Soft Matter

RSC Publishing

PAPER

View Article Online
View Journal | View Issue

Cite this: *Soft Matter*, 2013, **9**, 5807

Mechano-responsive calix[4]arene-based molecular gels: agitation induced gelation and hardening†

Xiuqin Cai,[ab] Ying Wu,[a] Liya Wang,[a] Ni Yan,[a] Jing Liu,[a] Xiaohua Fang[a] and Yu Fang*[a]

Received 25th February 2013
Accepted 6th April 2013

DOI: 10.1039/c3sm50577d

www.rsc.org/softmatter

Two novel cholesteryl derivatives of calix[4]arene with L- or D-phenylalanine residues in the linkers (**1** and **2**, respectively) were designed and synthesized. The gelation behaviors of the compounds in 30 organic solvents were tested. It was demonstrated that **1** gels *n*-butanol and *n*-pentanol at room temperature, but **2** gels isopropanol only under the treatment of heating–cooling cycling or energy supplementing *via* sonication, vortex or agitation at room temperature. AFM and SEM measurements revealed that the structures of the gel networks are greatly affected by the spatial configurations of the linkers contained in the calix[4]arene derivatives. Furthermore, mechanical treatment not only promotes the gelation of the system of **2**–isopropanol, but also enhances the strength of the gel. Specifically, 18 min of agitation at room temperature makes the storage modulus and the yield stress of the gel (3.5%, w/v) exceed 1×10^6 Pa and 6×10^3 Pa, respectively, which are second only to the mechanically strongest low molecular mass gelator-based molecular gel reported until now. XRD analysis revealed the hexagonal packing structure of **1** in its *n*-pentanol gel.

Introduction

As a kind of smart material, low molecular mass gelator (LMMG)-based stimulus-responsive molecular gels have received increasing attention during the last few years due to their potential applications[1–3] in a variety of fields such as controlled release,[4] mild separation,[5] smart cleaning,[6] and new mediums for preparation[7] and purification.[8,9] Similar to chemical gels, formation of a gelator network in a gel system is a prerequirement for the gelation of the system. It is, however, also different from a chemical gel, as the gelator network in a molecular gel is formed through the self-assembly of the molecules of the gelator, rather than chemical cross-linking. The driving forces behind the self-assembly could either be one or a combination of weak interactions, including but not limited to hydrogen bonding, π–π stacking, cation–π interactions, van der Waals interactions, dipole–dipole interactions, coordination interactions, electrostatic interactions, hydrophobic or hydrophilic interactions *etc.*, among the molecules of the LMMGs.[10–12] As for the stimulus, it could be light,[13,14] electric/magnetic field,[15] ultrasound,[16,17] shear stress,[18] and even chemical.[19,20]

Creation of LMMG-based stimulus-responsive molecular gels is always a challenge. A commonly adopted strategy is to introduce a specific structural unit, which shows a structural response when stimulated.[21–26] For example, Yi and co-workers created a photochromic switch in an organogel system by employing a change between the open and closed structure of a diarylethane.[27] Haldar *et al.* synthesized a tripodal peptide and used it as a LMMG to gel benzene, toluene, xylene, cyclohexane, kerosene and petroleum. However, unlike commonly found molecular gels, sonication is a necessity for the gelation of these systems.[28] Wei and co-workers designed and prepared two different metal ligands, which gel water in the presence of Cd^{2+}. Interestingly, the introduction of EDTA turns the hydrogels back into solutions. The phase transition could be reverted by providing more Cd^{2+}. Moreover, acid–base exchange can also be used to switch the process.[29] Zhu's group reported two LMMGs adopting a redox active tetrathiafulvalene unit and a urea structure, one of which gels 2-propanol under sonication, and the other gels polar solvents. The system could easily be destroyed by oxidation.[15] Very recently, Shinkai and colleagues reported a few mechano-responsive molecular gels by employing some specifically designed anthracene derivatives as LMMGs.[30] However, compared with other stimulus-responsive molecular gels, mechano-responsive gels have been rarely studied until now, due to the fact that it is hard to find a key structural unit sensitive to shear stress.

[a]*Key Laboratory of Applied Surface and Colloid Chemistry of Ministry of Education, School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an, Shaanxi 710062, P. R. China. E-mail: yfang@snnu.edu.cn; Fax: +86-29-85307566; Tel: +86-29-85310081*

[b]*College of Chemistry and Life Science, Weinan Normal University, Weinan, Shaanxi 714000, P. R. China*

† Electronic supplementary information (ESI) available: Synthesis routes and gelation behaviors of gelators; AFM and SEM of concentration dependence of the gel-networks of **1**–pentanol and sonication time dependence of the gel-networks of **2**–isopropanol; ^{1}H NMR spectra of compounds **1** and **2**. See DOI: 10.1039/c3sm50577d

Recently, we developed a calix[4]arene-based dimeric-cholesteryl derivative which gels the mixture of *n*-decane and acetonitrile, and the gel as produced exhibits unprecedented and fully reversible thixotropic properties[31]—a property exhibited by some gels or fluids that are generally viscous or thick under normal conditions, but turn to a less viscous state when shaken, stirred or agitated, and the gels later take a certain period of time to return to their original state when allowed to stand without being disturbed.[32–34] However, strictly speaking, the classical definition of thixotropy pertains only to those fluids that exhibit reversible structural changes. From this point of view, it is only possible for physical gels, such as the molecular gels under discussion, to possess this extraordinary property. For example, Weiss *et al.* reported a gel system of a naphthalene-based cholesteryl derivative in dodecane, and studied its thixotropic properties by conducting rheological measurements.[35] Recently, Shinkai and co-workers reported a naphthalenediimide-based organogel which shows a thixotropic phenomenon at concentrations higher than 0.075 wt%.[36] Rowan and co-workers synthesized a compound of 2,6-bis(1-alkyl-benzimidazolyl) pyridine attached with an open chain crown ether, and found that its acetonitrile gel possessed thixotropic properties.[37] No doubt, thixotropy is a complex phenomenon, especially for systems like molecular gels. The structural details and the nature behind this property are far from being thoroughly understood, and in fact, almost all of the molecular gels possessing thixotropic properties have been discovered by serendipity rather than by design. Therefore, the creation of molecular gels with thixotropic properties and figuring out the structural features of the corresponding gelators still remains a big challenge.

It is well known that chirality plays a crucial role in molecular assembly processes, taking place not only in solution but also on surfaces and interfaces.[38–40] Furthermore, the chirality of the molecules of a LMMG could be transferred to its assemblies, which frequently gives rise to the assemblies' abnormal properties.[41–44] Accordingly, we tried to embed a chiral phenylalanine residue in the linker connecting a calix[4]-arene unit and a cholesteryl structure. Gelation tests revealed that the compound with L-phenylalanine in the linker (**1**, Fig. 1) gels *n*-butanol and *n*-pentanol efficiently, and the formed gels are stable. When *n*-propanol or *n*-hexanol is used, instead of the other two solvents, the system is only a partial gel. In contrast, isopropanol could be gelled by the compound containing D-phenylalanine in its linker (**2**, Fig. 1) *via* a heating–cooling cycle, and furthermore, the gelation is so slow that at least 30 h is needed for the system to lose its fluidity. However, mechanical agitation or sonication not only promotes the gelation,[45] but also enhances the strength of the gel. Considering the fact that for almost all of the thixotropic and LMMG-based molecular gels reported, shear stress or agitation induces a gel-to-solution phase transition rather than the reverse, hence the **2**–isopropanol gel system may be recognized as the second example of shear stress or agitation induced gelation. Details are reported in the following section.

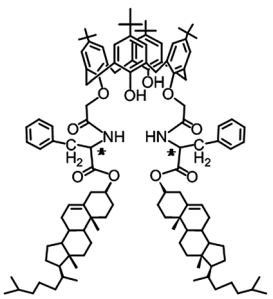

Fig. 1 Structure of the cholesteryl derivatives of calix[4]arene with L- or D-phenylanine in the linkers (**1** and **2**, respectively).

Experimental section

Reagents and materials

Cholesteryl, L-phenylalanine, D-phenylalanine, dicyclohexylcarbodiimide (DCC), *N*,*N*-dimethylaminopyridine (DMAP) (Sinopharm Group Co. Ltd) and *p-tert*-butylphenol (98%, Aladdin Chemistry Co. Ltd.) were used directly without further purification. Tetrahydrofuran (THF) was distilled over sodium in the presence of benzophenone under a nitrogen atmosphere before use. All other reagents were of analytical grade and used directly without further purification.

Synthetic procedures

The synthetic routes to the target compounds **1** and **2** are schematically shown in Scheme S1 (ESI†).

Synthesis of cholesteryl L-(D)-phenylalaninate (intermediates A and A′). Intermediates **A** and **A′** were synthesized as reported previously by us.[46,47]

Synthesis of calix[4]arene (intermediate B). Intermediate **B** was synthesized by a slightly modified method reported by Gutsche *et al.*[48] Specifically, 20.5 g (140 mmol) of *p-tert*-butylphenol, 14.5 mL of 37% formalin (200.2 mmol), and 0.5 mL of 12.5 mmol mL^{-1} NaOH solution were mixed together in a 500 mL four-necked flask. The mixture was then stirred and heated under a nitrogen atmosphere for 2 h in an oil bath at 110–120 °C, resulting in an orange-colored viscous mixture. Finally, a solid-like residue was obtained by allowing this mixture to be cooled to room temperature. The residue was dispersed in 200 mL of diphenyl ether under a nitrogen atmosphere by continuous stirring. The suspension was refluxed for 2 h, when the color of the system eventually became dark red. 200 mL of ethyl acetate was added after the system reached room temperature, was stirred for another 30 min, and then was allowed to stand for at least 30 min. The precipitate formed in the system was collected *via* filtration and washed twice with ethyl acetate and acetic acid, separately. The obtained product was purified by re-crystallization from toluene to give a white product (**B**) in 50% yield. For **B**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 1.21 (s, 36H, $-C(CH_2)_3$), 3.47 (d, $J = 12.0$, 4H, $-ArCH_2Ar-$), 4.23 (d, $J = 12.0$, 4H, $-ArCH_2Ar-$), 7.04 (s, 8H, –ArH), 10.34 (s, 4H, –OH); HRMS: *m*/*z* calcd for $[(M + Na)^+]$: 671.4071, found: 671.4071.

Synthesis of intermediate C. Intermediate **B** (0.648 g, 1 mmol), potassium carbonate (0.166 g, 1.2 mmol) and

potassium iodide (0.017 g, 0.1 mmol) were dissolved in 80 mL of acetone, and then ethyl chloroacetate (0.294 g, 2 mmol) was slowly added with stirring. The mixture was then refluxed for 10 h under a nitrogen atmosphere, followed by the evaporation of the solvent. The residue was dried and dissolved/suspended in chloroform. The organic system was extracted with 10% hydrochloric acid 3 times, and then collected and dried with anhydrous magnesium sulfate. The resulting clear solution was evaporated to dryness. The crude product as prepared was firstly purified by column chromatography (silicone gel, 200–300 mesh; acetone–petroleum ether, v : v = 1 : 9), and then by re-crystallization from petroleum ether three times to give intermediate **C** as white crystals in a yield of 51%. For intermediate C: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 1.04 (s, 18H, –$C(CH_2)_3$), 1.25 (s, 18H, –$C(CH_2)_3$), 1.31 (t, 6H, –CH_3), 3.29 (d, J = 15.0, 4H, –$ArCH_2Ar$–), 4.26 (q, 4H, –CH_2CH_3), 4.10 (d, J = 15.0, 4H, –$ArCH_2Ar$–), 4.72 (s, 4H, –$ArOCH_2$), 6.81 (s, 4H, –ArH), 7.01 (s, 4H, –ArH), 7.09 (s, 2H, –OH); HRMS: m/z calcd for [(M + Na)$^+$]: 843.4806, found: 843.4821.

Synthesis of intermediate D.[49] Intermediate **C** (0.820 g, 1 mmol) and 15% NaOH (2.8 mL) were dissolved in 60 mL of ethanol, and the mixture was stirred and heated under reflux for 6 h. The residue was diluted with cold distilled water (50 mL), then hydrochloric acid (3 M) was added with vigorous stirring until the pH value reached 1, and then the formed solid was collected *via* filtration. Finally, the residue was dried in air and dissolved in chloroform. The solution was first washed with hydrochloric acid (3 M) and brine, and was then dried and concentrated to afford intermediate **D** (yield: 97%). For **D**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm): 1.08 (s, 18H, –$C(CH_2)_3$), 1.25 (s, 18H, –$C(CH_2)_3$), 3.43 (d, J = 14.0, 4H, –$ArCH_2Ar$–), 4.13 (d, J = 14.0, 4H, –$ArCH_2Ar$–), 4.70 (s, 4H, –$ArOCH_2$), 6.97 (s, 4H, –ArH), 7.06 (s, 4H, –ArH), and 7.82 (br s, 4H, OH and COOH). HRMS: m/z calcd for [(M + Na)$^+$]: 787.4180, found: 787.4170.

Synthesis of intermediate E. Intermediate **D** (0.764 g, 1 mmol) was dissolved in 50 mL of toluene containing thionyl chloride (290 μL), and the mixture was stirred and refluxed for 3.5 h. Removal of the solvent and the un-reacted thionyl chloride *via* distillation under reduced pressure furnished the product, diacyl chloride (**E**), as an off-white solid in quantitative yield. The product as obtained was used directly in subsequent preparations without purification.

Preparation of compound 1. Intermediate **A** (0.9 g, 2 mmol) and triethylamine (280 μL) were dissolved in 50 mL of toluene, and then 20 mL of toluene containing intermediate **E** (0.8 g, 1 mmol) was added dropwise to the above solution when stirring, which was stirred at 0 °C for 12 h. After the reaction, the mixture was filtered, and the solvent in the solution was evaporated, leading us to the crude product. Purification of the product was first conducted by chromatography (silicone gel, 200–300 mesh; THF–petroleum ether, v : v = 10 : 1), and then by re-crystallization from ethanol. The purified product, **1**, a white powder, was obtained in a yield of 60%. The procedures used for the preparation of compound **2** are almost the same, and satisfactory results were also obtained. For compound **1**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm): 0.68–2.34 (m, 122H, –$C(CH_3)_3$, cholesteryl protons), 3.04 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 3.15 (d, J = 12.0, 4H, $ArCH_2CH$), 3.43 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 3.97 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 4.12 (d, J = 12.0, 2H, –$ArOCH_2$), 4.19 (d, J = 12.0, 2H, –$ArOCH_2$), 4.51 (m, 2H, oxycyclohexyl), 4.86 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 4.99 (m, 2H, –$NHCHCO(CH_2)$), 5.47 (s, 2H, alkenyl), 8.96 (m, 4H, –ArH), 7.01 (s, 14H, –ArH), 7.75 (s, 2H, OH) and 9.38 (d, 2H, –NH–); FTIR, ν_{max}/cm^{-1}: 3437 (NH, OH), 2954 (CH_3), 2929 (CH_2), 2858 (CH), 1715 (C=O, –O), 1653 (C=O, NH), 1534 (NH, bending vibration), and 1462 (–C–O). HRMS: m/z calcd for [(M + Na)$^+$]: 1818.2435, found: 1818.2426; anal. calcd for $C_{120}H_{166}N_2O_{10}$ (%): C 80.22, H 9.31, N 1.56; found: C 79.73, H 9.39, N 1.59. For compound **2**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm): 0.68–2.34 (m, 122H, –$C(CH_3)_3$, cholesteryl protons), 3.04 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 3.15 (d, J = 12.0, 4H, $ArCH_2CH$), 3.43 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 3.97 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 4.12 (d, J = 12.0, 2H, –$ArOCH_2$), 4.19 (d, J = 12.0, 2H, –$ArOCH_2$), 4.51 (m, 2H, oxycyclohexyl), 4.86 (d, J = 12.0, 2H, –$ArCH_2Ar$–), 4.99 (m, 2H, –$NHCHCO(CH_2)$), 5.47 (s, 2H, alkenyl), 8.96 (m, 4H, –ArH), 7.01 (s, 14H, –ArH), 7.76 (s, 2H, OH) and 9.31 (d, 2H, –NH–); FTIR, ν_{max}/cm^{-1}: 3437 (NH, OH), 2954 (CH_3), 2929 (CH_2), 2858 (CH), 1715 (C=O, –O), 1653 (C=O, NH), 1534 (NH, bending vibration), and 1462 (–C–O). HRMS: m/z calcd for [(M + Na)$^+$]: 1818.2435, found: 1818.2355; anal. calcd for $C_{120}H_{166}N_2O_{10}$ (%): C 80.22, H 9.31, N 1.56; found: C 79.92, H 9.39, N 1.58.

General methods

Gel preparation. In a typical gelation test, a weighed amount of the potential gelator and a measured volume of the solvent mixture were placed in a sealed test tube, then shaken or sonicated. Later, the system was left to equilibrate. Finally, the test tube was placed upside-down to observe if the solution inside could still flow. The systems which lose their fluidity are denoted as "G", those with only solutions left are referred to as "S". Systems with precipitates or crystals are named as "P", and the systems, in which the potential gelator could not be dissolved even at the boiling point of the solvent, are assigned with "I".

SEM pictures of the xerogels were taken on a Quanta 200 Scanning Electron Microscopy Spectrometer (Philips-FEI). The acceleration voltage was 20 kV and the emission was 10 mA. The xerogel was prepared by placing a block of gel onto a freshly cleaved mica surface then freeze-dried. Prior to examination, the mica with the xerogel was attached to a copper holder by using conductive adhesive tape and then coated with a thin layer of gold.

AFM measurements were conducted on a SOLVER P47 PRO Atomic Force Microscope. The sample was prepared by drop casting a solution of the system to be studied onto a freshly cleaved mica surface.

All FTIR measurements were performed on a Brucher EQUINX55 spectrometer in an Attenuated Total Reflection (ATR) mode with a ZnSe sample slot. The KBr pellets mixed with samples were measured in transmittance mode.

Rheological measurements were carried out with a stress-controlled rheometer (TA instrument AR-G2) equipped with

steel-coated parallel-plate geometry (20 mm diameter). The gap distance was fixed at 1000 μm. The following procedure was used to load the fresh gel sample: (1) the hot solutions of **1** in *n*-pentanol were placed between the parallel plates of the rheometer and heated to 80 °C to ensure that solutions were present. The samples were cooled to 15 °C at ~20 °C min^{-1} and incubated there for 4 h to reform the gels. (2) The hot solutions of **2** in isopropanol were cooled to room temperature and agitated on a stirrer at 200 rpm for different time periods. The obtained viscous solutions were placed between parallel plates and incubated there at 15 °C for 4 h to form gels. A solvent-trapping device was placed above the plate to avoid evaporation. All measurements were conducted at 15 °C, where two sweeps were investigated: stress sweep and frequency sweep. It was believed that this sweep provides information about the mechanical strength of the gel sample. The latter was finished at a constant shear stress of 1 Pa from 0.1 to 100 Hz.

^{1}H NMR data were collected on a Bruker AVANCE 300 MHz spectrometer. HRMS data were recorded on a Bruker Apex IV FTMS with ESI source.

The XRD data of the samples were collected on a D/Max-2550/PC with Cu KR X-ray radiation generated under a voltage of 40 kV and a current of 40 mA. The scans were conducted at a rate of 0.5° min^{-1}. The xerogels used in the measurements were prepared by freeze-drying the gels in liquid nitrogen, and then evaporating using a vacuum pump at a temperature of −60 °C for 12–24 h. The extended molecular lengths of **1** were calculated using Materials Studio 5.0 software. The energy minimization of the gelator conformations was made using the Discover module.

Result and discussion

Gelation behaviors of the compounds

Gelation behaviors of **1** and **2** were studied in 30 different organic solvents including protic/aprotic and polar/apolar solvents at a concentration of 2.5% (w/v), and the results are summarized in Table S1 (ESI†). It was found that **1** gels *n*-butanol and *n*-pentanol, and partially gels *n*-propanol and *n*-hexanol. In contrast, **2** gels isopropanol only. The effect of chirality upon the gelation behavior of the two compounds is not only reflected in the number of solvents they can gel, but also reflected in the conditions required by the gelation processes.

In the examination of the gelation behaviors of the compounds, it was observed that the gels of **1**–*n*-butanol and **1**–*n*-pentanol formed at room temperature spontaneously without agitation, sonication, or heating–cooling treatment. Yet for **2**, gelation of isopropanol is not so easy. The gel formed 30 h later after dissolution of **2** in the solvent (2.5%, w/v) *via* heating. However, mechanical agitation or sonication is able to accelerate the gelation process significantly. To be precise, it only took 12 min for the system to become a gel after vigorous agitation or sonication, indicating that the chiral structure of the phenylalanine residue connecting the cholesteryl units and the calix[4]arene structure show a pronounced effect upon the gelling performances of the compounds.

Morphology studies

The morphologies of the molecular assemblies of the compounds in dilute solutions and in the gels were studied *via* AFM and SEM measurements. Samples of the **2**–isopropanol gel had been prepared through stirring the system at a speed of 200 rpm at room temperature for 15 min, and then leaving for gelation. The corresponding xerogels used in the SEM measurements were prepared by freeze-drying the gels with liquid nitrogen, and then evaporating using a vacuum pump at −60 °C for 12–24 h. For other systems, gelation was induced by heating–cooling treatment, and the subsequent xerogel preparation remained the same as that described for the **2**–isopropanol gel system.

Fig. 2 shows the concentration-dependent morphologies of the molecular assemblies existing in a **2**–isopropanol solution and gel. With reference to the images, it can be seen that the morphologies of the aggregates of **2** in isopropanol at low concentrations are granules (*cf.* Fig. 2a). With increasing concentration of **2**, the granules start to fuse and form rod-like aggregates. At even higher concentrations, the rods blend to form network structures (*cf.* Fig. 2e and f). As for **1**, similar studies were also conducted and the results are shown in Fig. S2.† It can be concluded that by increasing the concentration of **1**, the morphologies of its aggregates change from particles and particle-based fibers (*cf.* Fig. S2a†) to rod-like structures, belts of narrow width, and belts of tens of micrometers width (*cf.* Fig. S2b–f†), suggesting that the network structures in the gel may originate from micro/nanoparticles which should be the primary aggregates of the molecules of **1**. Further comparison of the structures of the aggregates of **1** and **2** in the two systems, with the aggregate of **1** being hard and crisp as proved by the fractured surfaces and the aggregate of **2** being soft and pliable, reveals that the chirality change in the linker affects the aggregation behavior of the cholesteryl derivatives of calix[4]arene significantly.

To gather further information on the effect of mechanical agitation on the self-assembly behavior of **2**, the evolution process of its aggregate morphology was monitored as a function of agitation time, and some typical results are shown in Fig. 3 (2.5%, w/v). Similar to the results in Fig. 2, with the

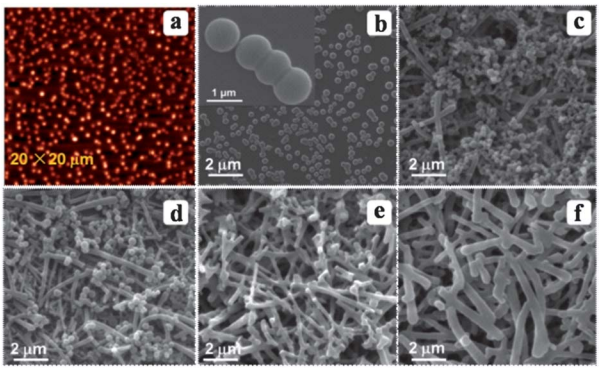

Fig. 2 AFM image (a) and SEM images (b–f) of **2**–isopropanol (a, 0.05%; b, 1%; c, 1.5%; d, 2%; e, 2.5%; f, 3%, w/v).

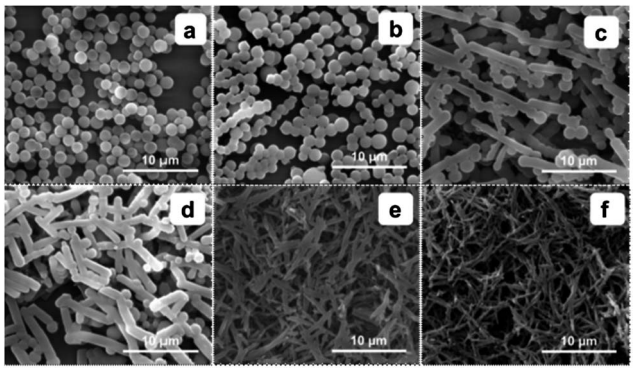

Fig. 3 SEM images of **2**–isopropanol gel networks present in the systems agitated for different lengths of time (a, 3 min; b, 6 min; c, 9 min; d, 12 min; e, 15 min; 30 min).

increase in the agitation time, the morphologies of the aggregates of **2** in the system change from globules, to globules and short rods then to short rods alone, and finally to rod-based networks. It is to be noted that there is a sharp transition between 12 min and 15 min of treatment time (*cf.* Fig. 3d and e). The aggregates appearing after 15 min of agitation look much thinner, and the networks are more homogeneous. A further increase in the agitation time, however, holds little effect on the morphologies of the gel networks since the image of the gel networks obtained after 15 min of agitation is almost the same as that obtained after 30 min (*cf.* Fig. 3f). Similar measurements through sonication treatment were also conducted for the gel system of **2**–isopropanol, and the received results are exhibited in Fig. S3.† It is obvious that a similar morphology evolution trend was observed. The morphological changes of the aggregates may explain why external energy is needed to make the systems change into gels.

Rheological studies

The mechanical properties of a material are extremely important for its practical uses, thereby the rheological properties of an example gel system of **2**–isopropanol were studied systematically. This system was chosen due to its specificity in preparation and in properties as afore-discussed. To explore these properties in detail, rheological measurements were conducted on a series of samples of the gel, which contained different amounts of the gelator and were agitated for various lengths of time.

Firstly, shear stress sweeps were conducted on the gels of **2** in isopropanol with an agitation time of 15 min (see Experimental section). In the measurement, the storage modulus, G', associated with energy storage, and the loss modulus, G'', associated with loss of energy, of the gel were measured as functions of shear stress at a constant frequency of 1.0 Hz at 15 °C (*cf.* Fig. 4a, to be clear, only the values of G' are shown). The value of G' increased from 9080 to 227 680 Pa along with increasing the concentration of **2** from 2.5 to 4.0% (w/v), and correspondingly, the yield stress changed from 40 to 1410 Pa. In contrast, the shear stress sweeps of the gels of **1** in

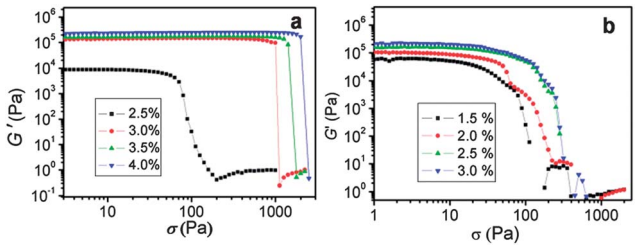

Fig. 4 Evolution of G' as a function of the applied shear stress at different concentrations of **2**–isopropanol gels (a, stirred at a speed of 200 rpm for 15 min), and **1**–pentanol gels (b).

n-pentanol with heating and cooling (see Experimental section) were also conducted, and the results are shown in Fig. 4b. It is seen that the value of G' increased from 58 050 to 227 640 along with increasing the concentration of **1** from 1.5% to 3.0% (w/v). Correspondingly, the yield stress increased from 10 to 30 Pa. These results indicate that both the stability and the elasticity of the gels are well dependent upon the structures of the gelators. Furthermore, increasing the concentration of the gelator in a gel also shows a positive role in enhancing the mechanical properties of the gel, but the only obvious effect is found when the concentration is below a certain value (*cf.* Fig. 4a and 5b).

As for the system of **2**–isopropanol, agitation not only promotes gelation and formation of the gel networks, but also enhances the mechanical strength of the gels. To understand the effect, the solutions of **2** in isopropanol with 3.5% (w/v) were agitated on the stirrer at a speed of 200 rpm for different time periods, followed by a stress sweep measurement (*cf.* Fig. 5a). Obviously, stronger agitation is needed for gels that were found after 18 and 24 min compared with that of 12 min. In further reference to the figure, it is seen that the value of G' of the system (3.5%, w/v) increased from 11 830 to 1 058 900 Pa along with increasing the agitation time from 12 to 24 min, and correspondingly, the yield stress increased from 110 to 6310 Pa. To the best of our knowledge, for LMMG-based molecular gels, the yield stress of 6310 Pa is only a little lower than the highest yield stress reported very recently.[50] Initially, these results seem to be counter-intuitive since ultrasound, agitation and other perturbation-like stimuli are reported to break network assemblies and eventually

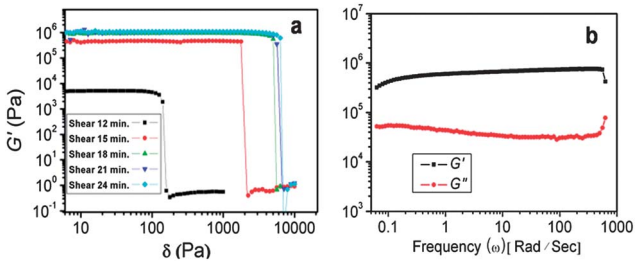

Fig. 5 Evolution of G' as a function of the applied shear stress for the **2**–isopropanol gels (3.5%, w/v) with different agitation times (a), and the traces from frequency scanning of the gel of **2**–isopropanol agitated for 15 min (3.5%, w/v).

result in dissolution of the gels in the vast majority of cases. However, there are an increasing number of reports highlighting the emergence of these stimuli as triggers of supramolecular gelation.[51–54]

Frequency sweep is an important method to examine the ability of a material to tolerate external forces.[55] Accordingly, a gel sample of **2**–isopropanol (3.5%, w/v) was employed to conduct the test at a shear stress of 1 Pa, which is well within the liner region of the gel sample (*cf.* Fig. 5a), and the result is shown in Fig. 5b. Reference to the figure reveals that the values of G' are always greater than those of the corresponding G'' of the gel within the frequency range from 0.1 rad s^{-1} to 500 rad s^{-1}. Further increasing the frequency, however, results in an abrupt decrease of the value of G' and a dramatic increase of G'', indicating break-down of the gel. Furthermore, within the frequency limit of 500 rad s^{-1}, both moduli exhibit weak dependence on frequency change, indicating typical visco-elastic behavior. All these results strongly demonstrate that the **2**–isopropanol gel shows good tolerance to external forces.

^{1}H NMR spectroscopy studies

To obtain further information on the structural nature of the gel networks of the gels, the aggregation behaviors of **1** and **2** in $CDCl_3$ were studied in detail by conducting temperature-dependent ^{1}H NMR measurements. The results are shown in Fig. 6. It is seen that the chemical shifts of the amide protons (>9 ppm) of **1** and **2** shifted remarkably up-field when the temperature was increased from 298 to 318 K. Specifically for **1**, the shifts are 0.15 ppm (*cf.* Fig. 6a), and 0.16 ppm for **2**, respectively (*cf.* Fig. 6b), suggesting that the amide groups in both compounds may have taken part in the aggregation process, and hydrogen bonding may be the most probable mode. Further reference to the data shows that the signals of the hydroxyl group protons (7.75 ppm) affixed to the calix[4]arene structure (*cf.* Fig. 1) also shifted to higher field with increasing temperature of the systems. The shifts for the two systems are as high as 0.22 and 0.24 ppm for **1** and **2**, respectively, supporting the argument that hydrogen bonding contributes to the self-assembly of the gelators. In addition, Fig. S5† shows the ^{1}H NMR spectrum of **1** in $CDCl_3$. The presence of four pairs of doublets between 3.0 and 5.0 ppm in the figure stands as strong evidence for the partial cone conformation possessed by the calix[4]arene residue of **1**,[56] which may provide a positive environment for host–guest interactions among the molecules of **1**, of which the guest might be the *tert*-butyl group connected to the benzene structure in the partial cone of a flipped calixarene.

FTIR spectroscopy studies

To further investigate the role of hydrogen bonding in the gelation process, FTIR spectra of the xerogels of **1**–*n*-pentanol, **2**–isopropanol, and those of their THF solutions were recorded. The results are shown in Fig. 7. It is seen that the characteristic bands of **1** in its THF solution at 3430, 1739 and 1682 cm^{-1} can be assigned to the stretching vibrations of OH(NH) and CO, as well as the bending vibration of NH, respectively.[57] Upon gelation, the band at 3430 cm^{-1} splits into two sharp bands, which appear at 3481 and 3306 cm^{-1}, respectively. Furthermore, the other two bands shift to 1733 and 1676 cm^{-1}, respectively. Fig. 7b shows the FTIR spectra of the THF solution of **2**, and the xerogel of **2**–isopropanol. By comparing the two spectra, it is seen that the characteristic bands of **2** shift from 1689 and 1652 cm^{-1} in the solution state to 1741 and 1689 cm^{-1} in the xerogel state, respectively. Similar to the system of **1**–*n*-pentanol, the broad signal at 3436 cm^{-1} for this system splits into two bands appearing at 3430 and 3345 cm^{-1}, respectively, along with gelation of this system. Change in the FTIR absorption positions of the carbonyl groups, the hydroxyl groups and the amide groups confirm the existence of hydrogen bonds in the gel networks, which should be one of the driving forces to promote gelation.

X-ray diffraction measurements

XRD analysis can be used to elucidate the molecular packing mode in the crystalline state and clarify the gelation mechanism of a LMMG in its gel phase.[58] Accordingly, the packing mode of **1** in the xerogel of its *n*-pentanol gel was studied *via* this technique, and the XRD trace is shown in Fig. 8. It is seen that the XRD pattern of the xerogel is characterized by four sharp reflection peaks at $2\theta = 4.06$, 5.18, 6.84 and 8.84°, of which the corresponding d values are 2.17, 1.72, 1.29 and 1.00 nm, respectively. Further interrogation of the data reveals that the ratio of the d values equals $(1/\sqrt{3}) : (1/2) : (1/\sqrt{7}) : (1/\sqrt{12})$,

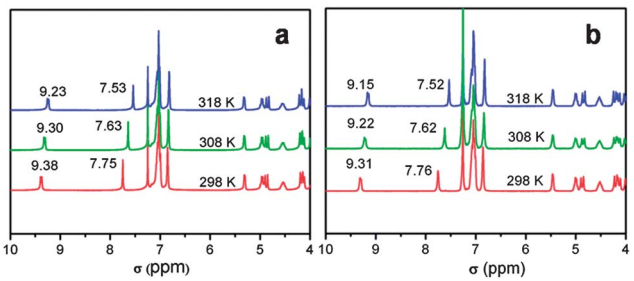

Fig. 6 Partial ^{1}H NMR spectra of **1** (a) and **2** (b) recorded in $CDCl_3$ at different temperatures at a concentration of 2% (w/v).

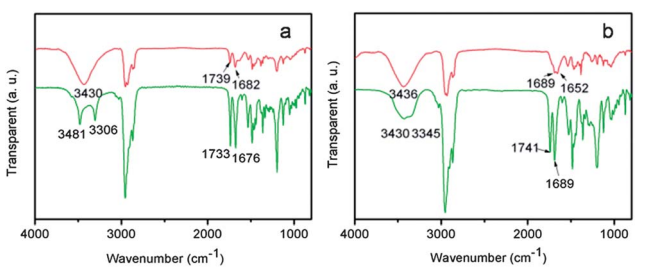

Fig. 7 FTIR spectra of **1** (a) and **2** (b) in their THF solutions (red) and xerogels (green) from **1**–*n*-pentanol and **2**–isopropanol.

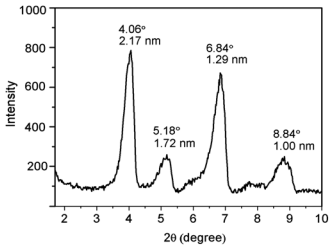

Fig. 8 XRD pattern of the xerogel of **1** from its *n*-pentanol gel.

which mainly follows the ratio of $1 : (1/\sqrt{3}) : (1/2) : (1/\sqrt{7}) : (1/3) : (1/\sqrt{12})$, characteristic of a hexagonal structure.[59] Therefore, the molecules of the gelator in the gel are probably assembled in a hexagonal mode, and accordingly the diffractions can be indexed in sequence of (110), (200), (300) and (220), which belongs to a hexagonal columnar lattice. As 2.17 nm is only $1/\sqrt{3}$ of the *d* value of the lattice, the first peak of the diffractions should appear at 3.76 nm, which is very close to the length (3.80 nm) of the molecules of **1** as calculated from molecular dynamics modeling (Fig. 9). Furthermore, it is to be noted that in the aggregate, one of the benzene units of the calix[4]arene residue of a component molecule functions as a guest, and is hosted by another calix[4]arene residue belonging to another component molecule. In other words, the component molecules within the aggregate are interlocked *via* host–guest interaction (*cf.* Fig. 9), which is different from the hexagonal packing of other calix[4]arene derivatives.[60,61] As the spacing is much smaller than the smallest size of the microstructure of the gel networks of **1** in its *n*-pentanol gel (*cf.* Fig. S1a†), it is supposed that the XRD data came from a fiber of the aggregates of **1** in the gel. The fibrous features of the primary structure is supported by the results that the aggregates do adopt a fiber-like structure as revealed by the AFM and SEM measurements (*cf.* Fig. S1†).

On the basis of the results obtained from FTIR, ^{1}H NMR, XRD measurements and the well-known fact that calix[4]arene units aggregate *via* van der Waals and host–guest interaction, a plausible possible structural mode (*cf.* Fig. 8) is proposed to describe the fundamental assembly of **1** in its *n*-pentanol gel.

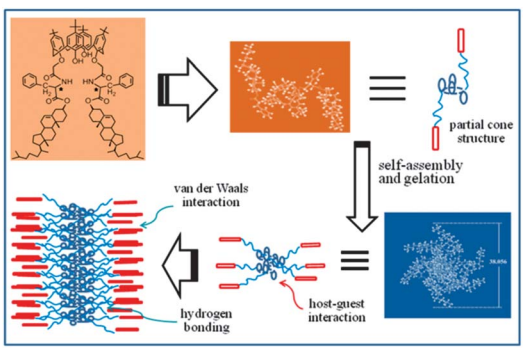

Fig. 9 Schematic representation of a plausible formation mechanism of the aggregate of **1** in *n*-pentanol.

Conclusion

Two novel cholesteryl derivatives of calix[4]arene with L- or D-phenylalanine residues in the linkers were designed and synthesized. Gelation tests in 30 organic solvents demonstrated that **1** gels *n*-butanol and *n*-pentanol at room temperature, but **2** gels isopropanol only. Moreover, the gelation for **2** occurs more than 30 h later, after heating–cooling treatment or in no more than 12 min after vigorous agitation or sonication. It was also revealed that shear force or sonication treatment accelerates the gelation of the system of **2**–isopropanol and enhances the strength of the gel. The value of the storage modulus, G', of the system (3.5%, w/v) increased to more than 1×10^6 Pa when agitated for 24 min, and correspondingly, the yield stress exceeded 6×10^3 Pa, which is second only to the mechanically strongest LMMG-based molecular gel reported by us very recently. XRD analysis revealed that **1** self-assembles into a hexagonal structure in its pentanol gel.

Acknowledgements

We thank the Natural Science Foundation of China (91027017 and 21273141) and the 13115 Project of Shaanxi Province (2010ZDKG-89) for financial support. This work is also supported by the "Program for Changjiang Scholars and Innovative Research Team in University" of China (IRT1070).

Notes and references

1 M. Zinić, F. Vögtle and F. Fages, *Top. Curr. Chem.*, 2005, **256**, 39–74.
2 M. M. Piepenbrock, G. O. Lloyd, N. Clarke and J. W. Steed, *Chem. Rev.*, 2010, **110**, 1960–2004.
3 J. W. Steed, *Chem. Commun.*, 2011, **47**, 1379–1383.
4 W. H. Binder, L. Petraru, H. Weinstabl, D. Gloger and R. Sachsenhofer, *Macromol. Symp.*, 2007, **254**, 62–66.
5 S. Yamamichi, Y. Jinno, N. Haraya, T. Oyoshi, H. Tomitori, K. Kashiwagi and M. Yamanaka, *Chem. Commun.*, 2011, **47**, 10344–10346.
6 *Molecular Gels: Materials with Self-Assembled Fibrillar Networks*, ed. R. G. Weiss and P. Terech, Springer, Dordrecht, 2006, ch. 22–27, pp. 773–920.
7 T. Naota and H. Koori, *J. Am. Chem. Soc.*, 2005, **127**, 9324–9325.
8 *Organic Nanostructure*, ed. J. L. Atwood and J. W. Steed, Wiley-VCH, Weinheim, 2008, ch. 5, pp. 111–154.
9 P. Jonkheijm, P. van der Schoot, A. P. H. J. Schenning and E. W. Meijer, *Science*, 2006, **313**, 80–83.
10 C. B. Aakeröy, P. D. Chopade, C. Ganser and J. Desper, *Chem. Commun.*, 2011, **47**, 4688–4690.
11 P. Terech and R. G. Weiss, *Chem. Rev.*, 1997, **97**, 3133–3159.
12 A. Aggeli, M. Bell, N. Boden, J. N. Keen, P. F. Knowles, T. C. B. McLeish, M. Pitkeathly and S. E. Radford, *Nature*, 1997, **386**, 259–262.
13 S. A. Ahmed, X. Sallenave, F. Fages, G. Mieden-Gundert, W. M. Müller, U. Müller, F. Vögtle and J. L. Pozzo, *Langmuir*, 2002, **18**, 7096–7101.

14 P. Xue, R. Lu, G. Chen, Y. Zhang, H. Nomoto, M. Takafuji and H. Ihara, *Chem.–Eur. J.*, 2007, **13**, 8231–8239.
15 C. Wang, D. Zhang and D. Zhu, *J. Am. Chem. Soc.*, 2005, **127**, 16372–16373.
16 D. Bardelang, *Soft Matter*, 2009, **5**, 1969–1971.
17 G. Cravotto and P. Cintas, *Chem. Soc. Rev.*, 2009, **38**, 2684–2697.
18 J. Liu, P. He, J. Yan, X. Fang, J. Peng, K. Liu and Y. Fang, *Adv. Mater.*, 2008, **20**, 2508–2511.
19 Z. Qi, P. M. Molina, W. Jiang, Q. Wang, K. Nowosinski, A. Schulz, M. Gradzielski and C. A. Schalley, *Chem. Sci.*, 2012, **3**, 2073–2082.
20 X. Yan, F. Wang, B. Zheng and F. Huang, *Chem. Soc. Rev.*, 2012, **41**, 6042–6065.
21 M. D. Segarra-Maset, V. J. Nebot, J. F. Miravent and B. Escuder, *Chem. Soc. Rev.*, 2013, DOI: 10.1039/c2cs35436e.
22 K. Sugiyasu, N. Fuijita and S. Shinkai, *Angew. Chem., Int. Ed.*, 2004, **43**, 1229–1233.
23 T. Nakashima and N. Kimizuka, *Adv. Mater.*, 2002, **14**, 1113–1116.
24 E. Kring, E. Shirman, H. Weissman, E. Shimoni, S. G. Wolf, I. Pinkas and B. Rybtchinski, *J. Am. Chem. Soc.*, 2009, **131**, 14365–14373.
25 X. Yan, D. Xu, X. Chi, J. Chen, S. Dong, X. Ding, Y. Yu and F. Huang, *Adv. Mater.*, 2012, **24**, 362–369.
26 L. Meazza, J. A. Foster, K. Fucke, P. Metrangolo, G. Resnati and J. W. Steed, *Nat. Chem.*, 2013, **5**, 42–47.
27 S. Xiao, Y. Zou, M. Yu, T. Yi, Y. Zhou, F. Li and C. Huang, *Chem. Commun.*, 2007, 4758–4760.
28 S. Maity, S. Sarkar, P. Jana, S. K. Maity, S. Bera, V. Mahalingam and D. Haldar, *Soft Matter*, 2012, **8**, 7960–7966.
29 Y. Zhang, W. Zhang, J. Li, J. Dang and T. Wei, *Mater. Lett.*, 2012, **82**, 227–229.
30 A. Dawn, T. Shiraki, H. Ichikawa, A. Takada, Y. Takahashi, Y. Tsuchiya, L. T. N. Lien and S. Shinkai, *J. Am. Chem. Soc.*, 2012, **134**, 2161–2171.
31 X. Cai, K. Liu, J. Yan, H. Zhang, X. Hou, Z. Liu and Y. Fang, *Soft Matter*, 2012, **8**, 3756–37661.
32 H. Barnes, *J. Non-Newtonian Fluid Mech.*, 1997, **70**, 1–33.
33 A. Sobczuk, Y. Tsuchiya, T. Shiraki, S. Tamaru and S. Shinkai, *Chem.–Eur. J.*, 2012, **18**, 2832–2838.
34 M. Shirakawa, N. Fujita and S. Shinkai, *J. Am. Chem. Soc.*, 2005, **127**, 4164–4165.
35 X. Huang, S. Raghavan, P. Terech and R. Weiss, *J. Am. Chem. Soc.*, 2006, **128**, 15341–15352.
36 P. Mukhopadhyay, N. Fujita, A. Takada, T. Kishida and S. Shinkai, *Angew. Chem., Int. Ed.*, 2010, **49**, 6338–6342.
37 W. Weng, J. Beck, A. Jamieson and S. Rowan, *J. Am. Chem. Soc.*, 2006, **128**, 11663–11672.
38 A. B. R. Oda and I. Huc, *Top. Curr. Chem.*, 2005, **15**, 3979–3986.
39 R. Oda, I. Huc and S. J. Candau, *Angew. Chem., Int. Ed.*, 1998, **37**, 2689–2691.
40 D. Berthier, T. Buffeteau, J. Lćger, R. Oda and I. Huc, *J. Am. Chem. Soc.*, 2002, **124**, 13486–13494.
41 J. Peng, K. Liu, J. Liu, Q. Zhang, X. Feng and Y. Fang, *Langmuir*, 2008, **24**, 2992–3000.
42 X. Chen, Z. Huang, S. Chen, K. Li, X. Yu and L. Pu, *J. Am. Chem. Soc.*, 2010, **132**, 7297–7299.
43 A. Brizard, R. Oda and I. Huc, *Top. Curr. Chem.*, 2005, **256**, 167–168.
44 T. Cardolaccia, Y. Li and K. S. Schanze, *J. Am. Chem. Soc.*, 2008, **130**, 2535–2545.
45 Z. Xie, A. Zhang, L. Ye, X. Wang and Z. Feng, *J. Mater. Chem.*, 2009, **19**, 6100–6102.
46 Y. Li, K. Liu, J. Liu, J. Peng, X. Feng and Y. Fang, *Langmuir*, 2006, **22**, 7016–7020.
47 Y. Li, Y. Fang, J. Liu and M. Wang, *J. Chin. Chem. Soc.*, 2006, **53**, 359–366.
48 C. D. Gutsche, M. Iqbal and D. Stewart, *J. Org. Chem.*, 1991, **51**, 743–748.
49 E. M. Collins, M. A. Mckervey, E. Madigan, M. B. Moran, M. Owens, G. Ferguson and S. J. Harris, *J. Chem. Soc., Perkin Trans. 1*, 1991, 3137–3142.
50 Z. Xu, J. Peng, N. Yan, H. Yu, S. Zhang, K. Liu and Y. Fang, *Soft Matter*, 2013, **9**, 1091–1099.
51 Y. Wang, C. Zhan, H. Fu, X. Li, X. Sheng, Y. Zhao, D. Xiao, Y. Ma, J. Ma and J. Yao, *Langmuir*, 2008, **24**, 7635–7638.
52 S. Maity, P. Kumar and D. Haldar, *Soft Matter*, 2011, **7**, 5239–5245.
53 X. Yu, X. Cao, L. Chen, H. Lan, B. Liu and T. Yi, *Soft Matter*, 2012, **8**, 3329–3334.
54 R. Afrasiabi and H.-B. Kraatz, *Chem.–Eur. J.*, 2013, **19**, 1769–1777.
55 M. G. Page, G. Gregory and G. G. Warr, *J. Phys. Chem. B*, 2004, **108**, 16983–16989.
56 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6052–6059.
57 J. H. Jung, G. Johm, M. Masuda, K. Yoshida, S. Shinkai and T. Shimizu, *Langmuir*, 2001, **17**, 7229–7232.
58 M. Xue, K. Liu, J. Peng, Q. Zhang and Y. Fang, *J. Colloid Interface Sci.*, 2008, **327**, 94–101.
59 J. J. van Gorp, Helices by Hydrogen Bonding: Folding and Stacking of Chiral Supramolecular Scaffolds, Doctorate thesis, Technische Universiteit Eindhoven, 2004, ch. 2, pp. 21–43.
60 A. N. Lazar, N. Dupont, A. Navaza and A. W. Coleman, *Chem. Commun.*, 2006, 1076–1078.
61 F. Perret, A. N. Lazar, O. Shkurenko, K. Suwinska, N. Dupont, A. Navaza and A. W. Coleman, *CrystEngComm*, 2006, **8**, 890–894.

