the corresponding isocyanates in the presence of various gelling solvents.[20] However, most of these gelators are obtained through time-consuming multistep organic syntheses that require extensive purification and often result in relatively low yields. Later, with the help of structure property correlation Dastidar group has been exclusively demonstrated that 1D and 2D hydrogen bonded network indeed played an important role in gelation even in a series of organic salts following supramolecular synthon approach; however it is not the necessary and sufficient conditions. [21] Salt formation is the easiest technique where equivalent amount of acid and base reacted to produce nearly quantitative yield in contrast to multistep covalent organic synthesis. Therefore, it immediately became obvious that such simple strategy (salt formation) could be advantageous in generating a large number of salts as potential LMWGs. Herein supramolecular synthon concept is involved to design a priori 1D molecular self-assembly so that the SAFiNs thus formed, under suitable conditions, would produce supramolecular gels. In this context, it is worth mentioned that urea derived supramolecular gels, driven by strong directional hydrogen bonding can readily self-assemble into stable fibrous networks in various organic solvents. These organogels can be functioned as structured media for crystallization, solvent immobilization, and organic templating.

In the present work, our objective was to design a gelator by employing both covalent and non-covalent synthetic strategies in order to evaluate the robustness of organic salt formation in the presence of additional hydrogen-bonding functionalities. In this context, salt formation through non-covalent interactions represents one of the simplest synthetic approaches, where equivalent amounts of an organic acid and an organic base react to afford the desired product in nearly quantitative yield, in contrast to conventional multistep covalent organic synthesis.

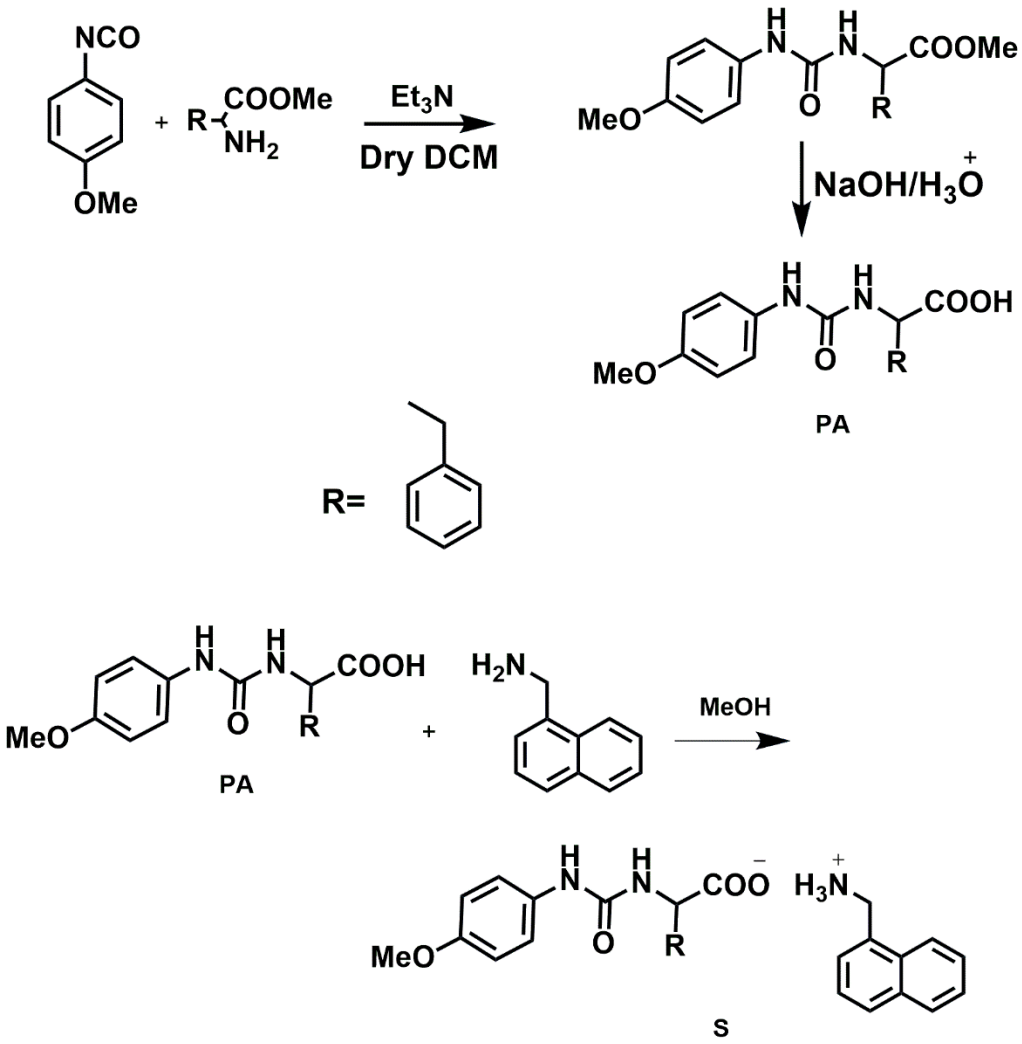
As noted earlier, salt formation can promote charge assisted directional hydrogen bonding that often plays important role in gelation. To achieve this, we have introduced urea functionalities in combination with a terminal carboxylic acid group derived from phenylalanine. The urea-based molecule containing a terminal carboxylic acid subsequently interacts with a primary amine to form a primary ammonium monocarboxylate (PAM) organic salt, which ultimately leads to the formation of a supramolecular gel. The deliberate choice of having additional hydrogen bond functionality i.e. urea in carboxylic acid was to study the robustness of primary ammonium monocarboxylate (PAM synthon) in the resulting organic salt and its implication in gelation. Interestingly, the salt forms gel in nonpolar solvent i.e. chlorobenzene. Gel was characterized by table-top and dynamic rheology. This bioconjugate, derived from a naturally occurring amino acid, offers a promising strategy for converting simple amino acids into functional supramolecular gelators that can be further applied in crystallization media, solvent immobilization, and organic templating in future.

Results & Discussion

Synthesis

In order to synthesize the bioconjugate, a time-efficient synthetic route was employed as depicted in Scheme 1. L-Phenylalanine methyl ester hydrochloride (5 mmol, 1080 mg) was dissolved in 30 mL of dry DCM in a 250 mL round-bottom flask, followed by the addition of triethylamine (500 μL). Subsequently, 4-methoxyphenyl isocyanate (5 mmol, 695 μL) was added drop wise to the reaction mixture at room temperature. The reaction was then stirred for 6 hours, after which the solvent was removed under reduced pressure. The resulting residue was then subjected to ester

hydrolysis using aqueous sodium hydroxide. The reaction mixture was subsequently acidified with HCl, resulting in the formation of a cream-colored solid (1256 mg, ~80% yield). The product (PA) was characterized by NMR spectroscopy.



Scheme 1. Synthetic procedure of bioconjugate (PA) and Salt (S).

The salt (S) was prepared by combining the synthesized acid (PA) and 1-napthylmethylamine in equimolar amounts in methanol at room temperature followed by sonication for 10 minutes. After evaporating the solvent, the resulting solids were subjected to FT-IR analysis. Interestingly, approximately 1 mmol of S (465 mg, 98% yield) was obtained from 1 mmol of PA. Complete disappearance of >C=O stretching frequency of corresponding COOH functionality of bioconjugate ~ 1733 cm $^{-1}$ and appearance of new bands at ~1645cm $^{-1}$ (for at COO -) clearly indicated the salt formation. The purity of the above-mentioned salts was checked by ^{1} H NMR (Experimental section).

Gel formulation

Next, the synthesized salt was subjected to gelation studies using seven selected solvents, including both polar and nonpolar types. Remarkably, the salt formed a translucent gel in chlorobenzene (Table 1). For the gelation study, 10 mg of salt (S) was transferred into a test tube, followed by the addition of 1 mL of solvent. The mixture was heated thoroughly until a clear homogeneous solution was obtained and then allowed to cool to room temperature. Interestingly, upon cooling, an organogel was formed in chlorobenzene, which was further confirmed by the test tube inversion

method. The gel was found to be thermoreversible, exhibiting a minimum gelator concentration (MGC) of 1 wt%, and a gel dissociation temperature (T_{Gel}) of 80 °C.

Table 1. Gelation Table of S

Solvent	Water	Acetonitrile	DMSO-H_20 (1:9)	Toluene	Methyl salicylate	Nitro benzene	Chlorobenzene
MGC (wt/vv) /T_{gel}	ppt	Soluble	Soluble	ppt	Gelatinous ppt	Gelatinous ppt	Gel 1/80 °C

ppt= precipitate. MGC= Minimum gelator concentration.

The T_{Gel} values at different concentrations were determined using dropping ball method. In a typical experiment, a glass ball (400 mg) was placed on 1 mL of the gel contained in a test tube. The test tube was then immersed in an oil bath and heated gradually. The temperature at which the ball reached at the bottom of the test tube was recorded as T_{Gel}. The T_{Gel} vs concentration plot further showed that T_{Gel} increased progressively with increasing gelator concentration, indicating that noncovalent interactions such as hydrogen bonding, π–π stacking, and C–H···π interactions play significant roles in the formation of gel network (Figure 1).

To investigate the internal morphology of the gel network, high-resolution transmission electron microscopy (HRTEM) analysis of the hydrogel was carried out. For sample preparation, a very dilute solution of the gelator was drop-cast onto a carbon-coated Cu TEM grid (300 mesh). The grid was dried under vacuum overnight. The resulting HRTEM images revealed an entangled fibrous network; corresponds to the assemblies formed through hydrogen bonding, π–π interaction, and other self-assembly interactions in the gel network (Figure 2).

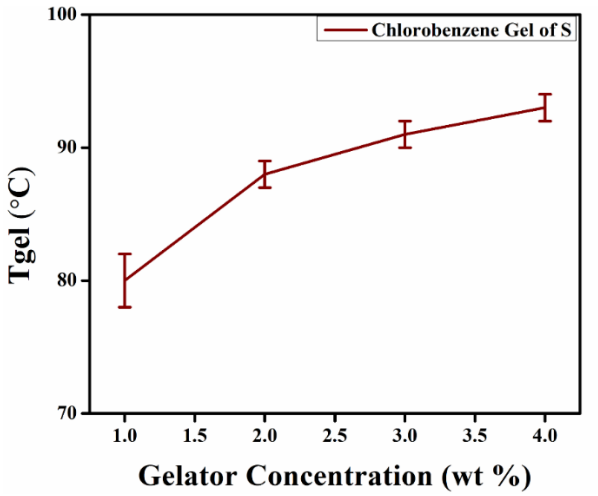


Figure 1. T_{gel} *vs* (wt % w/v) plot for organogel.

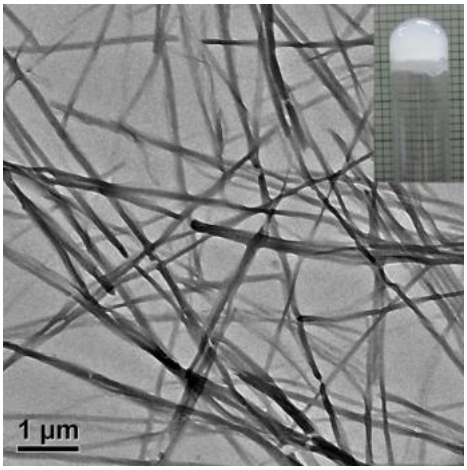


Figure 2. TEM morphology of the organogel along with gel picture.

The viscoelastic properties of the 1 wt% organogel were further examined using a series of dynamic rheological measurements. Initially, an amplitude sweep test was conducted to determine the linear viscoelastic (LVE) region. The elastic modulus (G′) gradually decreased with increasing strain and dropped below the viscous modulus (G″) at a critical strain of 3.23%, indicating a typical gel-like response. Subsequently, a frequency sweep experiment was performed at a constant strain of 0.1%, as determined from the amplitude sweep. The organogel exhibited characteristic viscoelastic behaviour, with the storage modulus (G′) significantly higher than the loss modulus (G″) and largely independent of frequency across the measured range (Figure 3).

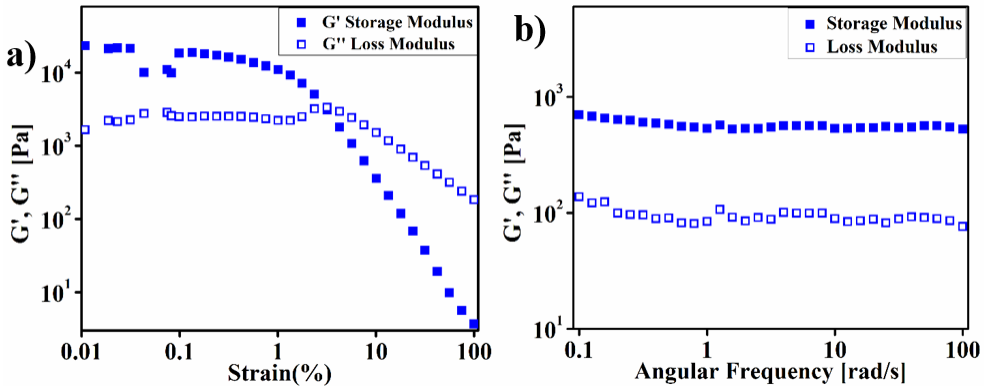


Figure 3. Rheological responses of the 1 wt % (w/v) organogel a) strain sweep and b) frequency sweep experiment at constant strain of 0.1 % at 25°C.

Conclusion

The present study focuses on the design, synthesis, and characterization of a urea derivative obtained from L-phenylalanine through a straightforward synthetic route. This bioconjugate was subsequently converted into an organic salt via a time-efficient salt-formation reaction with a primary amine. The resulting noncovalently assembled salt exhibited excellent gelation ability in chlorobenzene. Microscopic analysis revealed an entangled fibrous network characteristic of supramolecular gels, while rheological measurements confirmed its viscoelastic, gel-like behaviour. Additionally, their well-defined fibrous networks render them promising candidates for applications in organic templating, controlled-release systems, and the development of thermoresponsive materials.

Experimental Section

Materials

All the chemicals including 4-methoxy phenyl isocyanate, L phenylalanine methyl ester hydrochloride and 1-naphthylmethylamine were purchased from Sigma Aldrich and used without further purification. Solvents were AR (Analytical Reagents) grade and used without any further purification.

Methods

FT-IR spectra for all compounds were recorded using a Shimadzu FTIR-8300 spectrometer. NMR spectra were obtained on a Bruker Ultrashield Plus 400 MHz spectrometer. Rheological measurements were carried out using an Anton Paar Modular Compact Rheometer (MCR 102). Transmission Electron Microscopy (TEM) images were acquired on a JEOL instrument using 300-mesh copper grids.

Characterization Data

Physico-chemical Data: FT- IR (NEAT)

PA: 3301 (s, urea N-H stretch), 1733 (b, acid C = O stretch) (Figure S1), ^{1}H NMR (400 MHz, DMSO-d_6, 25°C): δ=8.46 (s, ,1H, NH of urea), 7.30-7.18 (m, 7H, Aromatic), 6.78-6.77 (d, 2H, 8Hz, Aromatic), 6.19-6.17 (d, 1H, 8Hz, NH of urea), 4.45-4.39 (m, 1H, chiral H of phenyl alanine), 3.67 (s, 3H, methyl of OMe,), 3.07-2.89 (m, 2H, diastereotopic H of phenyl alanine) (Figure S2).

S: 1645 (C=O stretch) cm^{-1}. ^{1}HNMR (400 MHz, DMSO-d_6, 25°C): δ=8.62 (s, ,1H, NH of urea), 8.14-8.12 (d, 2H, 8Hz, Aromatic), 7.98-7.96 (d, 2H, 8Hz, Aromatic), 7.91-7.89 (d, 2H, 8Hz, Aromatic), 7.61-7.50 (m, 4H, Aromatic), 7.27-7.15 (m, 7H, Aromatic of napthyl amine), 6.80-6.78 (d, 2H, 8Hz, Aromatic), 6.19-6.17 (d, 1H, 8Hz, NH of urea), 4.38 (s, 2H,

CH2 of napthylmethyl amine), 4.22-4.18 (1H, m, chiral H of phenyl alanine), 3.68 (s, 3H, methyl of OMe), 3.09-2.96 (m, 2H, diastereotopic H of phenyl alanine) (Figure S3).

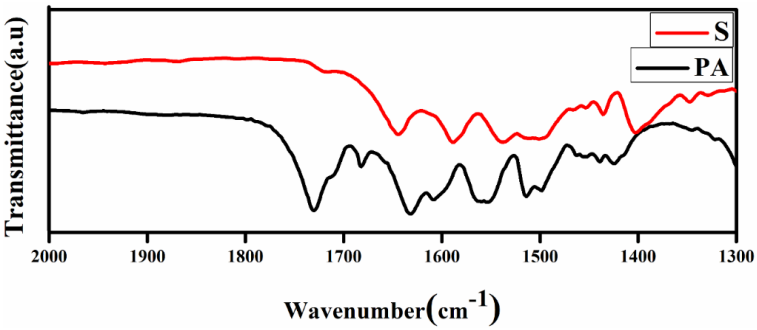


Figure S1. FT-IR spectra of bioconjugate acid and salt.

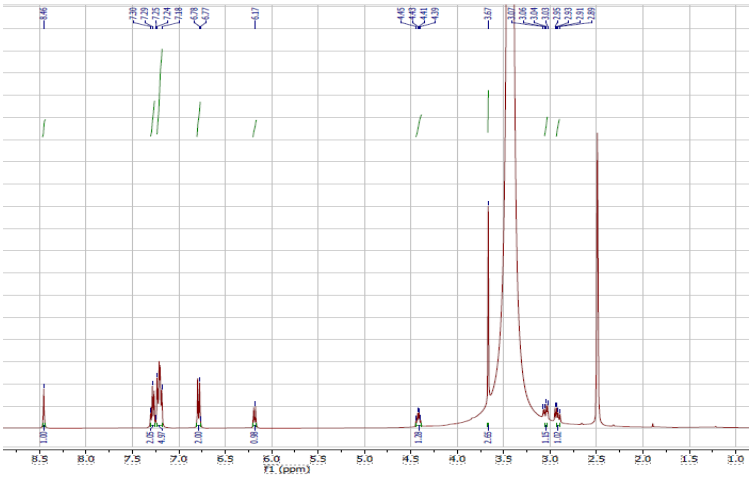


Figure S2. ^{1}H NMR spectra of **PA** in DMSO-d6.

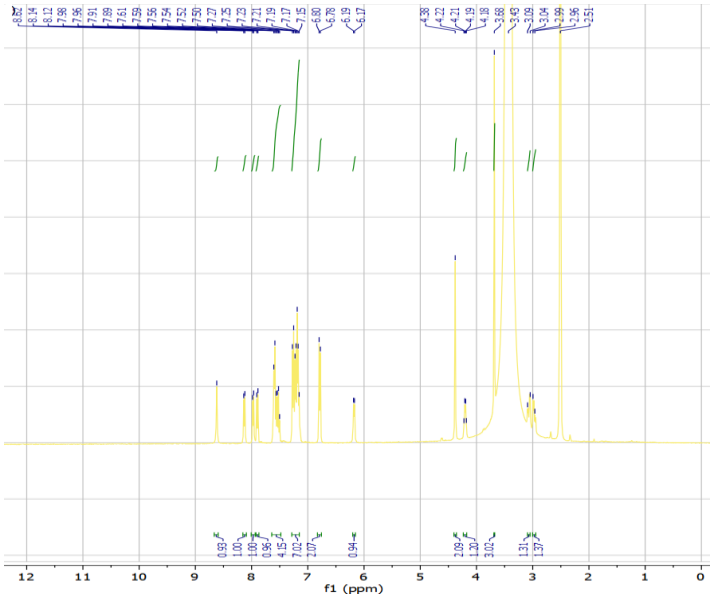


Figure S3. ^{1}H NMR spectra of **S** in DMSO-d6.

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Reference

1. Terech, P, Weiss, RG. Low Molecular Mass Gelators of Organic Liquids and the Properties of Their Gels. Chemical Reviews 1997, 97(8):3133–3160.
2. Suzuki, M, Hanabusa, K. L-Lysine-based low-molecular-weight gelators. Chemical Society Reviews 2009, 38(4):967–975.
3. Piepenbrock, M-OM, Lloyd, GO, Clarke, N, Steed, JW. Metal- and Anion-Binding Supramolecular Gels. Chemical Reviews 2010, 110(4):1960–2004.
4. Weiss, RG, Terech, P (eds.). Eds. Molecular Gels: Materials with Self- Assembled Fibrillar Networks, Springer: Dordrecht, The Netherlands, 2005.
5. Tomasini, C, Castellucci, N. Peptides and peptidomimetics that behave as low molecular weight gelators. Chemical Society Reviews 2013, 42(1):156–172.
6. Edwards, W, Smith, DK. Dynamic Evolving Two-Component Supramolecular Gels—Hierarchical Control over Component Selection in Complex Mixtures. Journal of the American Chemical Society 2013, 135(15):5911–5920.
7. Prasanthkumar, S, Ghosh, S, Nair, VC, Saeki, A, Seki, S, Ajayaghosh, A. Organic Donor–Acceptor Assemblies form Coaxial p–n Heterojunctions with High Photoconductivity. Angewandte Chemie 2015, 127(3):960–964.
8. Ikeda, M, Fukuda, K, Tanida, T, Yoshii, T, Hamachi, I. A supramolecular hydrogel containing boronic acid-appended receptor for fluorocolorimetric sensing of polyols with a paper platform. Chemical Communications 2012, 48(21):2716–2718.
9. Wynne, A, Whitefield, M, Dixon, A, Anderson, S. An effective, cosmetically acceptable, novel hydro-gel emollient for the management of dry skin conditions. Journal of Dermatological Treatment 2002, 13(2):61–66.
10. Basit, H, Pal, A, Sen, S, Bhattacharya, S. Two-Component Hydrogels Comprising Fatty Acids and Amines: Structure, Properties, and Application as a Template for the Synthesis of Metal Nanoparticles. Chemistry – A European Journal 2008, 14(21):6534–6545.
11. Carretti, E, Bonini, M, Dei, L, Berrie, BH, Angelova, LV, Baglioni, P, Weiss, RG. New Frontiers in Materials Science for Art Conservation: Responsive Gels and Beyond. Accounts of Chemical Research 2010, 43(6):751–760.
12. Escuder, B, Rodríguez-Llansola, F, Miravet, JF. Supramolecular gels as active media for organic reactions and catalysis. New Journal of Chemistry 2010, 34(6):1044–1054.
13. Wang, Q, Yang, Z, Zhang, X, Xiao, X, Chang, CK, Xu, B. A Supramolecular-Hydrogel-Encapsulated Hemin as an Artificial Enzyme to Mimic Peroxidase. Angewandte Chemie International Edition 2007, 46(23):4285–4289.
14. Jayawarna, V, Ali, M, Jowitt, TA, Miller, AE, Saiani, A, Gough, JE, Ulijn, RV. Nanostructured hydrogels for three-dimensional cell culture through self-assembly of fluorenylmethoxycarbonyl-dipeptides. Advanced materials 2006, 18(5):611–614.
15. Khademhosseini, A, Langer, R. Microengineered hydrogels for tissue engineering. Biomaterials 2007, 28(34):5087–5092.
16. Bommel, KJ van, Stuart, MC, Feringa, BL, Esch, J van. Two-stage enzyme mediated drug release from LMWG hydrogels. Organic & biomolecular chemistry 2005, 3(16):2917–2920.
17. George, M, Weiss, RG. Molecular Organogels. Soft Matter Comprised of Low-Molecular-Mass Organic Gelators and Organic Liquids. Accounts of Chemical Research 2006, 39(8):489–497.
18. Luboradzki, R, Gronwald, O, Ikeda, M, Shinkai, S, Reinhoudt, DN. An attempt to predict the gelation ability of hydrogen-bond-based gelators utilizing a glycoside library. Tetrahedron 2000, 56(49):9595–9599.
19. Schoonbeek, FS, Esch, J van, Hulst, R, Kellogg, RM, Feringa, BL. Geminal Bis-ureas as Gelators for Organic Solvents: Gelation Properties and Structural Studies in Solution and in the Gel State. Chem. Eur. J. 2000, 6, 2633-2643.
20. Suzuki, M, Nakajima, Y, Yumoto, M, Kimura, M, Shirai, H, Hanabusa, K. In situ organogelation at room temperature: direct synthesis of gelators in organic solvents. Org. Biomol. Chem. 2004, 2, 1155-1159.
21. Dastidar, P. Supramolecular gelling agents: can they be designed? Chemical Society Reviews 2008, 37(12):2699–2715.