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## Aliphatic alcohols induced opaque to transparent transformation and application of solubility theory in a bis-dipeptide based supramolecular gel

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#### Dedication

**Abstract:** Gel-to-gel phase transformations under external stimuli, which are visible to the naked eye, have great application potentials in the field of sensors and specific recognitions. Herein, a bis-dipeptide supramolecular gelator (DMPV) was prepared base on L-valine moieties having pyridinyl group and a long fatty diamine. It was found that the gelator could immobilize organic/water binary mixed solvents, and gel-to-gel transitions with unprecedented opaque to transparent transformations were observed when aliphatic alcohols, such as methanol, ethanol, 1-propyl alcohol and isopropanol were used as the organic components. Morphological investigations indicated a re-assembly process was occurred, and microstructure evolutions from agglomerates to nanofibers were observed. Opaque and transparent assemblies could interconvert and respectively respond and restore under mechanical force and pH stimuli. Moreover, Hansen and Flory–Huggins parameters were used to investigate the effect of solvent on the gelation performance of DMPV. This would facilitate the structure and solvent optimizations and improve developing of advanced gel systems.

#### Introduction

Phase transformation is a general physical phenomenon presented in materials, it is induced by the variation of intermolecular interactions and distance, molecular assembly mode and thermal movements. This process is ordinarily accompanied by energy absorption and release, which make the phase change materials have huge application potentials in the field of energy storage, temperature control and smart device.<sup>[1]</sup> Nowadays, supramolecular gels constructed by low molecular weight gelators (LMWGs) have attracted great attention for researchers. These solid-like soft materials are formed by the assembly of small molecules through noncovalent interactions, and reversible phase transformations such as sol-to-crystal, sol-to-gel and gel-to-gel transitions under the stimuli of mechanical stress,<sup>[2]</sup> ultrasound,<sup>[3]</sup> light,<sup>[4]</sup> electric or magnetic fields<sup>[5]</sup> are thus more easily take place. In contrast to polymer gels, the supramolecular assemblies are more suitable for specific recognition and controlled release.<sup>[6]</sup>

Various phase transformations under external stimuli w-

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hich could be distinguished by naked-eyes are of great value.<sup>[7,8]</sup> It is not only essential for the study of dynamic properties for supramolecular assemblies, but also useful in developing of advanced sensors. <sup>[9,10]</sup> Among all of the variations, the gel-to-gel transitions brought in volume and color changes attracted a great deal of attentions recently. Liu et al developed a hydrogel composed of the dendron gelator based on L-glutamic acid and positively charged azobenzene derivative. The system showed obvious volume variations with shrinking and swelling upon photoirradiation.<sup>[11]</sup> Mallia and co-workers synthesized a series of organogelators constituted with long alkyl chain, hydroxyl and secondary amine. The gelators assembled into fibrillar networks in CCl<sub>4</sub> and exhibited temperature induced gel-to-gel phase transitions with opaquetransparent changes in the appearance.<sup>[12]</sup> Banerjee's group reported a time-dependent changes from transparent to turbid of a peptide derived gel.<sup>[13]</sup> All of the above macroscopic changes are on behalf of the dynamic and metastable state properties of supramolecular systems. However, to the best our knowledge, the gel-to-gel transformations with visible macroscopic appearance reported so far are either temperature-induced or timedependent, and the examples induced by specific chemicals are rare.

In addition, with the imperative requirement of modern smart devices and biomedical engineering, many supramolecular gels based on natural organics usually could not meet the demand over special situations. Therefore, novel molecules which have excellent gelation

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Figure 1. Formation of gels and gel-to-gel transitions of DMPV at CGC. V(organic solvent)/V(H<sub>2</sub>O)=1/2.

properties need to be prepared. The structure design and investigation on solvent effect are fundamental. Despite the cognition of the importance of hydrogen bonding,  $\pi$ - $\pi$ stacking, coordination and hydrophobic interactions for gelation, selection of the solvent system should be tried repeatedly.<sup>[14,15]</sup> Several solubility theories have thus been proposed for the prediction of gel performance of a gelator and reduction of tedious attempts, such as Hansen solubility parameters, Hildebrand solubility parameters, Kamlet-Taft parameters, etc.<sup>[16,17]</sup> In the article, we report a gel-to-gel transition with interesting opaque to transparent transformation. The gelator was prepared based on L-valine and a long fatty diamine. It was found that gel could not be formed by the gelator in a single organic solvent. However, when amounts of water was introduced, the gelation process occurred instantaneously without time delay. In particular, a macroscopic phase transformation was observed when aliphatic alcohols were used as the organic solvent. Moreover, Hansen parameters and Flory-Huggins parameters were tentatively used for the prediction of gel performance of the gelator. The utilization of empirical equation provided a strategy for solvent screening and improved the progress for practical application of the gel.

#### **Results and Discussion**

#### **Gelation studies**

The synthesis procedure of this bis-dipeptide gelator is shown in Scheme 1. DMPV was designed inspired by peptide gels which have been investigated in many researches. Chiral functional groups have been demonstrated a key factor in the construction of supramolecular gels. Helical structure induced by the chiral centre makes the molecules orderly packed, it facilitates the formation of noncovalent intermolecular interactions, which conducted the supramolecular selfassemblies. Therefore L-valine was selected as the building block, and bis-dipeptide structure was prepared. The solubility of DMPV was investigated in detail. It is completely insoluble in water and only soluble in polar organic solvents including DMF, DMSO, 1,4-dioxane, etc. It could not form gel as a gelator in a single solvent. Therefore, the gelation propensity of DMPV was initially investigated in polar organic solvents by adding different proportions of pure water. A weighted sample of DMPV (0.01g) was mixed with an organic solvent in a septumcapped vial and stirred until the solid was fully dissolved.



By introducing a certain amount of water, gels could be formed immediately. If no flow was observed when inverting the vial, the gelation and a stable gel were denoted. All of the systems exhibited an opaque appearance, and the obtained gels of DMPV were stable for several months at room temperature (Figure 2). The gelation test (Table S1) indicated that the constitution of mixed solvents are crucial to the formation of gel. The solvents could not be immobilized when the volume fraction of water was less than 50%. Meanwhile, if the volume fraction of water exceeded 90%, precipitation was obtained instead of the gel. In particular, the water content of 50% contributed to the fastest gelation behavior and the best stability, thus the following detailed investigations on the gel was conducted based on this composition. The gelation behaviors of DMPV were studied by the standard heating-cooling method. The systems were heated in an oil bath, and all of the formed gels could be transformed into sol upon heating. Subsequently, the sample vial was cooled down to room temperature, and the aggregation state was then assessed. To our surprise, the gel in the mixture of ethanol and water transformed to a transparent

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status, whereas another mixtures were all recovered to the original opaque appearance. The critical concentrations (CGCs) and Tgel of DMPV depended on the solvents were listed in Table S2 and S3. Inspired by the phenomenon presented above in ethanol/H2O, methanol, isopropanol and n-butyl alcohol were also used for investigation, considering the intersolubility of aliphatic and aromatic alcohols with water. Interestingly, all of these gel systems exhibited the opaque-to-transparent transitions as in the mixture of ethanol/H<sub>2</sub>O (Figure S3). DMPV based gels displayed specific discrimination capacity for aliphatic alcohols. To the best of our knowledge, the changes between transparent and opaque in the gel-based soft materials reported so far are either time-dependent<sup>[13]</sup> or temperature-induced.<sup>[18]</sup> However, this gel-to-gel transformation in our case occurs based on specific chemical environment, and the aliphatic alcohols triggered transformation happened immediately without time delay. This would be potential for developing a sensor for prompt and facile selective recognitions. To analyze the relationship between structural details and the gelation behavior of this type of gelator, we synthesized a similar bis-dipeptide compound (DMBV) using benzaldehyde instead of 4-pyridine carboxaldehyde. Interestingly, DMBV could form the gel in a sole organic solvent. While heated upon  $T_{gel}$  and water was added, it could not gel again and the precipitation was observed. This result indicates that the nitrogen atom of pyridine plays a key role



Figure 2. Photographs of DMPV at different mixed solvents (v/v =1/2) a) 1,4-dioxane/H<sub>2</sub>O, b) DMF/H<sub>2</sub>O, c) DMSO/H<sub>2</sub>O, d) acetonitrile/H<sub>2</sub>O, e) 1-propyl alcohol/ H<sub>2</sub>O, f) isopropanol/H<sub>2</sub>O, g) methanol/H<sub>2</sub>O, h) ethanol/H<sub>2</sub>O.



**Figure 3.** SEM images of assembles obtained before heating/cooling process in different mixed solvents (v/v = 1/2) at the CGC: a) 1,4-dioxane/H<sub>2</sub>O, b) acetonitrile/H<sub>2</sub>O, c) DMF/H<sub>2</sub>O, d) DMSO/H<sub>2</sub>O, e) methanol/H<sub>2</sub>O, f) ethanol/H<sub>2</sub>O, g) 1-propyl alcohol/ H<sub>2</sub>O, h) isopropanol/H<sub>2</sub>O. Upon heating/cooling process: i) 1,4-dioxane/H<sub>2</sub>O, j) acetonitrile/H<sub>2</sub>O, k) DMF/H<sub>2</sub>O, l) DMSO/H<sub>2</sub>O, m) methanol/H<sub>2</sub>O, n) ethanol/H<sub>2</sub>O, o) 1-propyl alcohol/ H<sub>2</sub>O, p) isopropanol/H<sub>2</sub>O.

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in gel formation of DMPV under mixed solvents and phase transformations.

#### Morphological analysis

Macroscopic changes are the reflection of microstructure evolutions, the above phenomenon indicates a reversible change in the structure of the supramolecular aggregates between the opaque and transparent gels. To gain insight into the mechanisms of gelation and phase transformation, the morphological details of the samples were firstly investigated by scanning electron microscopy (SEM). As displayed in Figure 3, the gels obtained in the mixed solvents of 1,4-dioxane/H2O, acetonitrile/H2O, DMF/H2O and DMSO/H<sub>2</sub>O exhibited crumpled appearances. Whereas, the assemblies in methanol/H<sub>2</sub>O, ethanol/H<sub>2</sub>O, 1-propyl alcohol/H<sub>2</sub>O and isopropanol/H<sub>2</sub>O presented the agglomerate structures under the same scales. Their opaque properties might be resulted from the large sizes of the aggregates. Upon heating and cooling process, gels in 1,4-dioxane/H<sub>2</sub>O, acetonitrile/H<sub>2</sub>O, DMF/H<sub>2</sub>O and DMSO/H<sub>2</sub>O displayed nearly the same morphologies. Therefore, the macroscopic features did not change, they remained opaque. It is worth noting that, fibrous structures were obtained in the mixture of aliphatic alcohols and water. DMPV re-assembled into interconnected 3D networks and a gel-to-gel phase transitions occurred. The variation of microstructures brought about the changes in the reflection of visible light, the transparent appearance was thus formed. However, the opaque gel both in original and reformed situations displayed agglomeration state over a large scale. This could explain the reason for their remaining opaque appearances.



**Figure 4.** (a, b) TEM and POM images of the opaque xerogel of DMPV obtained from ethanol/H<sub>2</sub>O (v/v=1/2). (c, d) TEM and POM images of the transparent xerogel of DMPV obtained from ethanol/H<sub>2</sub>O (v/v=1/2).

Transmission electron microscopy (TEM) and polarized optical microscope (POM) analyses are further performed for the investigation of transformations between opaque and transparency in the gel obtained from ethanol/H<sub>2</sub>O. As it can be seen, TEM image for the opaque xerogel demonstrated random aggregates of DMPV. Upon heating/cooling process, re-self assemble to small and thin aggregates occurred as the gel went to transparent, which presented interconnected networks consisted of welldefined nanofibers with the diameter between 50-100 nm and several micrometers in length. These observations are in accordance with the SEM images. The achievement of a stable transparent gel over the progress indicates the formation of new aggregates that have no scattering effect to the visible light. POM was also used for demonstration of this gel-to-gel transformations, and bright region was existed in both of the gel states. It indicated the formation of anisotropic architectures, and DMPV self-assembled into some organized structures could be confirmed. Moreover, agglomerate and fibrillar textures could be differentiated between Figure 4b and Figure 4d, which consistent with the SEM and TEM analyses and further declared the different assemble processes.

#### Spectral analysis

FT-IR was also used to identify the structure variations of opaque to transparency for the gels assembled in aliphatic alcohols/H<sub>2</sub>O mixture. As shown in Figure 5a, the original synthesized DMPV exhibited significant absorptions at 3280 cm<sup>-1</sup>, 2961 cm<sup>-1</sup>,1631 cm<sup>-1</sup>,1338 cm<sup>-1</sup> and 1225 cm<sup>-1</sup>, which corresponded to the N-H stretching, alkyl stretching C=O stretching (amide I), N-H bending (amide II) and C-N stretching (amide III) vibrations, respectively. After the self-assembly in the mixture of ethanol and water, the bands corresponding to N-H and C=O stretching vibrations at 3280 cm<sup>-1</sup> and 1631 cm<sup>-1</sup> red-shifted to lower frequencies both in the opaque and transparent gels. It signified that hydrogen bondings played a key role in the assembly process. It is worth noting that, the transparent gel obtained in aliphatic alcohols/H2O binary mixture redshifted further compared with the opaque one. FT-IR spectra of the xerogels obtained from methanol/H<sub>2</sub>O, 1propyl alcohol/H<sub>2</sub>O and isopropanol/H<sub>2</sub>O are showed in Figure S4, and they all exhibited the same trends of the red-shift. These observations indicate a more ordered hydrogen-bond networks in the fibrous structure, which could only be constructed favored by aliphatic alcohols.

To gain further insight into the structures, X-ray powder diffraction investigations were carried out and displayed in Figure 5b. The powdery sample exhibited nearly no obvious diffractions, which demonstrated an amorphous structure. After the assembly, the opaque xerogel exhibited an intense peak at 19.2°, implying the formation of ordered molecular packings in this self-assembled system. For the transparent xerogel re-assembled in ethanol/H<sub>2</sub>O, prominent reflections were observed at 20 of 19.2° and 22.4°, which corresponded to d-spacing of 4.6701 Å and 3.8696 Å. The appearance of new sharper peaks for transparent gel indicates that there is an obvious transformation from one gel phase to the other gel state, more orderly regions were formed by gelator molecules.

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These analyses were in accordance with the microscopic morphology observations. The presence of one peak at almost same position (around 19.2°) for both opaque and transparent xerogels suggests the similar ordered packings for them. The d spacing of 4.6701 Å could be assigned to the distance between adjacent peptide strands, indicating the formation of hydrogen bondings.<sup>[19]</sup> Notably, a characteristic peak with d spacing of 3.8696 Å arised for the transparent xerogel. This could be assigned to the distance between adjacent layers, which contributed to the formation of nanofibers.<sup>[20]</sup> Based on the morphology, <sup>1</sup>H NMR, FT-IR, and XRD investigations, the molecular packings of transparent gel is proposed in Figure 5d.



Figure 5. (a) FT-IR spectra and (b) XRD patterns of the pristine DMPV, the opaque and transparent DMPV xerogels obtained from ethanol/H<sub>2</sub>O (v/v=1/2). (c) Hydrogen bondings of DMPV. (d) Proposed molecular packings of DMPV.

#### Thixotropic and rheological studies

To demonstrate the strength of the gels before and after the gel-to-gel transitions, oscillatory rheological measurements were conducted. As depicted in Figure 6, from the strain sweep profiles, the average storage modulus ( $G' > 10^3$  Pa) was one order of magnitude higher than the loss modulus (G'') for opaque gel assembled in ethanol/H<sub>2</sub>O. This confirmed the formation of stable supramolecular gel and its dominant elastic property. The average storage modulus decreased intensely and became less than the loss modulus upon 10% of the stress for the

opaque gel, it was destroyed and changed to sol. In contrast to the opaque gel, it should be noting that the average storage modulus increased ( $G' \ge 10^4$  Pa), and it was one order of magnitude higher than the loss modulus (G") over the entire range of stresses (0.1% - 100%) for the transparent gel. Dynamic frequency sweep (DFS) experiments were also performed and the results were exhibited in Figure 6c. G' and G" displayed a slight dependence upon the frequency, which signified a good tolerance of both opaque and transparent gels against external force. Moreover, the transparent gel showed an almost four fold increase in the storage modulus value (G') compared with the opaque one, which signified an appreciable difference in the mechanical properties for them. The transparent gel with fibrillar textures possessed better mechanical strength than the opaque gel with agglomerate structure. However, the dissipation factors of tan  $\delta$  (G"/G') for both opaque gel and transparent gel are 0.14 and 0.18 respectively, there is not much difference of tan  $\delta$  values.



Figure 6. Dynamic strain sweep (DSS) plots of (a) opaque and (b) transparent DMPV gels. (c)Dynamic frequency sweep (DFS) experiments at constant strain of 0.1%. The DMPV gels were prepared at the CGC, ethanol/H<sub>2</sub>O (v/v=1/2).

#### Multistimuli-responsive study

As a soft material, multi-responsive and self-healing characteristic are fundamental properties for supramolecular gels, which are vital to their smart applications. The response to thixotropic force of the gel was examined by the shaking and resting tests. As displayed in Figure 7, the opaque and transparent gels transformed into turbid liquids through vigorous shaking by hand. After resting for a few seconds, they quickly restored to self-supported gels. Meanwhile, chemical stimuli was performed by the addition of acid and base. When hydrochloric acid was added, both of the gels transformed into transparent liquids due to disruption of the hydrogen bondings. The solutions would quickly restore to the original gel after adding an equivalent

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amount of ammonia into the system. It was worth noting that, both of the opaque and transparent gels could recover to their original states, DMPV based gels exhibited well features mentioned above suffered from both physical and chemical stimuli.



Figure 7. Reversible gel-sol transitions of the opaque (a) and transparent (b) DMPV gels triggered by mechanical and pH stimuli.

#### Solubility theory application

The formation of a gel is the results of gelator–solvent and gelator–gelator interactions.<sup>[21]</sup> To predict the range of solvents which are likely to be gelled by this bis-dipeptide gelator of DMPV, and facilitate the further investigation and application of the gelator, Hansen and Flory–Huggins parameters were both used for clarification of the relationship between the structure of DMPV and different solvents. Unfortunately, as shown in Figure S5, the gelation behaviors of our compound toward the tested solvents were not in accordance with the Hansen parameter analysis based on  $\delta_d$ ,  $\delta_p$  and  $\delta_h$ . It was not suitable for the DMPV gelator. So the Flory–Huggins parameter of  $\chi$  was alternatively used. Generally,  $\chi$  is estimated from the Hildebrand solubility parameters as follows,

#### $\chi_{12} = V_1 (\delta_2 - \delta_1)^2 / RT$

(1)

where  $\delta_1$ ,  $\delta_2$  and  $V_1$  are denoted as Hilderbrand solubility parameters of the solvent and gelator, the solvent molar volume, respectively. The Hilderbrand solubility parameters of bis-dipeptide gelator can be calculated according to the Fedors group contribution method (Table S5). The values of Flory-Huggins parameter of the gelator in each solvent were calculated as described above (Table S6) and plotted in Figure 8. It showed a strong correlation between the solvent and  $\chi$ . The stable gel would form in the range from 2.15 to 3.17 for  $\chi$ , whereas the sol and precipitation would generate in a range less than 1.63 and more than 3.81. It should be noting that, the mixture of sol and gel was existed between 1.63 and 2.15. The gelation was a metastable state between the dissolution and precipitation. From the above point of view, if an untested solvent lies in the gelation domain, it would be gelled by DMPV. In order to test the hypothesis, we carried out the gelation test for DMPV in untested solvents of acetonitrile/H<sub>2</sub>O (1:1 v/v), which possessed a  $\chi$  of 1.72. As expected, this binary mixed solvents were gelled by DMPV. By virtue of the above model, a lot of tedious attempts on different solvents could be avoided, the progress on morphology and performance siftings for application are largely shortened.



Figure 8. The calculated Flory–Huggins parameters of DMPV and solvents in the gelation test. S: solution, black squares; G: gelation, red circles; P: precipitation, blue triangles.

#### Conclusions

In conclusion, we designed an L-valine derived bisdipeptide gelator of DMPV and investigated its gelling behaviors, self-assembled nanostructures and stimuliresponsiveness. The gelation was induced by addition of water into the organic solutions of DMPV, and the resultant supramolecular gels exhibited an unprecedented opaque to transparent transformations when aliphatic alcohols were used as the organic components. Evolutions of the assembled status from agglomerates to nanofibers by the stimulation of aliphatic alcohols were observed. Whereas, the crumpled morphologies remained upon heating/cooling process in another binary mixed solvents. The opaque and transparent assemblies could respectively respond and restore under both of the chemical and physical stimuli. Meanwhile, Flory-Huggins parameters were successfully used to predict the gelling performance of DMPV in untested solvents, it would considerably improve the schedules involved during the identification of a suitable gel system for a particular field, and the further solvent screening and application for special recognition of chemicals are in progress.

#### **Experimental Section**

#### Materials and instruments

L-valine, 1-ethyl-3-(3dimethyllaminopropyl)carbodiimide hydrochloride (EDC.HCl), pyridine-4-carboxaldehyde, Benzaldehyde, 1-Hydroxybenzotriazole (HOBt) and triethylamine were purchased from Aladdin. Methanol and all of the other solvents were all the products of Shanghai Chemical Reagent Company and distilled prior to use. Other chemicals were used as received without further

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purification. FT-IR spectra were obtained on a Bruker Tensor 27 FT-IR spectrometer using KBr pellets. <sup>1</sup>H NMR spectra measurements were recorded on a Bruker AVANCE 500 MHz NMR spectrometer. X-ray diffraction (XRD) measurements were recorded using a Brucker D8 Advance diffractometer equipped with a Cu target tube and a graphite monochromator. Morphologies of the xerogels were investigated by scanning electron microscopy (FEI Quanta 250F). Transmission electron microscopy (TEM) images were recorded by a FEI Tecnai 20 microscope. Polarizing optical microscopy (POM) of RX500MRT was used for visual observations at 25°C. Rheology measurements were used by Anton Paar MCR-102 rheometer.

#### Preparation of N-4-Pyridylmethyl-L-valine (PV)

PV was prepared according to literatures<sup>[22,23]</sup> with some modification. To an aqueous solution (20 mL) of L-valine (2g, 17mmol) and Na<sub>2</sub>CO<sub>3</sub> (0.92g, 8.5 mmol), Pyridine-4carboxaldehyde (1.84g, 17 mmol) in MeOH (15 mL) was dropped slowly. The solution was stirred for 5 h at room temperature and cooled in an ice bath. Then NaBH<sub>4</sub> (0.76g, 20.4mmol) was added. The mixture was stirred for another 12 h, and 36% hydrochloric acid was used to adjust the basic (pH~11) system to acerbic (pH~5-6). The mixture was stirred further for 2h and subsequently evaporated to dryness. The resultant solid was extracted with hot and dry EtOH, and the filtrate was evaporated to obtain the white powdery PV. FT-IR (KBr, cm<sup>-1</sup>): v(N-H), 3385; v(O-H), 3255; v(C=O), 1690; v(C=N), 1430. <sup>1</sup>H-NMR (500MHz, D<sub>2</sub>O, ppm): δ 8.446~8.455 (d, J=4.5Hz, 2H), δ 7.324~7.334 (d, J=5Hz, 2H), δ 3.546~3.858 (dd, J<sub>1</sub>=15Hz,  $J_2=14.5Hz$ , 2H),  $\delta$  2.782~2.793(d, J=5.5Hz, 1H),  $\delta$ 1.847~1.930 (m,1H), δ 0.859~0.884 (t, J<sub>1</sub>=6Hz,J<sub>2</sub>=6.5Hz, 6H).

# Preparation of dodecamethylene-1,12-bis(N-L-valine) (DM)

The compound DM was prepared following a modified literature procedure.<sup>[24]</sup> L-Valine (5.85g, 0.05mol), KOH (2.8g, 0.05mol) and ethyl 3-oxobutanoate (7.0mL, 0.055mol) were dissolved in isopropyl acetate (100mL). The mixture was heated to reflux for 2h and isopropyl acetate (200mL) was added. The solution was cooled to  $12^{\circ}$ C in an ice bath. Pivaloylchloride (12.3, 0.05mol) was added and the reaction mixture was stirred for 1h. Then 1,12-diaminododecane (4.55g, 0.023mol) was added to the solution and stirred at room temperature for 30 min. Water (300mL) was added to the reaction mixture and the pH was adjusted to 1-2 by addition of HCL. The aqueous phase was separated and washed with isopropyl acetate. The pH was adjusted to 10-11 by addition of NaOH solution. The solution was cooled to  $0^{\circ}$ C and the precipitate was filtered off, washed with cold isopropyl acetate and dried at 60°C in vacuum. FT-IR (KBr, cm<sup>-1</sup>): v(N-H), 3281; v(C-H), 3092; 2921; 2851; v(C=O), 1632. <sup>1</sup>H-NMR (500MHz, DMSO, ppm):  $\delta$  7.63~7.786 (t, J<sub>1</sub>=5.5Hz, J<sub>2</sub>=6Hz, 2H),  $\delta$  3.347 (s, 2H),  $\delta$  3.008~3.077 (m, 4H),  $\delta$  2.867~2.878 (d, J=5.5Hz, 2H),  $\delta$  1.80~1.851 (m, 2H),  $\delta$  1.585 (s, 4H),  $\delta$  1.366~1.392 (t, J<sub>1</sub>=6.5Hz, J<sub>2</sub>=6.5Hz, 4H),  $\delta$  1.232 (s, 16H),  $\delta$  0.763~0.855 (dd, J<sub>1</sub>=6.5Hz, J<sub>2</sub>=6.5Hz, 12H).

# Preparation of dodecamethylene-1,12-bis(N-(N-(4-pyridylmethyl-L-valyl))-L-valine)(DMPV)

Dodecamethylene-1,12-bis(N-L-valine) (1.99g, 0.005mol) and N-(4-Pyridylmethyl)-L-valine (2.184g, 0.0105mol) were dissolved in DMF (120 mL). Then EDC HCl (2.865g 0.015mol) and HOBT (2.057g, 0.015mol) were added. The reaction mixture was stirred at 50°C for 12 h. After poured into 0.5% of Na<sub>2</sub>CO<sub>3</sub> aqueous solution (1L). The collected precipitate was recrystallized from CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub> (1:10, v/v) to obtain the pure products. FT-IR (KBr, cm<sup>-1</sup>): v(NH), 3215; v(CH), 3012; v(CH), 2987; v(C=C), 1723; v(C=O), 1690; v(N-H), 1580; v(C=N), 1430; v(C-N), 1292. <sup>1</sup>H-NMR (500MHz, DMSO, ppm): δ 8.471~8.480 (d, J=4.5Hz, 4H), δ 7.974~7.979 (m, 4H), δ 7.321~7.330 (d, J=5.5Hz, 4H), δ 4.147~4.179 (t, 2H). 3.456~3.728  $J_1 = 8Hz, J_2 = 8Hz,$ δ (dd.  $J_1=14.5Hz, J_2=15Hz$  4H),  $\delta$  2.982~3.089 (m, 4H),  $\delta$ 2.771~2.782 (d, J=6Hz, 2H), δ 2.536~2.610 (brs, 2H), δ 1.766~1.940 (m, 4H), δ 1.350~1.361 (brs,4H), δ 1.194~1.233 (brs, 16H), δ 0.832~0.914 (m, 24H).

# Preparation of dodecamethylene-1,12-bis (N-(N-(phenylmethyl-L-valyl))-L-valine (DMBV)

Dodecamethylene-1,12-bis (N-(N-(phenylmethyl-L-valyl))-L-valine (DMBV) was synthesized in the similar way with the DMPV using benzaldehyde instead of pyridine-4-carboxaldehyde. FT-IR (KBr, cm<sup>-1</sup>): v(NH), 3282; v(CH), 3012; v(CH), 2987; v(C=C), 1723; v(C=O), 1690; v(N-H), 1580; v(C-N), 1292. <sup>1</sup>H-NMR (500MHz, DMSO, ppm):  $\delta$  7.917~8.048 (m, 4H),  $\delta$  7.201~7.324 (m, 10H),  $\delta$  4.174~4.207 (t, J<sub>1</sub>=7.5Hz, J<sub>2</sub>=9Hz, 2H),  $\delta$  3.432~3.690 (dd, J<sub>1</sub>=13Hz, J<sub>2</sub>=13Hz, 4H),  $\delta$  3.040~3.076 (m, 4H),  $\delta$  2.791~2.802 (d, J=5.5Hz, 2H),  $\delta$  2.307 (brs, 2H),  $\delta$  1.775~1.936 (m, 4H),  $\delta$  1.362~1.375 (brs, 4H),  $\delta$  1.191~1.209 (brs, 16H),  $\delta$  0.831~0.995 (m, 24H).

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**Keywords:** bis-dipeptide • L-valine • opaque to transparent transformations • aliphatic alcohols • Flory–Huggins parameters

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#### Supramolecular Chemistry

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Aliphatic alcohols induced opaque to transparent transformation and application of solubility theory in a bisdipeptide based supramolecular gel

Opaque to transparent transformation of the bis-dipeptide based supramolecular gel occurred when aliphatic alcohols were used as the component of  $\operatorname{organic/H_2O}$  binary mixed solvents for gelation. This would be potential for developing a sensor for prompt and facile selective recognitions. A re-assembly process with microstructure evolutions from agglomerates to nanofibers was observed during this gel-to-gel phase transition. Moreover, solubility theory of Flory–Huggins parameter was successfully used for the prediction of gelling performance of this gelator, it would improve the progress of system screening for practical applications.