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A new gelator based on tetraphenylethylene and diphenylalanine: Gel formation and reversible fluorescence tuning

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A new gelator **1** based on tetraphenylethylene (TPE) and diphenylalanine was designed and synthesized. Compound **1** was non-emissive in solution, but its fluorescence turned on after the formation of gels, due to the aggregation-induced emission (AIE) feature of TPE. Interestingly, the fluorescence was reversibly switched "on-off" upon the "gel-sol" transition. Scanning electron microscope (SEM), confocal laser scanning microscope (CLSM) and X-ray diffraction (XRD) were employed to study the gels.

tetraphenylethylene, diphenylalanine, gel, aggregation-induced emission (AIE)

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It is known that low-molecular-weight gelators (LMWGs) are able to immobilize certain solvents at low concentrations (less than 5% in weight percentage), due to weak intermolecular interactions, such as hydrogen bonding, van der waals force, π–π stacking and hydrophobic effect, etc. These gelator molecules can self-assemble into three-dimensional (3D) networks leading to gel formation [1,2]. A number of organic compounds have been investigated for the development of gelators, including cholesterol derivatives [3–5], amides and urea derivatives [6–9], nucleotides [10], saccharides [11–13], amino acids and peptides [14–22], oligo(para-phenylene vinylene) derivatives [23–25] and dendrimers [26–29]. Gelators can be categorized into organogelators and hydrogelators.

Currently, more efforts have been paid to fabricate multi-responsive or multi-functional smart gels. However, there are only a few reports about tuning the fluorescence upon gel-solution (gel-sol) transition [9,23,29–32]. In this report, we describe a new gelator **1** based on tetraphenylethylene (TPE) and diphenylalanine, in which TPE is well-known for the aggregation-induced emission (AIE) feature [33–35] and diphenylalanine is extensively utilized to develop hydrogelators [14–16]. The results reveal that **1** can gelate several solvent systems and the fluorescence can be reversibly tuned upon gel-sol transition.

1 Experimental

1.1 Materials and characterization techniques

4-Methoxybenzophenone **2** was purchased from Alfa Aesar and diphenylalanine **6** was purchased from GL Biochem (Shanghai) Ltd, and they were used as received. Compounds **3** and **4** were prepared according to reported procedures [29].

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 400 MHz. High-resolution mass spectra (HRMS) were obtained with Bruker Apex II FT-ICRMS. Fluorescence spectra were measured with a Hitachi F-4500 spectrometer. Scanning electron microscope (SEM) images were studied on a Hitachi S-4800 microscope. Confocal laser scanning microscope (CLSM) imaging experiments were performed with an Olympus FV-1000 laser scanning microscopy system. X-ray diffraction (XRD) data were

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collected with Rigaku D/max 2500.

1.2 Synthesis

The synthesis started from 4-methoxybenzophenone **2** and this was self-coupled into compound **3**, which was demethylated to get compound **4**. Reaction of compound **4** with bromoacetate and subsequent hydrolysis led to compound **5**. In the presence of NHS and DCC, compound **5** was activated and further reacted with diphenylalanine **6** to afford compound **1** (Figure 1).

Synthesis of **5**: To a flask were added compound **4** (410 mg, 1.08 mmol), ethyl bromoacetate (0.6 mL, 5.4 mmol), K_2CO_3 (1.5 g, 10.9 mmol) and anhydrous CH_3CN (25 mL) under nitrogen atmosphere. The mixture was heated to reflux and stirred for 8 h. After the reaction was complete, water (20 mL) and CH_2Cl_2 (20 mL) were added. The organic layer was extracted and washed successively with brine and water, and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure. The yellowish residue was dissolved in a mixture of CH_3OH (6.4 mL) and H_2O (0.8 mL), and KOH (300 mg, 5.4 mmol) was further added. The mixture was heated to reflux and stirred for 4 h. After being cooled to room temperature, the solvent was evaporated under reduced pressure. Water (20 mL) and 3 mol/L HCl (aq) were added by droplets until the residue was completely dissolved (pH 1.0). The mixture was taken up in CH_2Cl_2 and the organic layer was washed successively with brine and water, and dried over anhydrous $MgSO_4$. After filtration and evaporation, the residue was subjected to column chromatography with CH_2Cl_2 / CH_3OH (v/v, 200/1) as eluant. Compound **5** was obtained as a yellowish powder (340 mg) in 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–6.85 (14H, m), 6.75–6.55 (4H, m), 4.62 (2H, s), 3.74 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 158.2, 155.8, 144.1, 140.4, 139.4, 136.3, 132.8, 132.6, 131.5, 127.8, 127.7, 126.4, 114.0, 113.9, 133.3, 133.2, 64.9, 55.2; HR-MS (SIMS, negative mode): calcd. for $C_{29}H_{23}O_4$ [M – H$^+$] (*m*/*z*): 435.1596; found: 435.1604.

Synthesis of **1**: A suspension of compound **5** (227 mg, 0.52 mmol), NHS (60 mg, 0.52 mmol) and DCC (113 mg, 0.55 mmol) in CH_2Cl_2 (10.0 mL) were stirred for 2 h. After filtration and evaporation under reduced pressure, the yellowish residue was dissolved into acetone (5.0 mL). Such solution was introduced into an aqueous solution of diphenylalanine **6** (63 mg, 0.52 mmol) and $NaHCO_3$ (88 mg, 1.05 mmol). The mixture was stirred overnight. After the reaction was complete, 3 mol/L HCl (aq) was added by droplets until pH reached 3.0. Then, CH_2Cl_2 (20 mL) was added and the organic layer was washed successively with brine and water, and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography with CH_2Cl_2/CH_3OH (v/v, 100/1) as eluant. Compound **1** was obtained as a yellowish powder (210 mg) in 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.20 (3H, m), 7.18–7.07 (10H, m), 7.06–6.97 (7H, m), 6.96–6.86 (3H, m), 6.70–6.60 (2H, m), 6.60–6.50 (2H, m), 6.43–6.37 (1H, m), 4.80–4.68 (2H, m), 4.35–4.25 (2H, m), 3.75–3.65 (3H, m), 3.16–3.06 (2H, m), 3.05–2.96 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 170.3, 168.9, 158.2, 155.3, 132.9, 132.6, 131.5, 129.5, 129.4, 128.9, 128.6, 127.9, 127.8, 127.7, 127.3, 126.5, 114.1, 114.0, 113.3, 113.2, 66.9, 55.2, 53.7, 53.4, 37.7, 37.5; HR-MS (SIMS, negative mode): calcd. for $C_{47}H_{41}N_2O_6$ [M – H$^+$] (*m*/*z*): 729.2965; found: 729.2976.

2 Results and discussion

2.1 Gelation test

At first the gelation ability of gelator **1** was studied.

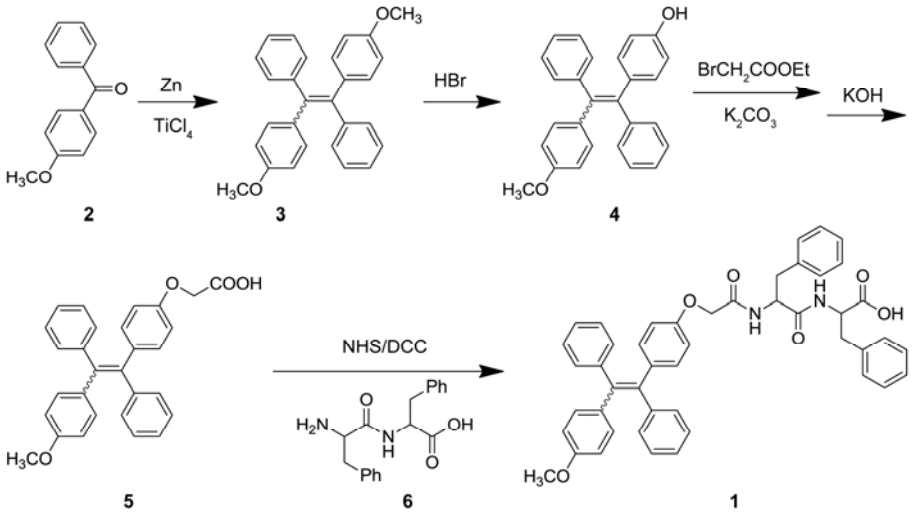

Figure 1 Chemical structure of **1** and the synthetic approach.

Generally, a weighed amount of the gelator and 1.0 mL of the solvent were placed in a vial, which was sealed and then heated until the gelator was completely dissolved. The solution was allowed to cool down and rest for a while. If the mixture was immobilized when the vial was inverted, then the gel was generated. According to previous reports [14–16], diphenylalanine is a good gelating moiety. However, **1** was hardly soluble in aqueous solution, even after tuning pH upon addition of NaOH (aq) or HCl (aq). Hence the mixture solution of water and organic solvent was used instead. The organic solvents which can be miscible with water, such as C_2H_5OH, CH_3OH, CH_3COCH_3, THF and CH_3CN, were used for the gelation experiments.

The results of gelation studies are listed in Table 1. Clearly, **1** could gel the first three mixture solvents, namely, H_2O/C_2H_5OH, H_2O/CH_3OH or H_2O/CH_3COCH_3. With H_2O/C_2H_5OH (1/1, v/v) as an example, to a vial was added a suspension of **1** at the concentration of 6.0 mg/mL; then, 0.5 mol/L NaOH (aq) was added until the mixture turned into a clear homogeneous solution (pH 12), followed by the addition of 1.0 mol/L HCl (aq) until slight precipitation appeared (pH 7.5). After that, the solution was heated to a clear solution and rested for about half an hour, a transparent gel was generated. After varying the concentration of **1** and pH of the solution, the critical gelation concentration (CGC) was measured to be 4.0 mg/mL, and critical pH was 7.5. Figure 2 depicts the photos of the solution and gel of **1** under daylight and UV light irradiation, respectively.

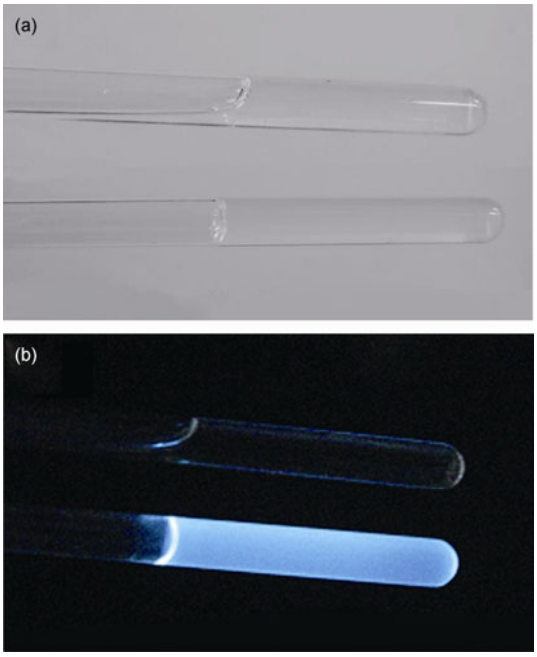

Figure 2 (Color online) (a) Photo of the solution and gel of **1** under daylight. (b) Photo of the solution and gel of **1** under UV light irradiation (λ_{ex} = 365 nm).

2.2 Characterization of the gel

After the gel was generated, it was lyophilized to obtain its xerogel as a yellowish fluffy powder. As displayed in Figure 3(a) and (b), the scanning electron microscope (SEM) micrograph showed that the xerogel was composed of tiny plates with the size of scores of square micrometers, and these tiny plates were entangled into three-dimensional networks. Meanwhile, confocal laser scanning microscope (CLSM) image indicated the xerogel was strongly emissive under UV light irradiation, as shown in Figure 3(c).

The X-ray diffraction (XRD) pattern of the xerogel formed with **1** was examined (Figure 4). A broad diffraction signal was detected with the peak at 1.92°. The corresponding *d*-spacing was 4.61 nm. The molecular length of **1** was 2.36 nm approximately, hence *d*-spacing may relate to the twofold of molecular length. There were a hydrophobic TPE unit and a hydrophilic diphenylalanine moiety in **1**. Therefore, the TPE units of neighboring molecules may be aggregated in the interior, for the hydrophobic interactions and π–π stacking; the diphenylalanine moieties may be assembled in the periphery via the intermolecular hydrogen bonding. In this way, molecules of **1** are assembled into interconnected networks leading to gelation as schematically

Table 1 Gelation studies of gelator **1** in different mixture solvents [a)]

Solvents	Results
H_2O/C_2H_5OH (1/1, v/v)	G
H_2O/CH_3OH (1/1, v/v)	G
H_2O/CH_3COCH_3 (1/1, v/v)	G
H_2O/THF (1/1, v/v)	S
H_2O/CH_3CN (1/1, v/v)	S

a) G, Gelation; S, Solution.

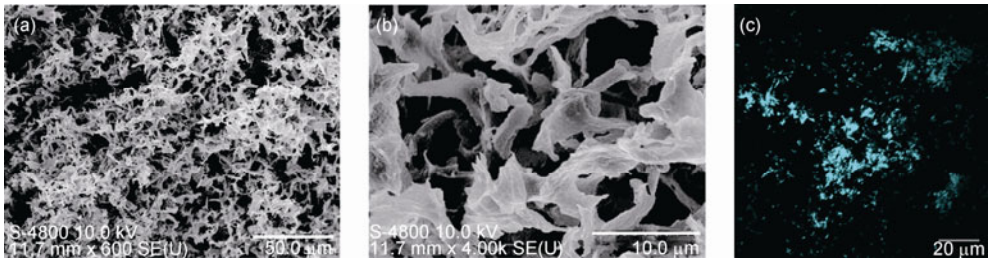

Figure 3 (Color online) (a) SEM image of the xerogel of **1**; the scale bar is 50 μm. (b) The magnified image of (a), the scale bar is 10 μm. (c) CLSM image of the xerogel of **1** (λ_{ex} = 375 nm); the scale bar is 20 μm.

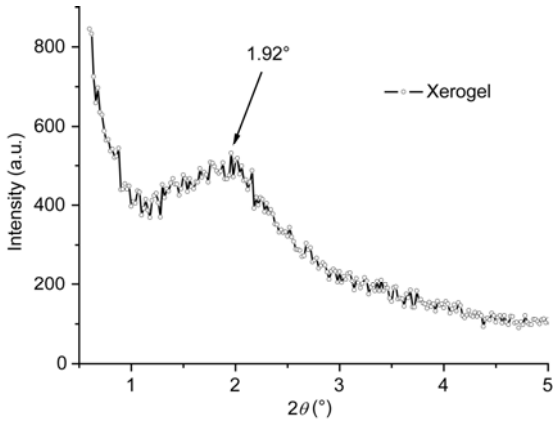

Figure 4 XRD pattern of the xerogel of **1**.

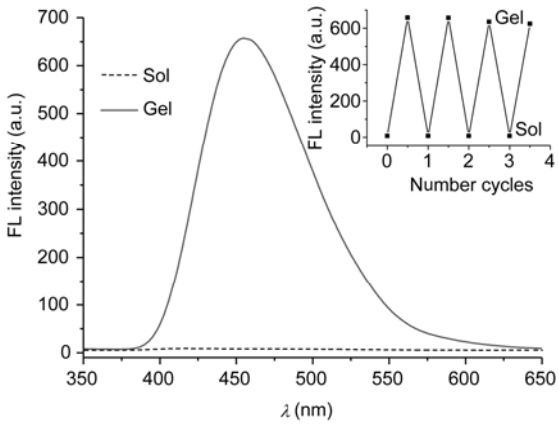

Figure 6 The fluorescence spectra of **1** (6.0 mg/mL, pH 7.5) in the solution state and gel state, respectively; inset shows the reversible variation of the emission intensity at 455 nm upon the sol-gel transition (λ_{ex} = 340 nm).

illustrated in Figure 5.

2.3 Fluorescence tuning

We studied the fluorescent properties of **1** in the solution and gel states, respectively. As revealed in Figure 2 (b), under UV light irradiation, the solution was almost non-fluorescent, but it emitted bright blue fluorescence after the gel formation. Figure 6 shows the fluorescence spectra of **1** in both solution and gel states. Apparently, there was no obvious fluorescence for the solution, while intensive fluorescence emerged upon the gel formation. For instance, the fluorescence intensity at 455 nm increased by nearly 80 times after gelation. This is in accordance with the CLSM image of xerogel as shown in Figure 3(c). Such fluorescence enhancement should be attributed to the TPE unit in **1**. It is known that TPE molecules are weakly fluorescent in solutions because of the internal rotations, but they become strongly emissive after aggregation [33–35]. Therefore, the fluorescence enhancement observed for **1** after gelation should be ascribed to the intermolecular interactions which lead to gelation and simultaneously restrict the internal rotations within TPE moiety.

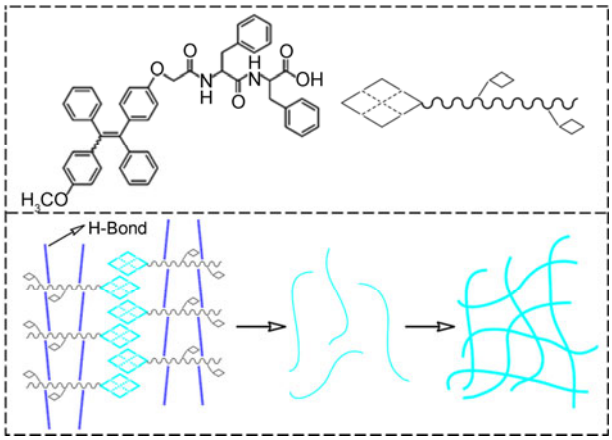

Figure 5 (Color online) The schematic illustration of the gelation with **1**.

Interestingly, the fluorescence intensity of **1** can be reversibly tuned upon the gel-sol transition as depicted in the inset of Figure 6. For instance, the fluorescence intensity of the gel of **1** (6.0 mg/mL) from H_2O/C_2H_5OH (1/1, v/v, pH 7.5) was high; however, after heating the gel was transformed into the solution which was almost non-emissive. Further cooling led to the formation of fluorescent gel again. In this way, the fluorescence of **1** can be switched on and off reversibly for several times.

3 Conclusions

A new gelator **1** based on TPE and diphenylalanine was synthesized. The gel can be formed with **1** in some miscible mixtures of water and organic solvents, such as H_2O/C_2H_5OH (1/1, v/v, pH 7.5). The solution of **1** was almost non-emissive, but the fluorescence was remarkably enhanced accompanying the gel formation. The gel can be easily and reversibly heated to the solution state, showing good thermal-reversibility. Accordingly, the fluorescence can be tuned "on-off" reversibly upon the gel-sol phase transition.

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