Amidourea-based homoduplex as a super organogelator

CHU WeiJun^{1,2} & CHEN ChuanFeng^{1*}

¹ Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China;

² Graduate University of Chinese Academy of Sciences, Beijing 100049, China

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The amidourea-based homoduplex was developed as a super organogelator, which could form stable gels in wide-tested solvents. And the reversible gel to solution transition was responsive to heat/cool and acid/base stimuli. The organogels were extensively investigated by ¹H NMR, UV-visible absorption spectroscopy, fluorescence spectroscopy, scanning electron microscopy, transmission electron microscopy and powder X-ray diffraction. Based on these data, the gelation mechanism was rationally proposed. The hydrogen-bonded homoduplexes served as the basic assembling units, and further aggregated into three dimensional networks via π - π stacking and van der Waals interactions, which consequently led to the entangled fibers for the gel formation.

amidourea, homoduplex, organogelator, gelation mechanism

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Gels are well-known soft materials with daily applications, such as hair gel, contact lenses, gelatin desserts, lithium grease and so on. Among them, one of the most emerging categories is organogels, which are composed of a self-assembled supramolecular structure of low-molecular-mass organic gelators (LMOGs) and a large volume of organic liquids immobilized therein [1–3]. Over the past decade, dramatically increased attention has been focused on the organogels [4], due to their widespread potential applications in sensors [5], photonics [6], electronic devices, regenerative medicine [7], catalysis [8], cosmetics and many other fields [2–4]. A number of compounds with diverse structures have been developed as LMOGs, including steroids [9,10], triterpenoids [11,12], amino acids [13–15], hydrazide [16–20], urea derivatives [21–23], and π -systems and chromophores [24–27]. In particular, many LMOGs have been developed as smart gel systems that are responsive to stimuli, such as ions [28,29], molecules [30,31], pH [32,33], redox [34,35], light [36,37], electric field [38], and ultrasound [39,40].

Generally, organogels are formed by LMOGs self-

assembling into reticular three-dimensional networks with solvent molecules entrapped inside through non-covalent interactions. However, the gelation mechanism on the molecular level is elusive, and a rational correlation of molecular structure and gelation ability in a given solvent still remains a challenge. The development of new LMOG with a well-understood gelation mechanism will provide valuable insights into the gelation process, and thus may promote the rational design of organogelators. Recently, hydrogen-bonded molecular duplexes based on the hydrazide [18] and amide [41] units are reported as LMOGs, but both of them gelate only in several apolar solvents.

As a continuation of our previous work on the amidourea-based hydrogen-bonded molecular duplexes [42], we herein report the amidourea-based homoduplex (Figure 1) as a super LMOG, which form stable gels in wide-tested solvents. And the reversible gel to solution transition is responsive to heat/cool and acid/base stimuli. Moreover, we investigated the organogels of **1** via ¹H NMR, UV-visible absorption spectroscopy, fluorescence spectroscopy, scanning electron microscopy (SEM), transmission electron microscopy (TEM) and powder X-ray diffraction (PXRD), and attempted to explore the gelation mechanism.

*Corresponding author (email: cchen@iccas.ac.cn)

Figure 1 Amidourea-based homoduplex **1·1** with proton-labeling.

1 Experimental

1.1 General methods

^1H NMR spectra were recorded on Bruker DMX 300 Spectrometer. UV-visible absorption spectra were measured on a UV 2041PC Shimadzu photometer. Fluorescence spectra were measured on a Hitachi F-4500 spectrometer. The morphologies of the xerogels were characterized by SEM. TEM was performed on a JEOL JEM-2011 microscope. XRD data were collected on a Rigaku D/MAX-2500 X-ray diffractometer at a scanning rate of $2^\circ/\text{min}$ in the 2θ range of 2° – 60° with Cu $K\alpha$ radiation ($\lambda = 1.54056 \text{ \AA}$). Gel in CH_2Cl_2 was coated on a glass plate and the solvent was free-dried. Then the glass plate with xerogel was fixed on a sample holder and subjected to XRD analysis at room temperature.

1.2 Gel formation

In a typical gelation experiment, a weighed amount of gelator **1** and 1.00 mL solvent were placed in a sealed glass vial, and then heated until the gelator was completely dissolved. The solution was then left for 0.5 h under ambient conditions, and the gel formation was verified by the “stable to inversion of the test tube” method [11].

2 Results and discussion

The gelation ability of **1** was examined in various organic solvents by the “stable to inversion of the test tube” method, and the results were summarized in Table 1. It was shown that organogelator **1** could form stable gels in wide-tested solvents, and the gels could remain without any change for more than three months under ambient conditions. We also found that gelator **1** formed transparent gels in aromatic solvents, while opaque gels in chloroalkanes, alcohols and cyclic ethers. Then we carefully determined the minimum gelation concentration (MGC) of **1** in the tested gelation solvents, which revealed that LMOG **1** possessed very strong gelation ability. Except 1,2-dichloroethane and chloroform, organogels of **1** in all the other gelation solvents could be obtained at impressively low concentrations

(0.19 wt%–0.67 wt%). Such an ability to gelate solvents at concentrations lower than 1 wt% is classified as super-gelation [2].

The reversible gel to solution phase transition responsive to heat/cool was the intrinsic property of supramolecular gels that occurred by dis-assembly and self-assembly processes, respectively. The thermo-reversibility of organogels of **1** was confirmed by repeated heating and cooling for several cycles (Figure 2). Furthermore, we studied the acid/base responsive property of the organogel of **1**. Interestingly, we found that the gel of **1** in CH_2Cl_2 converted into fluid solution immediately upon the addition of 10 equiv of trifluoroacetic acid (TFA), and the solution could regenerate gel upon the addition of 12 equiv of triethylamine (TEA) after several minutes at room temperature (Figure 2). And the acid/base responsive process of the organogel could be repeated for at least five cycles. Then we investigated the acid/base responsive process by ^1H NMR (Figure 3). When adding 10 equiv of TFA into the solution of **1** in CDCl_3 (5.0 mmol/L), all the NH proton signals significantly shifted upfield and broadened, and some NH proton signals even disappeared, which indicated that TFA broke the hydrogen bonds in **1** and might thus lead to the disruption of the gel. After adding 12 equiv of TEA, all the NH proton signals returned to their original positions, which suggested that the hydrogen bonds formed again, and the gel could thus be regenerated. These observations indicated that hydrogen bonding was the main driving force in the gel formation of **1**.

In our previous work [42], we have demonstrated that compound **1** existed as homoduplex **1·1** through eight intermolecular tricenter hydrogen bonds in low polar solvents (Figure 1). The dimerization constant of homoduplex **1·1** still reached up to $4.4 \times 10^4 \text{ L/mol}$ in 1% $\text{DMSO-}d_6/\text{CDCl}_3$

Table 1 Results of gelation tests for **1** in various organic solvents ^{a)}

Solvent	State	MGC (mmol/L)	MGC (wt%)
Benzene	TG	4.4	0.35
Toluene	TG	4.1	0.33
Xylene	TG	4.2	0.34
Chlorobenzene	TG	4.0	0.25
1,2-Dichlorobenzene	TG	5.5	0.29
CH_2Cl_2	OG	7.7	0.40
CHCl_3	OG	29.1	1.37
1,2-Dichloroethane	OG	19.6	1.10
Methanol	OG	3.9	0.34
Ethanol	OG	3.6	0.32
2-Propanol	OG	2.1	0.19
1,4-Dioxane	OG	2.8	0.19
THF	OG	8.6	0.67
Diethyl ether	I		
Hexane	I		
EtOAc	P		
DMF	S		
DMSO	S		

^{a)} TG: transparent gel; OG: opaque gel; S: soluble; I: insoluble; P: precipitate.

Figure 2 The reversible gel to solution transition of **1** in CH_2Cl_2 responsive to heat/cool and TFA/TEA.

(v/v). Thus, it was reasonable to propose that the hydrogen-bonded homoduplexes should serve as the basic units for assembling into supramolecular networks. Compared with individual strands, the duplex structure was significantly rigidified, leading to a well-defined and largely planar surface that should facilitate the further intermolecular aggregation via π - π stacking interactions and the consequent gel formation. The aggregation of **1** in the gel was first evidenced by variable-temperature ^1H NMR study of **1** in benzene- d_6 (Figure 4). Compared with the well-resolved ^1H NMR of **1** in CDCl_3 (Figure 3), the ^1H NMR of **1** (5.0 mmol/L) in benzene- d_6 at 298 K showed almost no peaks because of the gelation. With the temperature increasing, the spectrum became gradually resolved. Above 323 K, the signals of aromatic and NH protons began to appear, and their intensities increased with the aggregation being weakened via further elevating the temperature. Eventually, a totally well-resolved ^1H NMR of **1** in benzene- d_6 was observed above 343 K. These results demonstrated the strong intermolecular aggregation of **1** in the gel state.

The self-assembly of **1** in the gel was then studied by UV-visible absorption spectroscopy and fluorescence spec-

troscopy. Compared with the corresponding dilute solution of **1** in CH_2Cl_2 (10^{-5} mol/L), the gel of **1** showed a much broadened and red-shifted UV-vis absorption spectrum, which suggested that π - π stacking interaction played an important role in the gel. In the fluorescence spectra, the solution of **1** in CH_2Cl_2 (10^{-4} mol/L) exhibited relatively weak fluorescence emission (Figure 5). In contrast, the fluorescence emission intensity of **1** in the gel state was largely enhanced, which referred to the aggregation-induced emission (AIE) enhancement [43]. Meanwhile, the fluorescence maximum emission was red shifted by about 10 nm in the gel of **1**. Combining with the UV-visible absorption spectra, it could be deduced that **1** formed J-aggregate in the gel, which was also a reason responsible for the fluorescence emission enhancement in the gel state relative to the solution of **1**. Another reason may be that the formation of homoduplex via strong intermolecular hydrogen-bonding restricted the bond rotation of **1**, and increased the rigidity and coplanarity of the backbones, and thus prohibited the non-radiative transitions to some extent. The AIE property may render the gel of **1** potentially applicable in the design of solid-state chemosensors.

To gain visual insight into the microscopic morphology of the organogels formed by **1**, SEM and TEM were utilized to investigate the assembly structures (Figure 6). The SEM images of the free-dried gels formed by **1** in benzene and in methanol both showed thread-like fibrous structures with widths of tens of nanometers and lengths of up to tens of micrometers. These fibers further interlaced and self-assembled into three-dimensional networks, which could entrap solvent molecules in their interstices. The TEM images of the free-dried gels formed by **1** in benzene and in methanol also revealed the nano-fibrous structures. Moreover, the SEM and TEM images of the gels in other solvents including CH_2Cl_2 , THF, toluene and ethanol, all revealed the similar morphologies, which indicated that the self-assembly of LMOG **1** in the gels was independent on the gelation solvents.

The xerogel formed by **1** in CH_2Cl_2 was then studied by PXRD (Figure 7), which provided further insight into the self-assembly of the gelators. The diffraction pattern showed

Figure 3 Partial ^1H NMR spectra of LMOG **1** in CDCl_3 (300 MHz, 298 K). (a) **1** (5.0 mmol/L); (b) after adding 10 equiv of TFA; (c) after adding 12 equiv of TEA.

Figure 4 Variable-temperature ^1H NMR spectra of LMOG **1** in benzene- d_6 (5.0 mmol/L).

Figure 5 Fluorescence spectra ($\lambda_{\text{ex}} = 343 \text{ nm}$) of gel **1** and solution **1** (10^{-4} mol/L) in CH_2Cl_2 .

two sharp strong diffractions at 22.0 and 15.8 Å in the small angle region, which fully corresponded to the length (23.6 Å) and width (16.7 Å) of the hydrogen-bonded homoduplex **1·1** obtained by the density functional theory (DFT) calculation. These data confirmed that the hydrogen-bonded duplexes were indeed the basic units for assembling into supramolecular networks. The diffractogram also revealed a sharp strong diffraction at 14.0 Å, suggesting a well-defined layer structure [44]. And a d -spacing of 3.85 Å consistent with the π - π stacking distance was shown, which supported that π - π stacking interaction was another driving force in the gel formation of **1**. In addition, the PXRD analyses of the xerogels of **1** from benzene or methanol afforded the

same information.

Based on the above experiment results, we rationally proposed the gelation mechanism of LMOG **1**. First, the eight intermolecular tricenter hydrogen-bonding interactions ensured that gelator **1** paired into the sequence-specific homoduplex. With their largely planar surfaces, the duplexes then aggregated into two dimensional lamellar structures via π - π stacking interactions. The long alkyl chains of **1** further promoted the 2D layers to assemble into three dimensional networks through van der Waals interactions. Consequently, the entangled fibers were formed and entrapped the solvent molecules in their interstices, and thereby led to the formation of organogels.

3 Conclusions

We found that the amidourea-based homoduplex as a super LMOG could form stable gels in wide-tested solvents. And the reversible gel to solution transition was responsive to heat/cool and acid/base stimuli. The organogels of **1** were extensively investigated by ^1H NMR, UV-visible absorption spectroscopy, fluorescence spectroscopy, SEM, TEM and PXRD. Based on these data, we rationally proposed the gelation mechanism of LMOG **1**. The hydrogen-bonded homoduplexes served as the basic assembling units, and further aggregated into three dimensional networks via π - π stacking and van der Waals interactions, which consequently led to the entangled fibers for the gel formation. The results

Figure 6 SEM images of the free-dried gel formed by **1** in benzene (a), in methanol (b). TEM images of the free-dried gel formed by **1** in benzene (c), in methanol (d).

Figure 7 XRD pattern of the xerogel formed by **1** in CH_2Cl_2 .

presented here may provide valuable insights into the gelation process, and promote the rational design of new organogelators.

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