SCIENCE CHINA
Chemistry

• ARTICLES •

March 2011 Vol.54 No.3: 475–482
doi: 10.1007/s11426-010-4208-4

Synthesis and gelation behaviors of five new dimeric cholesteryl derivatives

LIU KaiQiang, PENG JunXia, XUE Min, YAN Ni, LIU Jing & FANG Yu*

Key Laboratory of Applied Surface and Colloid Chemistry (Shaanxi Normal University), Ministry of Education; School of Chemistry and Materials Science, Shaanxi Normal University, Xi'an 710062, China

Received March 21, 2010; accepted May 4, 2010

Five new diacid amides of di-cholesteryl L-glycinates were designed and prepared. The compounds with linkers containing 0, 1, 2, 3, or 4 methylene units are denoted as **1**, **2**, **3**, **4**, and **5**, respectively. Their gelation behaviors in 25 solvents were tested as novel low-molecular-mass organic gelators (LMOGs). It was shown that the length of the linker connecting the two-cholesteryl residues in a gelator plays a crucial role in the gelation behavior of the compound. **1** gels 11 of the 25 solvents tested at a concentration lower than 1.0%, while **2** gels 17 of the solvents tested. **4** and **5**, however, gel only 2 and 4 of them, respectively. SEM observation reveals that the lengths of the linkers and the identity of the solvents are the main factors affecting the structures of the aggregates in the gels. Experimentally, a clear linker effect on the microstructures of the gels was observed. As example, the aggregates of **1, 2** and **3** in benzene or 1-heptanol adopt structures of thin fibers, rods or lamellas, respectively. Furthermore, it was found that the gelation and aggregation behaviors of **2**, **3**, **4**, and **5** in DMSO showed an even-odd effect.

organogelators, cholesterol, linker effect, solvent effect

1 Introduction

The phenomenon that some organic compounds with low molecular mass can solidify organic solvents at low concentrations was discovered more than 50 years ago. These compounds have been known as low-molecular-mass organic gelators (LMOGs). In recent years, physical gelation of organic solvents by LMOGs has become one of the hot areas in soft matter research because of its abundant potential applications [1–10]. The gels based on LMOGs are usually considered as supramolecular gels, in which the gelator molecules self-assemble into three-dimensional (3-D) networks via various non-covalent interactions, such as hydrogen bonding, π-π stacking, van der Waals interaction, dipole-dipole interaction, coordination, solvophobic interaction, and host-guest interaction [1–9, 11, 12]. The non-covalent nature of the 3-D networks within the supramolecular gels promises accessibility for designing and constructing sensors, actuators, and other molecular devices [13–15]. Most of the gels based on LMOGs have been obtained by a heating-cooling method.

The control of self-assembling mode at the molecular level and the balance between precipitation and dissolution in a given solvent are critical to the design of new LMOGs [1–9]. This is because the gelation of a solvent by a LMOG is the result of gelator-gelator and gelator-solvent interactions, which involve specific and nonspecific intermolecular forces. Therefore, the aggregation behavior of a gelator in solvents can be adjusted by varying its structure, for example, introducing directional self-assembling units, such as amides, and urea [1–9]. As a versatile unit, the covalently bound cholesteryl group with four rings fused together, of which three rings are six-member rings and one is five-member ring, has been widely chosen for designing new LMOGs because of its unique directional self-association

*Corresponding author (email: yfang@snnu.edu.cn)

through van der Waals interactions in the aggregates of the gelators comprising it [3]. Historically, molecules comprising an aromatic (A) moiety and a steroidal (S) group, of which the two units are connected by a linker (L), are called ALS type LMOGs. These compounds can gel a range of solvents including polar and apolar solvents, mainly depending on the nature of A, L, and S components [1, 3, 16]. Another class of LMOGs is dimeric cholesterol-based derivatives denoted as $A(LS)_2$ or LS_2 gelators. Via the components of A and L, various functional units such as chromophores, ligands, and polymerizable units have been successfully incorporated into gelator structures, laying a foundation for the applications of the gels [3, 17–22]. As an example, Shinkai prepared a series of dimeric cholesterol derivatives bearing various functional linkers as versatile gelators, and some organogels comprising them were used successfully as templates for the preparation of inorganic materials possessing unique structures.

In recent years, we designed and prepared some ALS, LS and LS_2 type gelators and studied their gelation behaviors in various solvents [23–25]. It was found that the gelators of LS_2 type structures are generally much more efficient than gelators of other structures. Furthermore, some organogels comprising LS_2 type gelators possess thixotropic properties [26]. On the bases of these works and the structural information cited above, we have designed and synthesized a new class of LS_2 type LMOGs, and regulated the gelation and aggregation behaviors of these compounds by changing the number of the methylene unit in the linker of them.

2 Experimental

2.1 Gelation test

A known weight of the potential gelator and a measured aliquot of liquid were placed into a sealed glass tube ($d = 10$ mm, $V = 3$ mL) and the system was heated in an oil or water bath until all solid materials were dissolved completely. Then, the solution was cooled to room temperature in air and the test tube was inversed to see if a gel was formed. When the gelator formed a transparent, translucent or white gel by immobilizing the solvent at this stage, it was denoted as "TG", "TLG" or "G". For the systems in which only solution remained until the end of the tests, they were referred to as solution (S). When the gelator formed into precipitate in some solvent, it was denoted as a "precipitate (P)". The system in which the potential gelator could not be dissolved even at the boiling point of the solvent was designated as an insoluble system (I). In a few cases, turbid solution (TUS) or viscous solution (VS) was also observed at 3.0% of the gelator. Critical gelation concentration (CGC) refers to the minimum concentration of the gelator for gel formation.

2.2 SEM measurement

SEM pictures of the xerogel were taken on a Quanta 200 scanning electron microscopy spectrometer (Philips-FEI). The xerogel was prepared by freezing the gel in liquid nitrogen, and then evaporated by a vacuum pump for 12–24 h. The dried sample thus obtained was attached to a mica or glass slice by conductive adhesive tape, and shielded by gold. The accelerating voltage was 15 kV, and the emission was 10 mA.

2.3 FTIR measurement

The solution and gel samples were measured by a Bruker EQUINX55 spectrometer in an attenuated total reflection (ATR) mode. The xerogel samples for measurements were coated on a glass or mica slice as a gel film and frozen in liquid nitrogen, and then evaporated by a vacuum pump for 12–24 h.

2.4 ^{1}H NMR measurement

The gel sample containing one gelator and d^6-benzene was prepared in a NMR tube, and the chemical shifts of the sample were detected by a Fourier Digital NMR spectrometer (AVANCF300MHZ, 300 MHz) at a given temperature between 318 K and 338 K.

2.5 X-ray diffraction (XRD) analysis

The measurement was conducted using a Rigaku/MSC D/Max-2550/PC X-ray diffraction system. Fresh gel sample was directly loaded onto a rectangular glass sample holder as smooth film, and then scanned immediately. The XRD pattern was obtained using CuKα radiation with an incident wavelength of 0.1542 nm under a voltage of 40 kV and a current of 50 mA. The scan rate was 0.5 °/min.

3 Synthesis of compounds

3.1 Cholesteryl glycinate primary amine

Step (a): 0.175 g (1 mmol) Boc-glycin and 0.387 g (1 mmol) cholesterol were dissolved in 40 mL dichloromethane. The solution was maintained at 0 °C using an ice bath. 0.206 g (1 mmol) dicyclohexylcarbodiimide (DCC) and 0.012 g (0.1 mmol) *N*,*N*-dimethylamino-pyridine (DMAP) were added, and the reaction mixture was being stirred for 4 h at 0 °C. After the reaction, the mixture was filtered and the filtrate was washed with 0.001 mol L^{-1} hydrochloric acid (30 mL × 3), 0.001 mol L^{-1} sodium hydroxide solutions (30 mL × 3) and pure water (30 mL × 3). The organic layer was evaporated to dryness. The residue was purified by a silica gel column eluting with THF/*n*-hexane (1:6, *v*/*v*) to give cholesteryl Boc-glycinate in 64% yield as a white solid. Step (b): 0.544 g (1 mmol) cholesteryl Boc-glycinate was dissolved in 100 mL dichloromethane and then bubbled dry HCl gas for 30 min. The mixture was filtered and the resi-

due was washed with dichloromethane three times and dried in vacuum to give the desired product in 90% yield as a white crystal. For hydrochloric salts of cholesteryl glycinate ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 5.37 (1H, alkenyl), 4.66–4.69 (1H, m, oxycyclohexyl), 3.98 (2H, d, CH_2CO), 2.31–2.34 (2H, d, CH_2), 0.67–1.85 (42H, m, cholesteryl protons). Elemental analysis, calculated for $C_{29}H_{50}O_2NCl$ (Mw = 479.35): C 72.54, H 10.50, N 2.92; Found: C, 72.21, H, 10.40, N, 2.88. Step (c): 1.45 mL triethylamine was added to the solution of 5.00 g hydrochloric salts of cholesteryl glycinate in 200 mL benzene. The mixture was stirred and refluxed for 5 h, after which the formed precipitate was filtered off, the resulting solution was evaporated to dryness, and the solid was dried in vacuo to give cholesteryl glycinate primary amine in 78% yield as a white or yellowish solid.

3.2 Dimeric cholesterol-based amino acid derivative 1

Two mmol (0.887 g) cholesteryl glycinate primary amine and 2 mmol (278.2 μL) TEA were dissolved in 40 mL dried benzene. The solution was maintained at 0 °C using an ice-water bath. 40 mL benzene with 1 mmol (85.8 μL) oxalyl chloride was added dropwise to the above solution under stirring. The reaction mixture was stirred for 4–5 h at 0 °C. After the reaction, the resulting mixture was filtered and the filtrate was evaporated to dryness. The solid was washed with hot methanol three times to give a dimeric cholesterol-based amino acid derivative **1** in 80% yield as a white solid. For **1**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 7.79 (2H, s, CONH), 5.39 (2H, s, alkenyl), 4.69–4.72 (2H, m, oxycyclohexyl), 4.07–4.08 (4H, d, CH_2COO, J = 5.25 Hz), 2.23–2.36 (4H, d, CH_2, J = 7.29), 0.68-1.99 (82H, m, cholesteryl protons). Elemental analysis, calculated for $C_{60}H_{96}N_2O_6$ (Mw = 941.41): C 76.55, H 10.28, N 2.98; Found: C 76.89, H 10.34, N 2.68.

3.3 Dimeric cholesterol-based amino acid derivative 2

Two mmol (0.887 g) cholesteryl glycinate primary amine and 1 mmol (0.104 g) malonic acid were dissolved in 40 mL dried THF. The solution was maintained at 40–50 °C using a thermostated water bath. 2 mmol (0.412 g) DCC was added, and the reaction mixture was stirred for 10–12 h at 40–50 °C. After the reaction, the mixture was filtered and the filtrate was evaporated to dryness. The resulting solid was washed with hot methanol three times to give a dimeric cholesterol-based amino acid derivative 2 in 78% yield as a white solid. For **2**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 7.19 (2H, CONH), 5.39 (2H, alkenyl), 4.67–4.79 (2H, m, oxycyclohexyl), 4.03–4.04 (4H, d, CH_2COO, J = 3.15 Hz), 2.32–2.35 (4H, d, CH_2, J = 7.03), 2.03 (4H, s, CH_2), 0.68–1.89 (82H, m, cholesteryl protons). Elemental analysis, calculated for $C_{61}H_{98}N_2O_6$ (Mw = 955.44): C 76.68, H 10.34, N 2.93; Found: C 76.48, H 9.99, N 2.84.

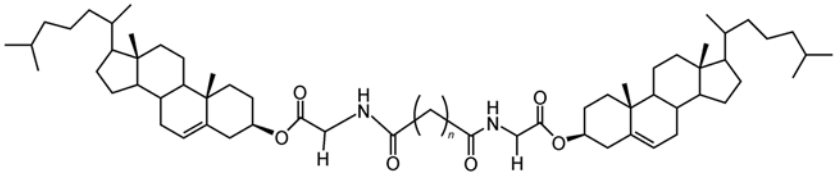
3.4 Dimeric cholesterol-based amino acid derivative 3–5

Two mmol (0.887 g) cholesteryl glycinate primary amine and 1 mmol dicarboxylic acid were dissolved in 40 mL THF. The solution was maintained at 0 °C using an ice bath. 2 mmol DCC and 0.2 mmol DMAP were added, and the reaction mixture was stirred for 4–7 h at 0 °C. After the reaction, the mixture was filtered and the filtrate was evaporated to dryness. The resulting solid was washed by hot methanol three times to give in a dimeric cholesterol-based amino acid derivative in 70%–90% yield as a white solid. For **3**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 6.51 (2H, s, CONH), 5.38 (2H, s, alkenyl), 4.64–4.67 (2H, m, oxycyclohexyl), 3.99–4.01 (4H, d, CH_2COO, J = 4.62 Hz), 2.31–2.34 (4H, d, CH_2, J = 7.52), 1.85–2.00 (4H, m, CH_2CH_2), 0.68–1.62 (82H, m, cholesteryl protons). Elemental analysis, calculated for $C_{62}H_{100}N_2O_6$ (Mw = 969.47): C 76.81, H 10.40, N 2.88; Found: C 75.48, H 10.38, N 2.79. For **4**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 7.77 (2H, CONH), 5.39 (2H, s, alkenyl), 4.65–4.67 (2H, m, oxycyclohexyl), 4.05–4.06 (4H, d, CH_2COO, J = 4.2 Hz), 2.30–2.33 (4H, d, CH_2, J = 8.99), 1.86–2.04 (6H, m, $CH_2CH_2CH_2$), 0.68–1.58 (82H, m, cholesteryl protons). Elemental analysis, calculated for $C_{63}H_{102}N_2O_6$ (Mw = 983.49): C 76.94, H 10.45, N 2.85; Found: C 76.76, H 10.13, N 2.847. For **5**: ^{1}H NMR ($CDCl_3$/Me_4Si, 300 MHz): δ (ppm) 7.77 (2H, CONH), 5.39 (2H, alkenyl), 4.65–4.67 (2H, m, oxycyclohexyl), 4.05–4.15 (4H, d, CH_2COO, J = 4.19 Hz), 2.30–2.33 (4H, d, CH_2, J = 2.99), 1.86–2.04 (8H, m, $CH_2CH_2CH_2CH_2$), 0.68–1.60 (82H, m, cholesteryl protons). Elemental analysis, calculated for $C_{64}H_{104}N_2O_6$ (Mw = 997.52): C 77.06, H 10.51, N 2.81; Found: C 76.84, H 10.38, N 2.75.

4 Results and discussion

4.1 Design and synthesis of the gelators

It has been demonstrated in former research that organic diacid monoamides of cholesteryl glycinate are poor gelators for organic solvents [25]. However, neutralization of the acids with ammonia enhanced their gelling ability significantly [25]. Referring to the structures of these compounds, another simple way to enhance their gelling ability is to modify their structures by connecting two molecules in order to change their structure from LS type to LS_2 type. In this way, novel dimeric cholesteryl derivatives should be formed (*c.f.* Scheme 1). It was expected that the new compounds are efficient LMOGs because (1) more cholesteryl units in a molecule are favorable for the aggregation of the compounds in solution, (2) similarly, increase in the number of amide residue is also favorable for the aggregation due to formation of hydrogen bonds and (3) change of the linker lengths is another factor to adjust the balance between



Scheme 1 Structure of amino acid derivatives of dimeric cholesterols. n = 0, 1, 2, 3, 4; named **1**, **2**, **3**, **4**, **5**.

dissolution and precipitation. This also increases the chance to find good LMOGs.

Synthesis of **1**–**5** has been accomplished by using two different routes. One is that the primary amine was coupled with acryl chloride in a suitable solvent. Another is the condensation between the two carboxyl groups of organic diacids and the primary amine group of the reactants with dicyclohexylcarbodiimide (DCC) and *N*,*N*-dimethylaminopyridine (DMAP) as catalysts. For the system, in which malonic acid was taken as a reactant, DMAP could not be used due to its reactivity with the methylene unit of the diacid.

4.2 Gelation behaviors of the compounds

The gelation performances of the compounds, **1**–**5**, in 25 solvents are listed in Table 1. Examination of the table reveals that **1**, **2**, and **3** are more versatile and efficient gelators than **4** and **5**. The data shown in Table 1 indicate that the increase of the linker length between the two-cholesteryl residues decreases the gelling abilities of the compounds. Specifically, **1**, **2** and **3** gel 11, 17 and 11 of the solvents tested, respectively. **4** and **5**, however, gel only 2 and 4 of them, respectively. This result shows that a longer linker in

Table 1 Gelation behaviors of some amino acid derivatives of dimeric cholesterols

Solvents	**1**	MGC	**2**	MGC	**3**	MGC	**4**	MGC	**5**	MGC
Methanol	I		I		I		I		P	
Ethanol	I		G	1.25	I		I		P	
1-Propanol	P		G	0.92	P		P		P	
1-Butanol	G	0.26	G	0.91	P		P		P	
1-Pentanol	G[a)]	0.33	G	0.76	P		P		P	
1-Hexanol	G[a)]	0.20	G	1.21	G	3.40	P		P	
1-Heptanol	G[a)]	0.28	G	1.20	G	3.31	P		P	
1-Octanol	G[a)]	0.40	G	1.19	G	1.79	P		P	
1-Nonanol	G[a)]	0.89	G	1.19	G	1.78	P		P	
1-Decanol	G[a)]	0.36	G	1.18	G	1.77	P		P	
Toluene	VS		TLG	1.70	TG	4.15	P		P	
Benzene	TLG	3.10	TLG	1.69	TG	3.47	P		P	
Xylene	TUS		P		TG	4.34	P		G	4.40
Ethyl acetate	P		G	1.10	P		I		G	3.23
Butyl acetate	G	0.38	G	1.12	G	3.36	TLG	3.37	P	
DMSO	TUS		G	2.70	P		G	2.57	P	
DMF	G[a)]	0.16	G	1.25	P		P		P	
Cyclohexane	I		TG[a]	0.17	G	0.43	I		TLG	1.5
1-Heptane	P		P		TUS		I		I	
TEA	P		P		G	1.02	P		P	
Acetic acid	G	0.94	G	0.81	P		P		G	0.38
Diethyl ether	I		I		I		I		I	
Acetone	P		P		P		I		I	
THF	TUS		S		S		S		S	
H_2O	I		I		I		I		I	

TLG, translucent gel; I, Insoluble; TG, transparent gel; TUS, turbid solution; S, transparent solution; P, precipitate. a) The color of gel is changing from white to translucent with the decrease of gelator concentration.

such gelators is not favorable for the gelation of most of the organic solvents. Moreover, in most cases, for a given solvent the minimum gelation concentrations (MGCs) of these gelators increase with increasing the linker lengths. The reasons for the linker effect on the gelation behaviors can be the change of the spatial conformation of the gelators as revealed by computer simulation (*c.f.* Figure S1 in Supporting Information), which may decrease the ability of the gelator molecules to self-assemble into ordered structures, a necessity for forming network structures.

4.3 Morphology studies

To obtain a visual insight into the gel microstructures, the linker effects, solvent effects and concentration effects on the structures of the gel networks were studied by SEM technique.

Figure 1 shows some typical SEM images of the gels. It shows that the microstructures of the xerogels of **1**, **2**, and **3** in benzene are significantly different from each other, and the morphologies of the aggregates change from the fiber, rod to lamella with increasing the linker lengths of the gelators. A similar linker effect was also observed in other systems as shown in Figures 1(d)–(f), and Figure S2 (*c.f.* Supporting Information). The morphologies of the aggregates shown in the SEM images may be rationalized by considering a commonly accepted idea that highly directional intermolecular interactions, such as hydrogen bonding or metal-ligand interactions, favor formation of fiber structures. The increase in the number of methylene unit in the linkers of the gelators provides the gelators more opportunities in adopting conformations of lower energies, which must weaken the hydrogen-bonding interactions between gelator molecules, and result in loss of flexible fine fibrous structure [27].

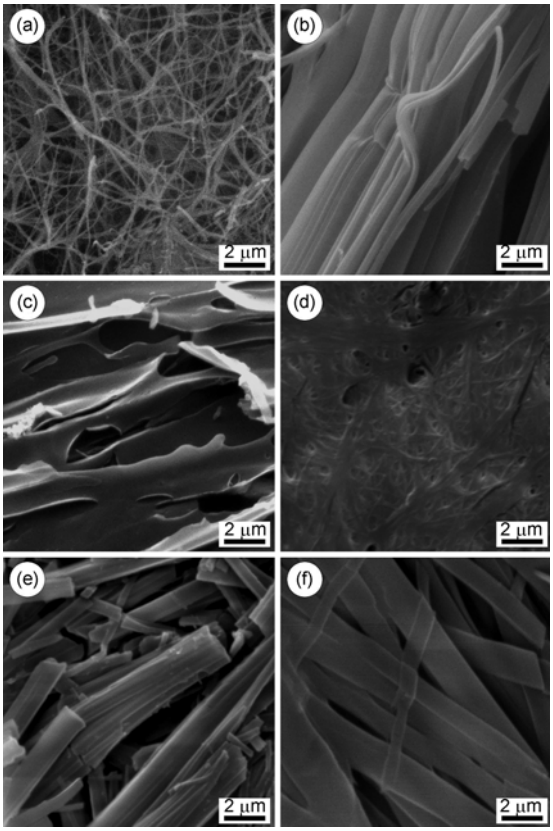


Figure 1 SEM images of the xerogels from the gels of **1**/benzene (a), **2**/benzene (b), and **3**/benzene (c) and those from **1**/1-heptanol (d), **2**/1-heptanol (e), and **3**/1-heptanol (f).

It is helpful to have a close inspection of the gelation behaviors of compounds **2**, **3**, **4** and **5** in DMSO. Table 1 shows that **3** and **5** do not gel DMSO even at a concentration of 5.0%, but **2** and **4** form stable gels in DMSO at concentrations below 3.0%. More interestingly, the structures of the xerogels of **2** and **4** from DMSO are characterized by lamellar structures (*c.f.* Figure 2(a), and (c)). By contrast, the precipitates of **3** and **5** from DMSO take micro-particle like structures (*c.f.* Figure 2(b) and (d)). Both the gelation behaviors of the compounds and their aggregate structures show an even-odd effect considering the number of the methylene units in the linkers. This kind of phenomena concerning the self-assembling morphologies has already been reported by other groups [28–30]. The reasons for the effect are not clear at this moment, but changes in the gelator-gelator and gelator-solvent interactions are the origin of the effect which may be interrogated by conducting FTIR measurements as described below.

The polarity of a solvent may have a great effect on its interaction with a given gelator. Accordingly, solvents of different polarities (The relative polarities of acetic acid, DMSO, benzene, and cyclohexane are 64.8, 44.4, 11.1, and 0.6, respectively.) have been chosen as sample solvents to investigate the solvent effect on the aggregation and gelation

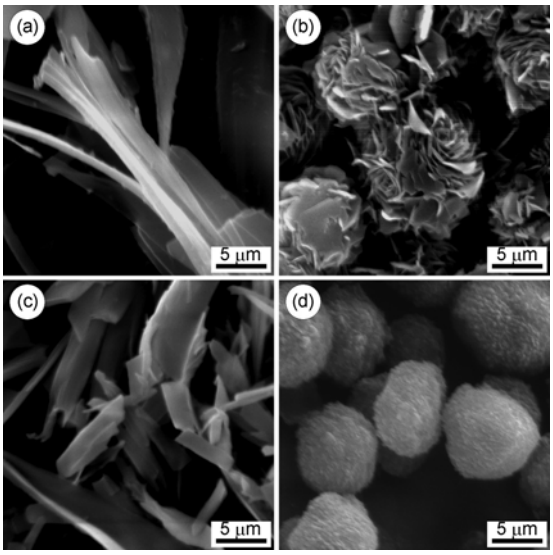


Figure 2 SEM images of the xerogels of **2** (a) and **4** (c) from DMSO and those of the precipitates of **3** (b) and **5** (d) from the same solvent.

behaviors of the compounds. The microstructures of the xerogels of **2** in these solvents are shown in Figure S3 (*c.f.* Supporting Information). It shows that **2** aggregated into thick fibers and lamella structures in acetic acid and DMSO, respectively. However, it aggregated into thin fabric bundles in cyclohexane and benzene. According to the opinion of Dordick [27], the different aggregation behavior of **2** in different solvents can be explained by considering the different strengths of the gelator-solvent interactions. It is believed that in the presence of stronger gelator-solvent interaction, particularly in the presence of specific gelator-solvent interaction, more solvent molecules will occupy the hydrogen bonding sites of the gelator, resulting in weakening of the gelator-gelator interaction. As a result, gelator molecules tend to form thicker fibers or lamellas via the mediation of solvent molecules.

To obtain information of the effect of gelator concentration on the molecular aggregation, the microstructures of freezing-dried cyclohexane gels of **2** at concentrations from 0.5% to 3.0% were studied by conducting SEM measurement. The results are shown in Figure 3. It shows that **2** aggregated into rigid and thick fibers at a high concentration (3.0%) in cyclohexane, and flexible and thin fibers at lower concentrations (2.0%, 1.0% and 0.5%). At the same time, the fresh gels changed from white to transparent with decreasing the gelator concentrations. These results suggest that the rigid and thick fiber may be clusters of many flexible fine fibers.

4.4 Hydrogen bond formation

FTIR spectroscopy is a powerful technique to verify hydrogen bond formation between molecules [31, 32]. Accordingly, the FTIR spectra of **2** in $CDCl_3$ (solution state, 2.0%) and **2** in benzene (gel state, 2.0%) were recorded and are shown in Figure 4. It shows that the three typical absorption bands of **2** corresponding to the stretching vibrations of N–H and C=O, and the bending vibration of N–H appeared at 3448.1 cm^{-1}, 1655.6 cm^{-1}, and 1537.6 cm^{-1}, respectively. Upon gelation, the bands shifted to 3420.3 cm^{-1}, 1640.3 cm^{-1} and 1558.4 cm^{-1}, respectively, suggesting direct participation of the groups to intermolecular interactions. Considering the aprotic identity of the solvents involved, the potential hydrogen bond formation properties of the groups and the relatively extended conformation adopted by **2** (*c.f.* Figure S1, Supporting Information), we believe changes in the FTIR absorptions may be indications of intermolecular hydrogen bond formation. This tentative conclusion was further supported by the result from temperature-dependent ^{1}H NMR studies. In the studies, the gel of **2**/d^6-benzene was used as a sample, and the dissolution of the gel was monitored by ^{1}H NMR measurement. The results are shown in Figure 5. Structurally, the solvent has no possibility to participate in the hydrogen bond formation, and thereby the hydrogen bond can solely be ascribed to the gelator-gelator interaction provided it is present in the system. With refer-

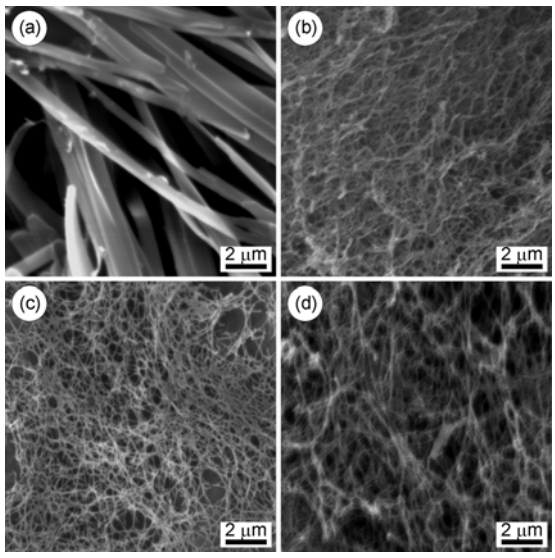


Figure 3 SEM images of the xerogels of **2** from cyclohexane at different concentrations. (1) 3.0%; (2) 2.0%; (3) 1.0%; (4) 0.5%.

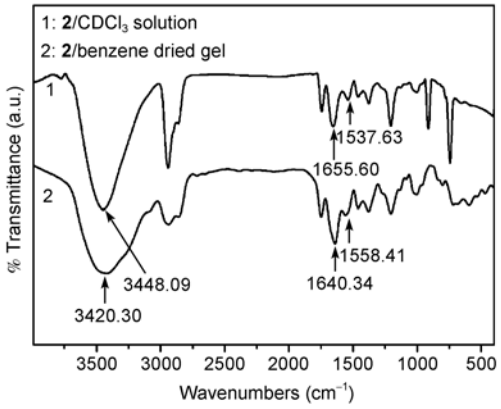


Figure 4 FTIR spectra of **2**/$CDCl_3$ solution and **2**/benzene gel.

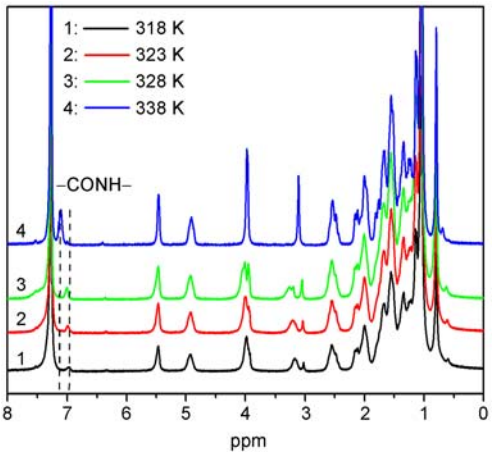


Figure 5 Temperature-dependent ^{1}H NMR spectra of **2**/benzene gel.

ence to Figure 5, the signal of the amide proton of **2** shifts to higher field along with increasing the temperature of the system, an evidence of disruption of the hydrogen bonds, in which the amide proton has been involved [33].

As mentioned previously, the gelation behaviors and the morphologies of the aggregates of **2**, **3**, **4**, and **5** in DMSO showed a remarkable even-odd effect (*c.f.* Table 1, and Figure 2). This effect is closely related with the effect of the linker length on the packing of both the headgroups and the linkers of the compounds, and the packing, particularly that based on hydrogen bond formation, could be investigated by conducting FTIR studies. Accordingly, the FTIR spectra of the aggregates of the four compounds from DMSO were measured, and the characteristic frequencies of the N–H and C=O stretching vibrations, and the N–H bending vibration of the amide groups in the linkers were recorded. The frequencies were plotted as functions of the methylene numbers in the linkers (*c.f.* Figures S4-S6, Supporting Information). The figures reveal, as expected, an even-odd phenomenon, which is a fluctuation change for the chain lengths ($1 \leqslant n \leqslant 4$), an indication of the difference in the strength of the intermolecular hydrogen-bonds of the four compounds, which may affect the balance of dissolution and precipitation and thereby results in different gelation behaviors.

4.5 XRD study

The XRD pattern of a fresh gel of **2**/benzene is shown in Figure 6. The curve for the fresh gel sample shows four peaks in the low angle region (2θ values, 2.12°, 4.26°, 6.42°, and 8.54°) corresponding to d values of 4.13 nm, 2.06 nm, 1.37 nm and 1.04 nm, respectively, suggesting a lamellar packing of the gelator in the gel. Similar XRD measurements were conducted on the fresh aggregates of **2**, **3**, **4**, and **5** from DMSO, and the results are shown in Figures S7–S10 (*c.f.* Supporting Information). The traces shown in Figures S7–S9 reveal that each trace possesses three sharp reflection peaks, and the corresponding *d* values follows a ratio of 1: 1/2: 1/3, suggesting a lamellar structure of the aggregates. It is noteworthy that the precipitate of **5** from DMSO did not show any significant XRD signals in the low angle region, indicating that **5** aggregated in an amorphic state. Further inspection of the figures, reveals that for each systems

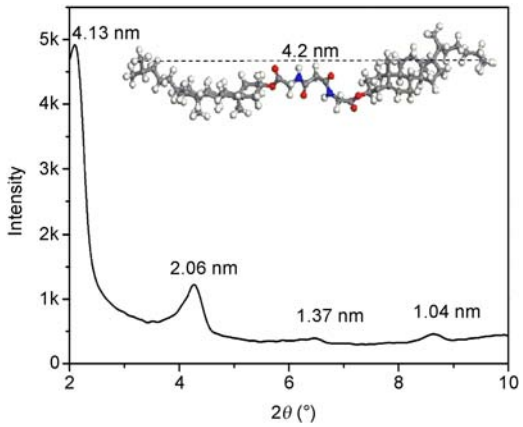


Figure 6 X-ray diffraction trace of the fresh gel of **2**/benzene (3%).

studied except the one containing **5**, the spacing of the first peak is very close to the length of a complex of two molecules, rather than the length of a molecule itself, particularly that of compound **4**. This demonstrates again that the linker length has a great effect on the packing mode of the compounds. It is noteworthy that the intensities of the XRD signals of the systems containing **2** or **4** are much higher than those of the systems containing **3** or **5**, which is another even-odd effect, confirming the observations obtained in the gelation test and in the SEM and FTIR studies of the compounds. Considering the XRD results described above and the hydrogen bonding nature of the linker packing of the compounds as confirmed by FTIR and ^{1}H NMR measurements, a possible packing mode of the compounds in the gels studied was proposed and is schematically shown in Figure 7.

5 Summary

In summary, it has been demonstrated that the gelation behaviors of the novel dimeric cholesteryl derivatives in various organic solvents can be regulated by changing the number of the methylene units of the linker part in the LS_2-type molecules. The compounds containing relatively shorter linkers can gel more solvents than their analogues with longer linkers. Increase in the lengths of the linkers of the compounds results in complete loss of the fibrous

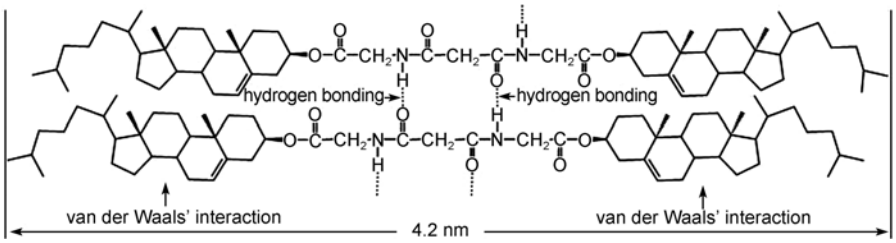


Figure 7 A possible aggregation mode of gelator **2** in benzene.

structure of the aggregates in the gel sate. The morphologies of the aggregates are also affected by the solvent nature. Generally, a less polar solvent favors formation of thin fibers. The gelator concentration is also a significant factor affecting the morphology of its aggregate in gels. Lower concentration is favorable for the formation of networks composed of flexible, thin fibers. FTIR and temperature-dependent ^{1}H NMR studies reveal that hydrogen bonding between the amide N–H and the amide C=O of the gelator is one of the main driving forces for the formation of **2**/benzene gel.

This work was supported by the Ministry of Science and Technology of China (2007AA03Z349), and the National Natural Science Foundation of China (20773083, 20902055).

1 Terech P, Weiss RG. Low molecular mass gelators of organic liquids and the properties of their gels. *Chem Rev*, 1997, 97: 3133–3160
2 Liu XY. Gelation with small molecules: From formation mechanism to nanostructure architecture. *Top Curr Chem*, 2005, 256: 1–37
3 Žinić M, Vögtle F, Fages F. Cholesterol-based gelators. *Top Curr Chem*, 2005, 256: 39–76
4 Fages F, Vögtle F, Žinić M. Systematic design of amide- and urea-type gelators with tailored properties. *Top Curr Chem*, 2005, 256: 77–131
5 Araki K, Yoshikawa I. Nucleobase-containing gelators. *Top Curr Chem*, 2005, 256: 133–165
6 Brizard A, Oda R, Huc I. Chirality effects in self-assembled fibrillar networks. *Top Curr Chem*, 2005, 256: 167–218
7 Kato T, Mizoshita N, Moriyama M, Kitamura T. Gelation of liquid crystals with self-assembled fibers. *Top Curr Chem*, 2005, 256: 219–236
8 Hirst AR, Smith DK. Dendritic gelators. *Top Curr Chem*, 2005, 256: 237–273
9 Carretti E, Dei L, Weiss RG. Soft matter and art conservation. Rheoreversible gels and beyond. *Soft Matter*, 2005, 1: 17–22
10 Xue PC, Lu R, Li DM, Jin M, Bao CY, Zhao YY, Wang ZM. Rearrangement of the aggregation of the gelator during sol-gel transcription of a dimeric cholesterol-based viologen derivative into fibrous silica. *Chem Mater*, 2004, 16: 3702–3707
11 Li CP, Yu Q, Du M. Structural modulation of Cd(II) supramolecular frameworks with a versatile 2,4-dipyridyl-type building block and different dicarboxylate ligands. *Sci China Ser B-Chem*, 2009, 52: 1470–1478
12 Lin YY, Qiao Y, Yan Y, Huang JB. Thermo-responsive viscoelastic wormlike micelle to elastic hydrogel transition in dual-component systems. *Soft Matter*, 2009, 5: 3047–3053
13 Balzani V, Credi A, Raymo FM, Stoddart JF. Artificial molecular machines. *Angew Chem Int Ed*, 2000, 39: 3348–3391
14 de Silva AP, Gunaratne HQN, Gunnlaugsson T, Huxley AJM, McCoy CP, Rademacher JT, Rice TE. Signaling recognition events with fluorescent sensors and switches. *Chem Rev*, 1997, 97: 515–1566
15 Yan XH, Cui Y, He Q, Wang KW, Li JB. Organogels based on self-assembly of diphenylalanine peptide and their application to immobilize quantum dots. *Chem Mater*, 2008, 20: 1522–1526
16 Wu JC, Yi T, Xia Q, Zou Y, Liu F, Dong J, Shu TM, Li FY, Huang CH. Tunable gel formation by both sonication and thermal processing in a cholesterol-based self-assembly system. *Chem Eur J*, 2009, 15: 6234–6243
17 Sugiyasu K, Fujita N, Shinkai S. Fluorescent organogels as templates for sol-gel transcription toward creation of optical nanofibers. *J Mater Chem*, 2005, 15: 2747–2754
18 Jong JH, Nakashima K, Shinkai S. Preparation of ultrastable mesoporous silica using a phenanthroline-appended cholesterol organogelator as a template. *Nano Lett*, 2001, 1: 145–148
19 Jong JH, Ono Y, Shinkai S. Novel silica structures which are prepared by transcription of various superstructures formed in organogels. *Langmuir*, 2000, 16: 1643–1649
20 Jung, JH, Kobayashi H, Masuda M, Shimizu T, Shinkai S. Helical ribbon aggregate composed of a crown-appended cholesterol derivative, which acts as an amphiphilic gelator of organic solvents and as a template for chiral silica transcription. *J Am Chem Soc,* 2001, 123: 8785–8789
21 Jung JH, Kobayashi H, van Bommel KJC, Shinkai S, Shimizu T. Creation of novel helical ribbon and double-layered nanotube TiO_2 structures using an organogel template. *Chem Mater*, 2002, 14: 1445–1447
22 Wu JC, YiT, Zou Y, XiaQ, Shu T, Liu F, Yang YH, Li FY, Chen ZG, Zhou ZG, Huang CH. Gelation induced reversible syneresis via structural evolution. *J Mater Chem*, 2009, 19: 3971–3978
23 Li YG, Liu KQ, Liu J, Peng JX, Feng XL, Fang Y. Amino acid derivatives of cholesterol as "latent" organogelators with hydrogen chloride as a protonation reagent. *Langmuir*, 2006, 22: 7016–7020
24 Li YG, Fang Y, Liu J, Wang MZ. Synthesis and gelation behavior of cholesteryl glycinate anthraquinone-2-carboxylamide and cholesteryl glycinate 9,10-dimethyloxyl anthracene-2-carboxylamide. *J Chin Chem Soc*, 2006, 53: 359–366
25 Liu KQ, Yan N, Peng JX, Liu J, Zhang QH, Fang Y. Supramolecular gels based on organic dioic acid mono-amides of cholesteryl glycinate. *J Colloid Interface Sci*, 2008, 327: 233–242
26 Peng JX, Liu KQ, Liu J, Zhang QH, Feng XL, Fang Y. New dicholesteryl-based gelators: Chirality and linker length effect. *Langmuir*, 2008, 24: 2992–3000
27 Zhu GY, Dordick JS. Solvent effect on organogel formation by low molecular weight molecules. *Chem Mater*, 2006, 18: 5988–5995
28 Kogiso M, Ohnishi S, Yase K, Masuda M, Shimizu T. Dicarboxylic oligopeptide bolaamphiphiles: Proton-triggered self-assembly of microtubes with loose solid surfaces. *Langmuir*, 1998, 14: 4978–4986
29 Nakazawa I, Masuda M, Okada Y, Hanada T, Yase K, Asai M, Shimizu T. Spontaneous formation of helically twisted fibers from 2-glucosamide bolaamphiphiles. *Langmuir*, 1999, 15: 4757–4764
30 Wang TY, Li YG, Liu MH. Gelation and self-assembly of glutamate bolaamphiphiles with hybrid linkers: Effect of the aromatic ring and alkyl linkers. *Soft Matter*, 2009, 5: 1066–1073
31 Shimizu T, Masuda M. Stereochemical effect of even-odd connecting links on supramolecular assemblies made of 1-glucosamide bolaamphiphiles. *J Am Chem Soc*, 1997, 119: 2812–2818
32 Kogiso M, Ohnishi S, Yase K, Masuda M, Shimizu T. Dicarboxylic oligopeptide bola-amphiphiles: Proton-triggered self-assembly of microtubes with loose solid surfaces. *Langmuir*, 1998, 14: 4978–4986
33 Liu J, Yan JL, Yuan XW, Liu KQ, Peng JX, Fang Y. A novel low- molecular-mass gelator with a redox active ferrocenyl group: Tuning gel formation by oxidation. *J Colloid Interface Sci*, 2008, 318: 397–404