Mutual Responsive Hydrazide-Based Low-Molecular-Mass Organic Gelators: Probing Gelation on the Molecular Level

Yong Yang, Ting Chen, Jun-Feng Xiang, Hui-Juan Yan, Chuan-Feng Chen,* and Li-Jun Wan*[a]

Organogels are a new class of soft materials, which are composed of a self-assembled suprastructure of low molecular-mass organic gelators (LMOGs) through specific interactions and a large volume of organic liquid immobilized therein.[1] Stimulated by their wide potential applications in nanomaterials and delivery or modification agents for paints, inks, cleaning agents, cosmetics, and drugs, great efforts have been paid to this kind of new materials during the past decade. Different types of LMOGs have been developed, including steroid,[2] amino acid,[3] anthryl derivatives,[4] urea and thiourea derivatives,[5] sugar compounds,[6] linear π-systems and chromophores.[7] However, most of these LMOGs were discovered largely serendipitously or via structural modification on the known gelators, and the relationship between the structures of LMOGs and the structural and rheological properties of their self-assembled fibrillar networks (SAFINs) is not well understood. Specially, stimuli sensitive or "smart" or "responsive" materials,[8] such as photoactive gelators[9] featuring azo and stilbene groups, pH-sensitive gelators,[9c, 10] and electroactive gelators[11] are very appealing for potential applications. In this paper, we report, to the best of our knowledge, for the first time two mutual "gel responsive" and solvent polarity sensitive hydrazide based LMOGs.[12] Their gel–solution phase transition can be achieved in a predictable fashion, which, we believe, will find wide applications in the design of functional materials.

During our ongoing project of hydrogen bonding mediated self-assembly,[13–15] we systematically modified the structures of hydrazide-based oligomers. When we tried to syn-

thesize diacetyl-terminated oligomer **1a** from N_1'-acetyl-4,6-bis(octyloxy)-benzene-1,3-dihydrazide and malonic acid using EDC·HCl as coupling agent in CH_2Cl_2 (Scheme 1), stirring at room temperature for several hours resulted in a viscous solution. With purified **1a** at hand, extensive heating also led to a solution in $CHCl_3$ at a concentration of about 2% (w/w) viscous enough to perform top-down experiment.

This viscous mixture demonstrated gravity-induced flow after a few minutes upon being inverted (Figure 1a). Addition of a small amount of methanol into the viscous mixture resulted in a clear solution. A precipitate then formed when more methanol was added. Similar results were also obtained with the dibutyryl-terminated oligomer **1b**. The only difference is that the concentration competent for top-down experiment dropped to as low as 1% (w/w). With isobutyloxy-derived oligomer **1c**, only a precipitate in chloroform was found. Atomic force microscope (AFM) images (Figure 1a) of xerogels of **1a** or **1b** showed needle-like nanofiber structures. Scanning electronic microscope (SEM) images also provided similar results.[16] We further investigated self-assembly of **1a** on HOPG (High Oriented Pyrolytic Graphite) by scanning tunneling microscope (STM) technology. As provided in Figure 1b, STM image revealed an offset dimeric structure for **1a**. We propose that in contrast to oligomers with complementary hydrogen boding sites,[15a] in addition to forming molecular duplex strands, abundant hydrogen bonding donor/acceptor sites that reside at the termini of each duplex may further interact intermolecularly to form a polymeric hydrogen bonding mediated supramolecular zipper structure (Scheme 1). Further entanglement of the polymeric zippers resulted in entrapment of solvent molecules. Van der Waals interactions among the interdigitated octyl side chains as found in the X-ray structure of diacetyl-terminated monomer[13a] may also play an important role in the formation of the viscous mixture. Because the main intermolecular interactions stabilizing the self-assembled networks are hydrogen bonding, addition of competitive solvents such as methanol can substantially affect the self-assembly process, and ultimately destroy the networks which

[a] Dr. Y. Yang, T. Chen, Dr. J.-F. Xiang, Dr. H.-J. Yan, Prof. C.-F. Chen, Prof. L.-J. Wan
Beijing National Laboratory for Molecular Sciences
Institute of Chemistry, Chinese Academy of Sciences
Beijing 100190 (China)
Fax: (+86) 10-62554449
E-mail: cchen@iccas.ac.cn

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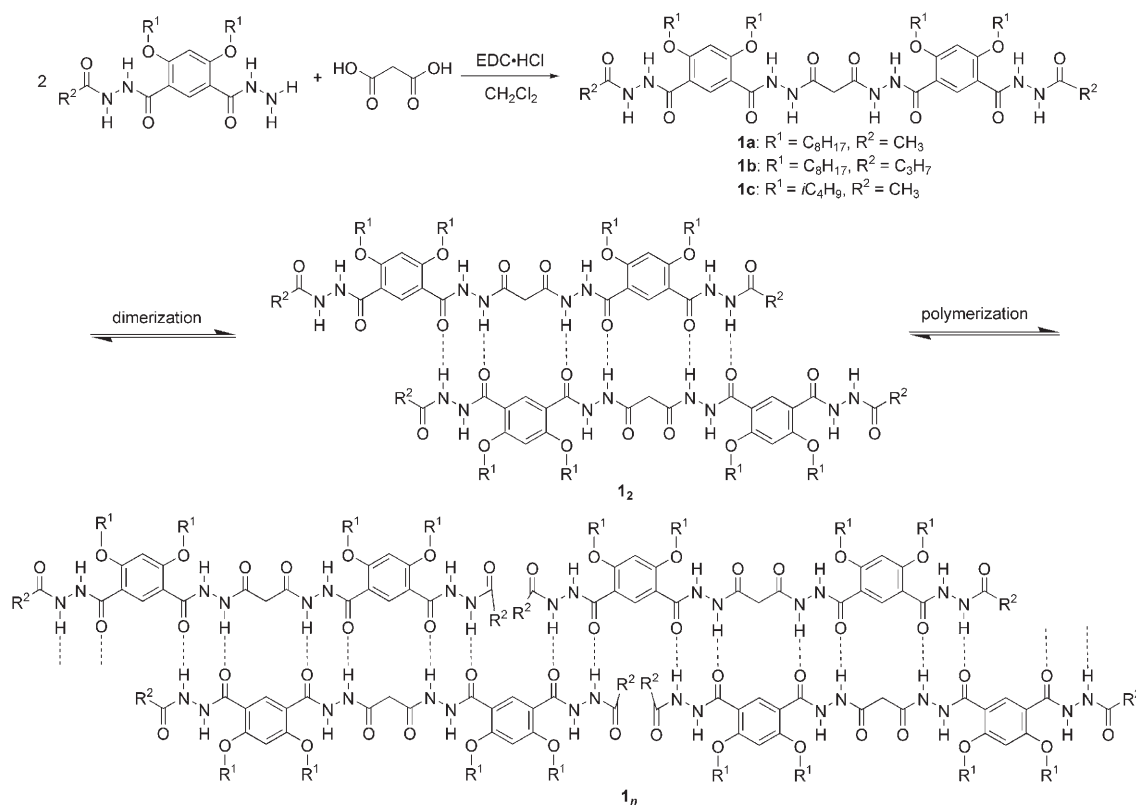
Scheme 1. Synthesis and representation of self-assembly of **1** in apolar solvent, with hydrogen bonding highlighted.

entrapped solvent molecules to form organogels. Compound **1a** in chloroform also displayed a concentration dependency in the ^{1}H NMR spectra. Because of the viscous mixtures, only a solution of **1a** in CDCl$_3$ as low concentration as 1 mM displayed a resolvable spectrum. Addition of 2% CD$_3$OD into a viscous solution of 5 mM of **1a** in CDCl$_3$ also rendered a resolvable spectrum. These findings also confirmed the above hypothesis.

Gelation was also observed with dinaphthyl terminated oligomer **2** (Scheme 2). As low concentration as 10 mM (ca.

0.8%, w/w) **2** in CHCl$_3$ could form a gel. Addition of a small amount of hydrogen bonding competitive solvents such as methanol also led to gel–sol transformation. AFM image (Figure 2a) on xerogel revealed entangled fibrous structure. The longest fibers reached micrometer scale. We propose that as in the case of **1**, abundant hydrogen bonding sites also led to a polymeric zipper structure as shown in Scheme 2. Gelation was not observed with other similar structures as diphenyl- or monophenyl-mononaphthyl terminated oligomers.[17] In addition to hydrogen bonding and van der Waals interactions, π–π stacking interactions between naphthalene rings as depicted in Scheme 2 may also play an important role in stabilizing the junction zone and further the gel formation. Interestingly, the STM image revealed a polymeric double helical structure for **2** on HOPG (Figure 2b).

As stated above, intermolecular hydrogen bonding interactions and/or π–π stacking interactions promoted aggregation along one dimension to form nanofiber structures, and further entanglement of these nanofibers into networks ach-
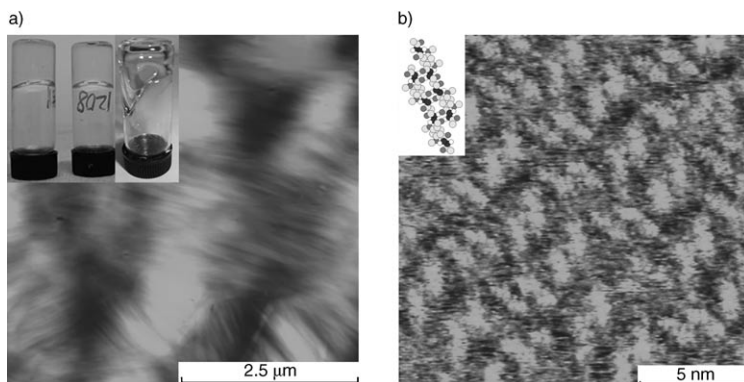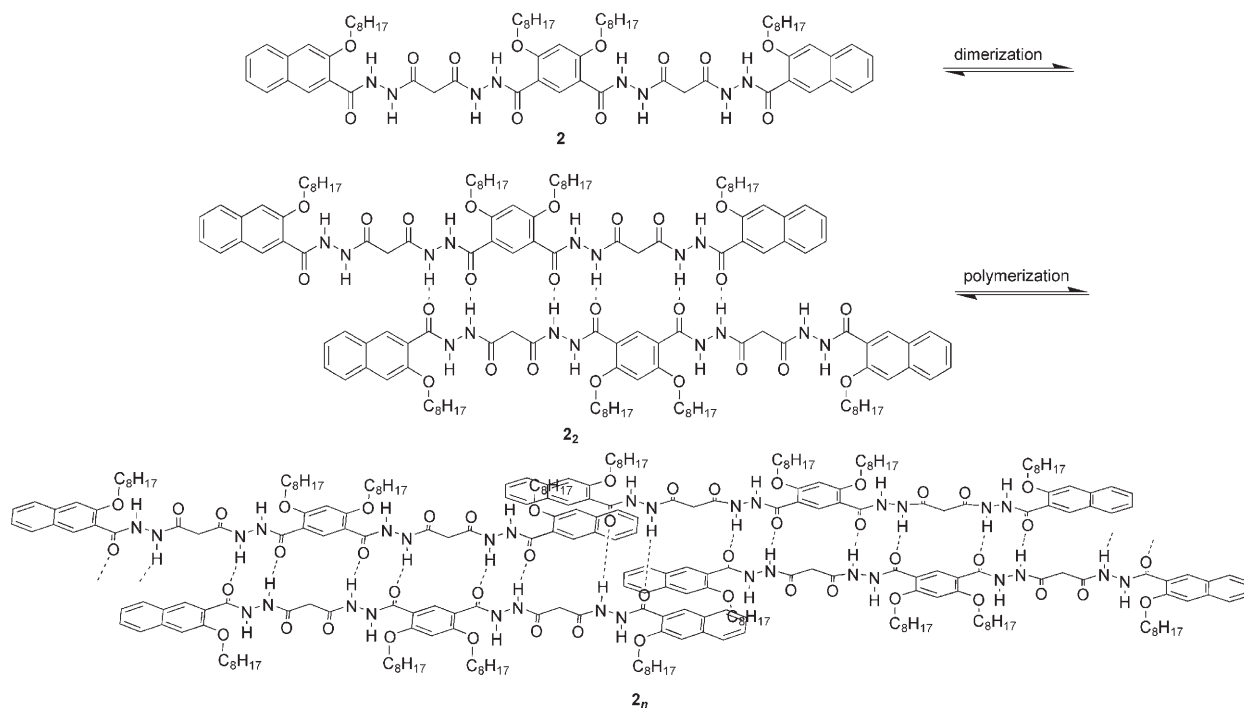

Figure 1. a) AFM image of **1a** on silica plate, showing the needle-like nanofiber structure, with digital photographs of (from left to right) gels of **1a** in CHCl$_3$, 2% (w/w); **1b** in CHCl$_3$, 1% (w/w); **1a** in CHCl$_3$, 2% (w/w) demonstrating gravity-induced flow inserted. Scan size = 5.00 um, Scan rate = 1.001 Hz, Data scale = 100 nm. b) STM image of **1a** on HOPG, showing the offset dimeric structure. The imaging conditions: E_{bias} = −500 mV, I_{tip} = 612.4 pA.

Scheme 2. Representation of self-assembly of **2** in apolar solvent, with hydrogen bonding and π–π stacking interactions highlighted.
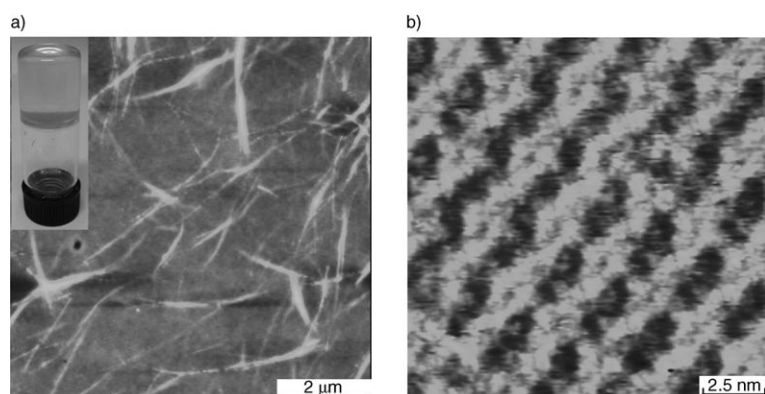

Figure 2. a) AFM image of **2** on silica plate, showing the entangled fibrillar networks structure, with digital photograph of gel from **2** in CHCl₃, 0.8% (w/w) inserted. Scan size = 8.00 um, Scan rate = 0.5003 Hz, Data scale = 20 nm. b) STM image of **2** on HOPG, showing the polymeric double helical structure. The imaging conditions: E_{bias} = 793.9 mV, I_{tip} = 570.6 pA.

ieved entrapment of apolar solvents. Examination of the chemical structures of **1** and **2** revealed that the hydrogen-bonding sites in **1** and **2** were complementary. We wonder if there exists a multipoint recognition directed supramolecular substitution reaction to form a discrete heterodimer via eight hydrogen bonds as depicted in Scheme 3, which blocks abundant hydrogen-bonding sites, renders polymeric zipper structures impossible and thus leads to mutual responsive organogels? Our hypothesis was first evidenced by 1:1 mixture of **1** and **2** in CDCl₃. A clear solution appeared (Scheme 3) and ¹H NMR experiment revealed a well resolved spectrum (Figure 3). However, **1** alone in CDCl₃ at 10 mM can not give a resolvable spectrum due to the viscous

solution. Signals for **2**-Hᵃ and **2**-Hᵉ displayed up-field shifts. This may result from their specific positions: they were at the frontier of complexation. Contacts between **1**-Hᶠ and **2**-Hᵉ, g zone and h zone were observed in the 2D NOESY spectrum (Figure 4), which provided a diagnostic evidence for the heterodimer structure. Variable temperature ¹H NMR experiments revealed unique dynamic behavior for complex **1·2**: multiple minor signals for NHs appeared in the area between δ 8 and 9 ppm and there displayed a complicated picture in the area between δ 10.5 and 12.5 ppm at low temperatures (Figure 3). A contact between **1**-Hᶠ and h zone was also observed in 2D NOESY spectrum. These findings might suggest intermolecular slide perpendicular to hydrogen bonds between the two constituent molecules of the heterodimer.

In conclusion, we reported in this paper two mutual responsive hydrazide based oligomers **1** and **2** as LMOGs. In addition to forming hydrogen bonded molecular duplex strands, abundant hydrogen-bonding sites and/or π–π stacking interactions further promoted aggregation along one-dimension to form fibrous structures. Because the main non-covalent forces stabilizing the self-assembled networks are hydrogen bonding, the gels are solvent polarity sensitive.
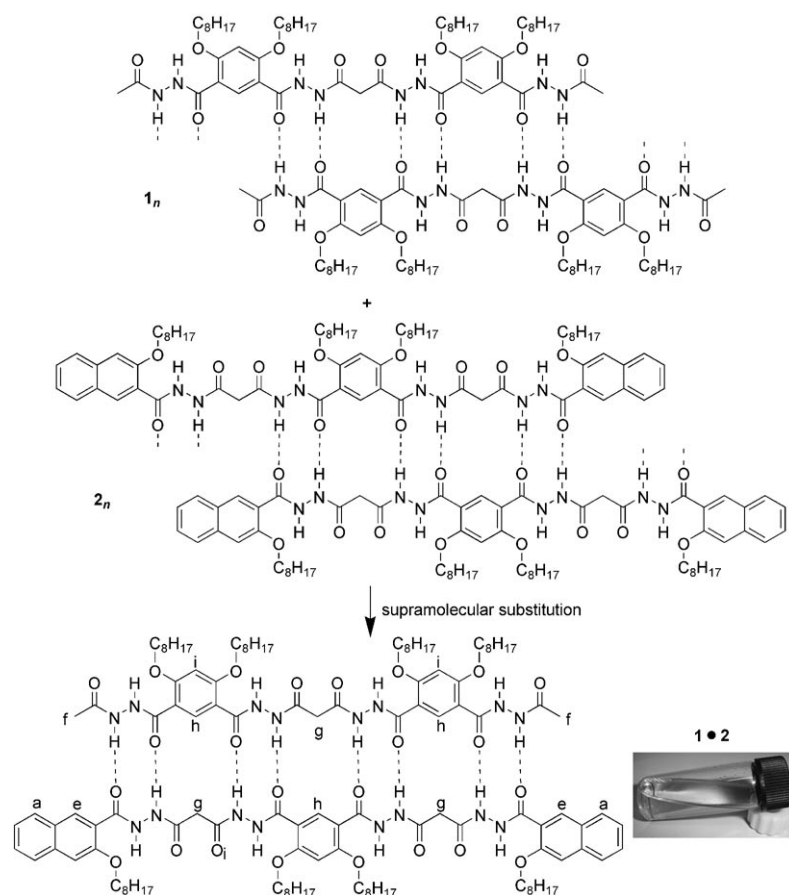
Scheme 3. Representation of supramolecular substitution reaction between **1** and **2**, which leads to gel–solution phase transition, with a photograph of a solution of **1** and **2** 1:1 in CHCl₃, each 2 % (*w/w*) inserted and proton-labeling Scheme indicated.

For a 1:1 ratio of **1** and **2** in apolar solvents, gelation was no longer observed, which could be explained on the basis of the chemical structures that the hydrogen-bonding sites in **1**

and **2** are complementary and a multipoint recognition directed supramolecular substitution reaction leads to gel–sol phase transition. Thus the gel–sol transition can be controlled in a predictable fashion. We believe the new gel systems we presented here will find wide applications in the future.

Experimental Section

Gel preparation: Gelators **1** or **2** in a sealed tube were heated extensively in methanol free chloroform (typically 2 mL) until all solids dissolved. Upon cooling at room temperature, gels were obtained.

STM measurement: A Nanoscope IIIa SPM (Digital Instruments, Santa Barbara, CA) was employed to carry out the STM experiments using a standard constant-current mode under ambient condition. The samples for the STM measurements were prepared by placing a drop of octylbenzene solution containing 1 mM corresponding compounds on a freshly cleaved atomically
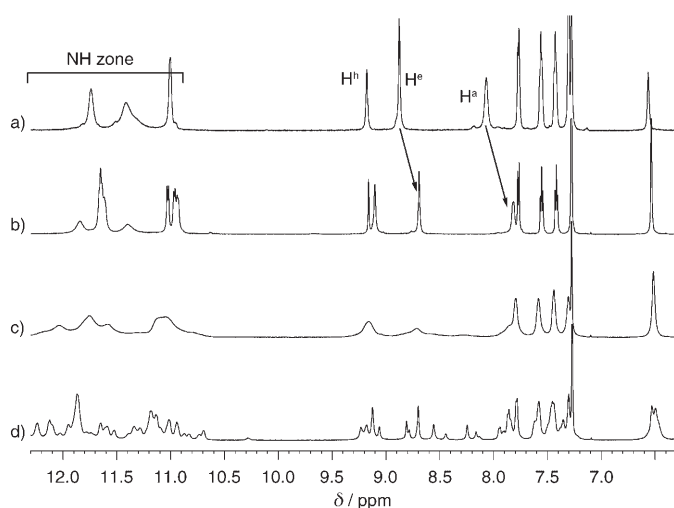

Figure 3. Stacked partial ¹H NMR spectra of a) **2** in CDCl₃ at 298 K (10 mM, gel state); **1** and **2** 1:1 in CDCl₃ at b) 298 K, c) 253 K, d) 223 K, each 10 mM, 600 MHz.
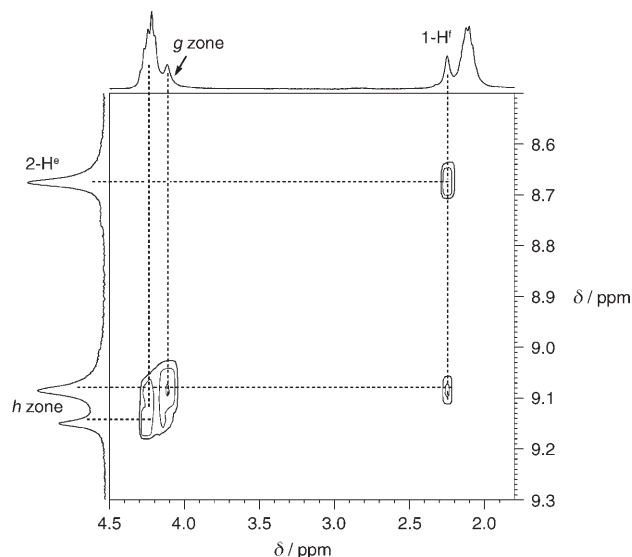

Figure 4. Partial 2D NOESY spectrum of **1** and **2** 1:1 in CDCl₃, with contacts between *g* zone and *h* zone, **1**-Hᶠ and **2**-Hᵉ, **1**-Hᶠ and *h* zone shown, each 10 mM, 300 MHz, 298 K.

flat surface of HOPG (ZYB quality). STM tips were mechanically cut Pt/Ir wire 90:10. All STM images are presented in the paper without further processing. The tunneling conditions used are given in the corresponding Figure captions.

AFM measurement: AFM measurements were carried out with a NanoScope IIIa Extended Multimode AFM (Digital Instruments, SantaBarbara, CA) and a "J" scanner. All images were obtained with Tapping mode AFM in air. Commercially available etched Si cantilevers (resonance frequency: ~300 KHz, Digital Instruments) were employed. A little drop of the viscous solution of **1a** or a little block of the gel from **2** was placed on the Si cantilever and the sample was dried under cooling condition. After all solvents were evaporated, the samples were subjected to measurement.

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[16] See Supporting Information for more details.

[17] Unpublished results.