Formation of the Large-scale Ordered Honeycomb Pattern by Organogelator via Self-assembly Process

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Electronic Supplementary Information

Experimental procedure

Materials and methods

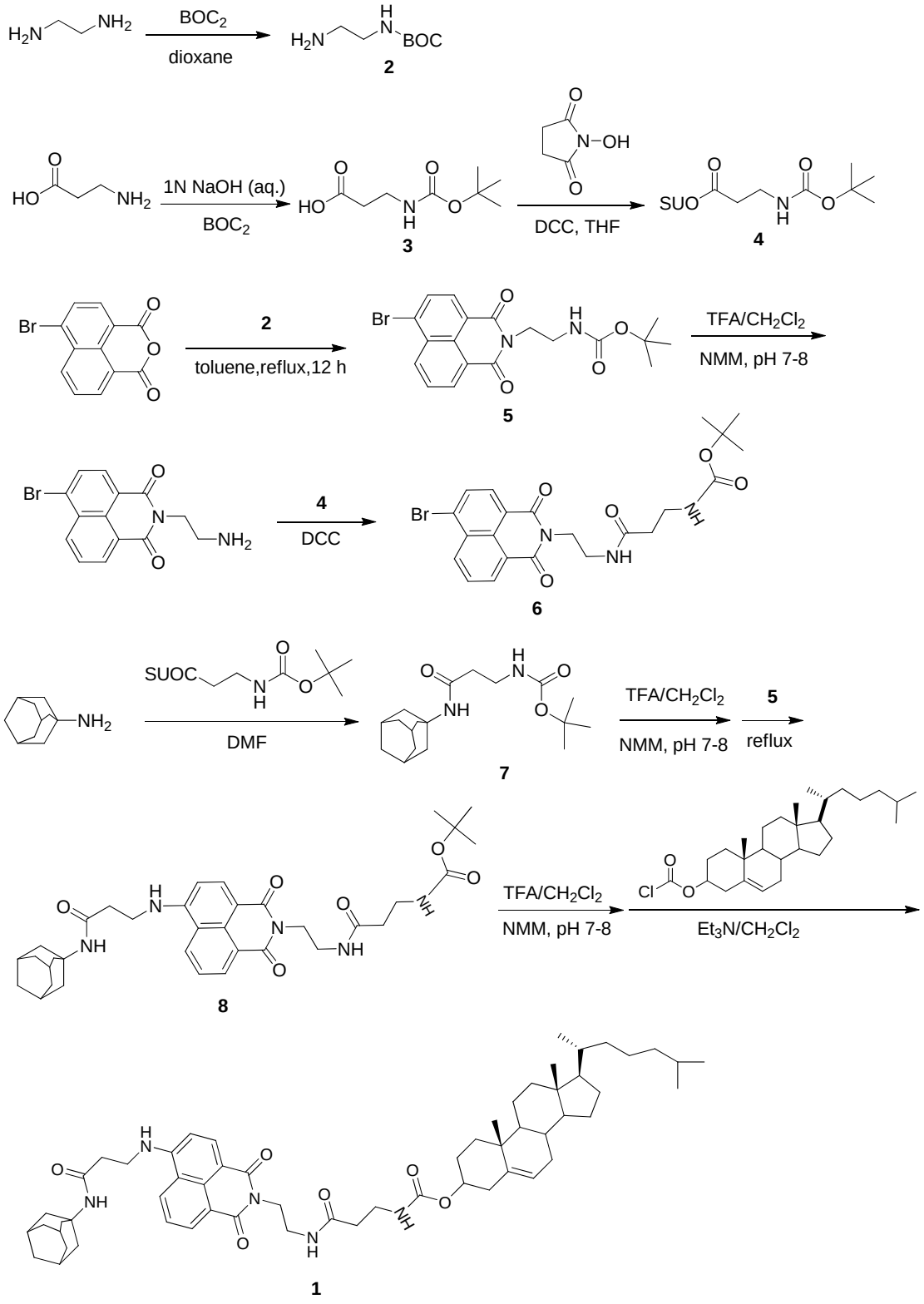
All starting materials were obtained from commercial supplies and used as received. Moisture sensitive reactions were performed under an atmosphere of dry argon. Amantadine Hydrochloride (99%), cholesteryl choroformate (99%), dicyclohexylcarbodiimide (DCC) (99%) and di-tert-butyl dicarbonate (97%) were provided from Alfa Aesar; 4-bromo-1,8-naphthalic anhydride (95%), β-alanine (98.5%), ethane-1,2-diamine (CP), morpholine (CP) and other chemicals were supplied from Sinopharm Chemical Reagent Co., Ltd. (Shanghai). Column chromatography was carried out on silica gel (200-300 mesh). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Mercuryplus-Varian instrument. Proton chemical shifts are reported in parts per million downfield from tetramethylsilane (TMS). MALDI-TOF-MS was recorded on BIFLEX III MALDI-TOF mass spectroscopy instrument (Bruker Daltonics Inc.). Elementary analysis data were obtained on an Elementar vario EL III (Germany). Melting points were determined on a hot-plate melting point apparatus XT4-100A without correction.

SEM images were obtained using a SSX-550 (Shimadzu) with an accelerating voltage of 15 KV and a FE-SEM S-4800 (Hitachi) instrument. Samples were prepared by spinning the samples on glass slices and coating with Au. SAXS diagrams were obtained on a NanoSTAR U SAXS system (Bruker), using a Cu Kα radiation source (λ = 0.1542 nm). The SAXS data

were corrected for absorption and background scattering. UV-Vis absorption and fluorescent spectra were recorded on a UV-Vis 2550 spectroscope (Shimadzu) and an Edinburgh Instruments (FLS 900), respectively. Fourier transform infrared (FTIR) spectra were collected by a Nexus 470 spectrometer (Nicolet Company) with a resolution of 4 cm^{-1}, and 64 scans were accumulated to obtain an acceptable S/N ratio, the samples were prepared with KBr pellets. Original spectra were baseline-corrected by use of Omnic 5.1 software. Particle size distribution was studied by Malvern Zeta Sizer Nano Series, Nanosizer ZS90 and Malvern Autosizer4700. Confocal laser scanning microscopy was performed with an OLYMPUS ZX81 laser scanning microscopy and a 60x oil-immersion objective lens.

Synthetic Methods and Characterizations:

Scheme S1



General procedure:

Compounds **2**, **3** and **4** were prepared according to the previously reported method. [1-3]

Preparation of compound 5

A mixture of 4-Bromo-1,8-naphthalic anhydride (20 g, 72 mmol) and (2-Aminoethyl) carbamic acid *tert*-butyl ester (6.0 g, 36 mmol) in toluene (600 mL) was refluxed for 12 h under nitrogen atmosphere. After removal of toluene, the residues was purified by silica gel column chromatography (SiO_2; dichloromethane) to give **5** as a buff solid (9.6 g, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67-8.65 (d, J = 5.6 Hz, 1H), 8.57-8.56 (d, J = 6.8 Hz, 1H), 8.42-8.41 (d, J = 6.4 Hz, 1H), 8.05-8.03 (d, J = 6.4 Hz, 1H), 7.86-7.83 (t, J = 6.2 Hz, 1H), 4.94 (s, 1H), 4.35 (m, 2H), 3.53 (d, 4.0H), 1.27 (s, 9H);

Preparation of compound 6

Trifluoroacetic acid (TFA, 12 mL) was added to a solution of **5** (8.80 g, 21 mmol) in CH_2Cl_2 (12 mL). The reaction mixture was stirred at room temperature for 10 h. Then, the solvent was evaporated in vacuo at 40 °C. The residue was dissolved in CH_2Cl_2 (50 mL) and the solution was neutralized with NMM to pH 7 - 8. Then, **4** (5.72 g, 0.02 mol) was added. The reaction mixture was stirred for 16 h at room temperature. The resulting solution was filtered. The filtrate was poured into water and extracted with ethyl acetate. The organic layer was then washed, dried and concentrated. The residues were purified by silica gel column chromatography (SiO_2; dichloromethane/ methanol = 50:1) to give **6** as a buff solid (7.8 g 80%). Mp> 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67-8.65 (d, J = 8.0 Hz, 1H), 8.59-8.57 (d, J = 8.0 Hz, 1H), 8.42-8.40 (d, J = 8.0 Hz, 1H), 8.05-8.03 (d, J = 8.0 Hz, 1H), 7.87-7.83 (t, J = 4.4 Hz, 1H), 6.42(s, 1H), 5.24 (s, 1H), 4.40-4.38 (t, J = 4.4 Hz, 2H), 3.68-3.64 (q, J = 4.0 Hz, 2H), 3.34-3.30(q, J = 4.0 Hz, 2H), 2.31-2.29 (t, J = 4.4 Hz, 2H), 1.38 (s, 9H).

Preparation of compound 7

To a suspension of 1-adamantanamine hydrochloride (4 g, 22 mmol) in DMF (60 mL), TEA (3 mL, 22 mmol) and Boc-β-Ala Osu (6 g, 20 mmol) were added. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness. The residue was taken

up in EtOAc (200 mL). The crude product was dissolved in ethyl acetate; the solution was washed with 10% citric acid, saturated sodium chloride, 5% sodium carbonate and saturated sodium chloride solutions, dried (Na_2SO_4), and evaporated to dryness. The residue was purified by column chromatography (SiO_2; ethyl acetate / Petroleum ether = 1:1) to yield **7** as a white solid (4.82 g, 75%). Mp> 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (s, 1H), 5.22 (s, 1H), 3.38-3.34 (q, J = 4.0 Hz, 2H), 2.33-2.30 (t, J = 4.0 Hz, 2H), 2.07 (s, 3H), 1.99 (s, 6H), 1.68 (s, 6H), 1.44 (s, 9H).

Preparation of compound 8

Trifluoroacetic acid (TFA, 21 mL) was added to a solution of **7** (4.82 g, 15 mmol) in CH_2Cl_2 (24 mL), the reaction mixture was stirred at room temperature for 10 h. Then, the solvent was evaporated in vacuo at 40 °C. The residue was dissolved in CH_2Cl_2 (50 mL) and the solution was neutralized with NMM to pH 7-8. Then, a mixture of **5** (5.39 g, 11 mmol), K_3PO_4 (4.3 g 20 mmol), CuI (1.9 g, 1 mmol), L-Proline (0.23 g, 2 mmol) was added to 10 mL of DMSO. The reaction mixture was stirred for 48 h at 120 °C under nitrogen atmosphere. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentration in vacuo. The residual oil was purified by column chromatography (SiO_2; ethyl acetate) to obtain **8** (1.6 g, 23%) as yellow solid. Mp > 300 °C. ^{1}H NMR (400 MHz, DMSO) δ 8.62-8.62 (d, J = 8.0 Hz, 1H), 8.45-8.43 (d, J = 8.0 Hz, 1H), 8.29-8.27 (d, J = 8.0 Hz, 1H), 7.98 (s, 1H), 7.77 (s, 1H), 7.70-7.68 (t, J = 4.0 Hz, 1H), 7.44(s, 1H), 6.82-6.80 (d, 1H), 6.63 (s, 1H), 4.12-4.09 (t, J = 4.4 Hz, *2*H), 3.60-3.56 (q, J = 4.0 Hz, *2*H), 3.08-3.04 (q, J = 4.4 Hz, *2*H), 2.13-2.10 (t, J = 4.4 Hz, 2H), 1.99 (s, 3H), 1.92 (s, 6H), 1.60 (s, 6H), 1.37 (s, 9H). ^{13}C NMR (100MHz, DMSO): δ 171.13, 170.28, 164.73, 163.88, 156.05, 151.02, 134.84, 131.26, 130.20, 129.01, 124.95, 122.70, 120.79, 108.59, 104.45, 78.25, 51.42, 40.80, 37.56, 36.71, 36.53, 36.43, 35.79, 29.46, 28.92.

Preparation of compound 1

Trifluoroacetic acid (TFA, 12 mL) was added to a solution of **8** (1.45 g, 2.3 mmol) in CH_2Cl_2 (15 mL), the reaction mixture was stirred at room temperature for 10 h. Then, the solvent was

evaporated in vacuo at 40 °C. The residue was dissolved in CH_2Cl_2 (18 mL) and the solution was neutralized with NMM to pH 7-8. Then, a dichloromethane solution (20 mL) of cholesteryl chloroformate (1.5 g, 3.3 mmol) was added drop wise over 1.5 h at 0 °C and the mixture was stirred for 12 h at room temperature, and concentrated in vacuo. The residue was purified by silica gel column chromatography (SiO_2; dichloromethane/methanol = 20:1) to obtain **1** as hyacinth solid (1.5 g 70%).

Mp > 300 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59-8.57 (d, J = 8.0, 1H), 8.46-8.44 (d, J = 8.0 Hz, 1H), 7.64-7.61 (d, J = 6.24 Hz, 1H), 6.68-6.67 (d, J = 4.0 Hz, 1H), 6.39 (s, 1H), 5.56 (s, 1H), 5.34-5.33 (m, 1H), 5.30 (s, 1H), 4.43 (s, 1H), 4.40-4.38 (t, J = 4.0 Hz, 1H), 3.69-3.67 (t, J = 4.0 Hz, 2H), 3.65-3.62 (q, J = 4.0 Hz, 2H), 3.57-3.50 (m, 1H), 3.41-3.38 (q, J = 4.0 Hz, 2H), 2.58-2.56 (t, J = 4.0 Hz, *2*H), 2.31-2.29 (m, 1H), 2.24-2.20 (m, 1H), 2.09 (s, 3H), 2.00 (s, 6H), 1.98-1.96 (m, 1H), 1.94-1.92 (m, 2H), 1.85-1.79 (m, 4H), 1.69 (s, 6H), 1.66-0.67 (m, 33H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 171.1, 165.4, 164.8, 156.6,150.2, 140.1, 134.9, 131.5, 129.9, 127.3, 124.7, 122.6, 122.3, 120.5, 109.2, 104.0, 77.6, 77.3, 77.0, 74.4, 56.9, 56.3, 52.6, 50.2, 42.5, 41.8, 40.1, 40.0, 39.7, 39.5, 38.8, 37.2, 36.7,36.4, 36.0, 35.3, 32.1, 29.6, 28.4, 28.2, 24.5, 24.1, 23.1, 22.8, 21.2, 19.6, 18.9, 12.1. MALDI-TOF-MS, 966.7 $[M+Na]^+$, Elemental analysis calcd (%) for $C_{58}H_{81}N_5O_6 \cdot 2H_2O$: C 71.06, H 8.74, N 7.14; Found: C, 71.32; H, 9.15; N, 6.98.

The gelation test: The gelation test on **1** was carried out with various solvents using a test tube inversion method. The gelators and the solvents were put in a septum-capped test tube and heated (> 75 ºC) until the solid was dissolved. Then the sample vial was cooled to 25 ºC (prepared sample). Gel was obtained when the prepared sample left for a period of time in a certain solvent (for example half an hour in methylene chloride) at the ambient conditions. Qualitatively, gelation was considered successful if no sample flow was observed upon inverting the container at room temperature.

Table S1 Gelation property of compound **1**

Solvent	**State**	**Tg** /°C	**Stable Period**
petroleum ether	I		
hexane	I		
cyclohexane	I		
n-heptane	I		
carbon tetrachloride	I		
Toluene	P		
p-xylene	I		
benzene	G (45)	64	> 1 week
Isobutyl alcohol	S		
Methylene chloride	G (25)	34.5	> 1 week
n-butanol	S		
n-butyl acetate	S		
n-propanol	P		
tetrahydrofuran	S		
ethanol	P		
ethyl acetate	G (50)	75	~1 day
i-propanol	G (50)	54	> 1 week
chloroform	S		
Dioxane	G (35)	89	> 1 week
Acetone	I		
Acetonitride	I		
methanol	I		
Dimethyl sulfoxide	I		
water	I		

State: G = gel; P = Precipitation; S = Solution; I = Insoluble. The critical gelation concentrations were included in the parentheses (mg mL^{-1})

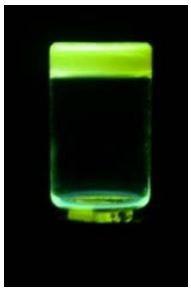


Fig. S1 Image of the gel in CH_2Cl_2 (25 mg/mL).

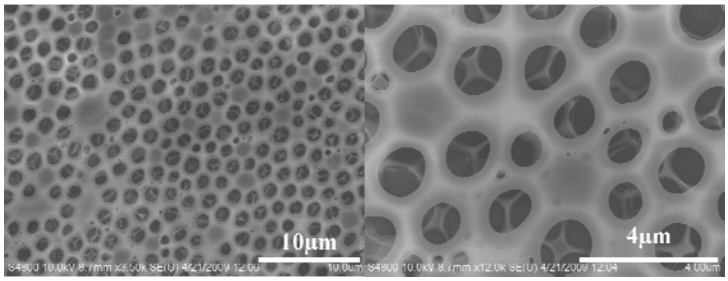


Fig. S2 SEM image of the multilayer pattern of **1** from CH_2Cl_2 (2.5 mg/mL)

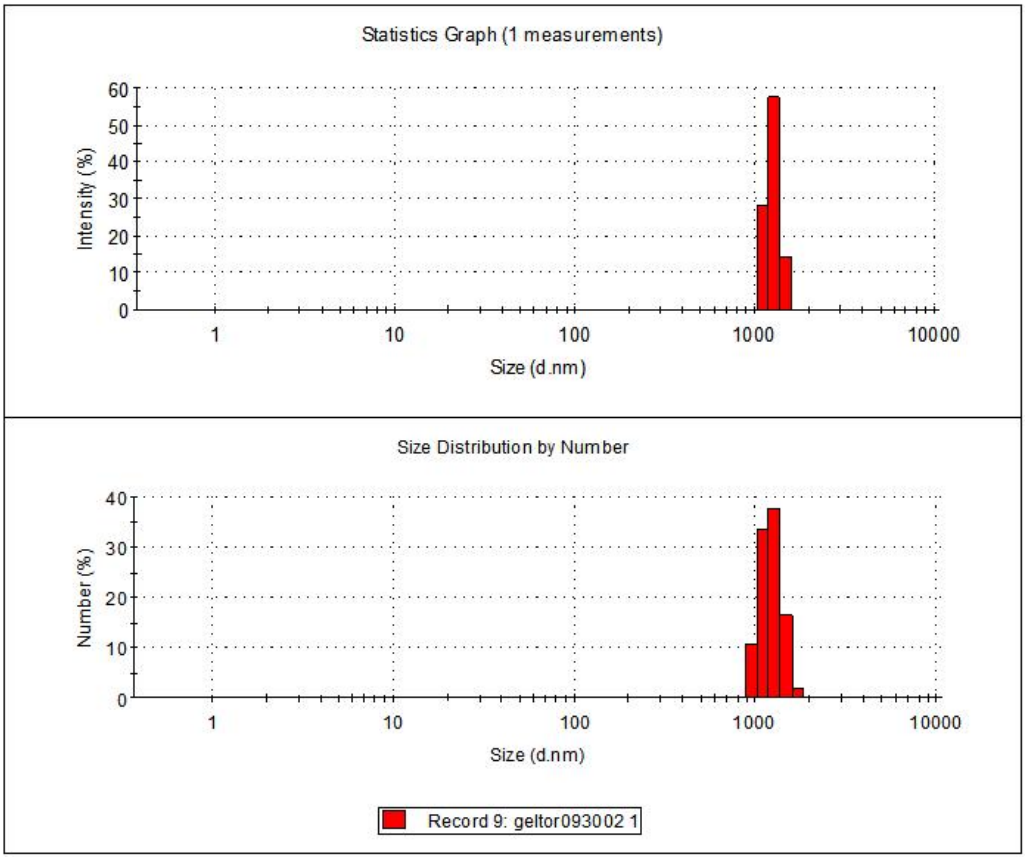


Fig. S3 The dynamic light scattering (DLS) of **1** in dichloromethane (5.0 mg/mL) in the size distribution by number and intensity, respectively.

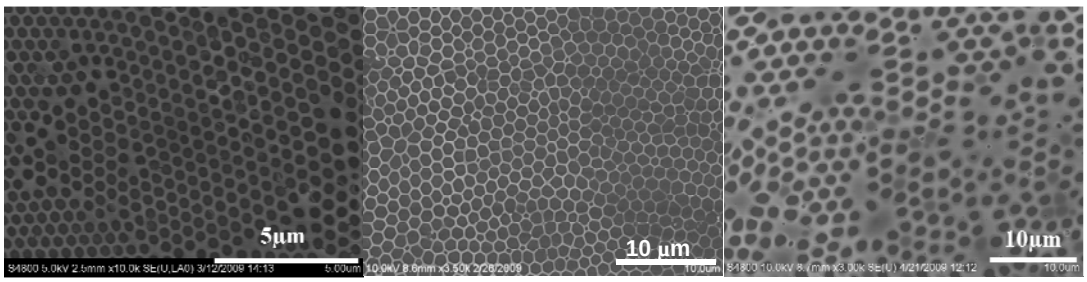


Fig. S4 SEM image of the macro porous structure formed by **1** in dichloromethane (2.5 mg/mL) on polished mica surface, glass surface and silica surface (left to right).

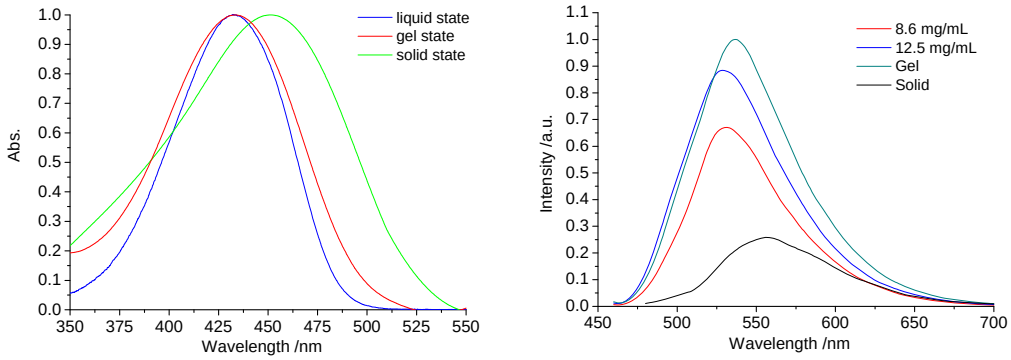


Fig. S5 Absorption and fluorescent emission spectra of **1** in solution (CH_2Cl_2, 30 mM), gel (CH_2Cl_2, 25 mg/mL) and solid state of at room temperature (λ_{ex} = 420 nm).

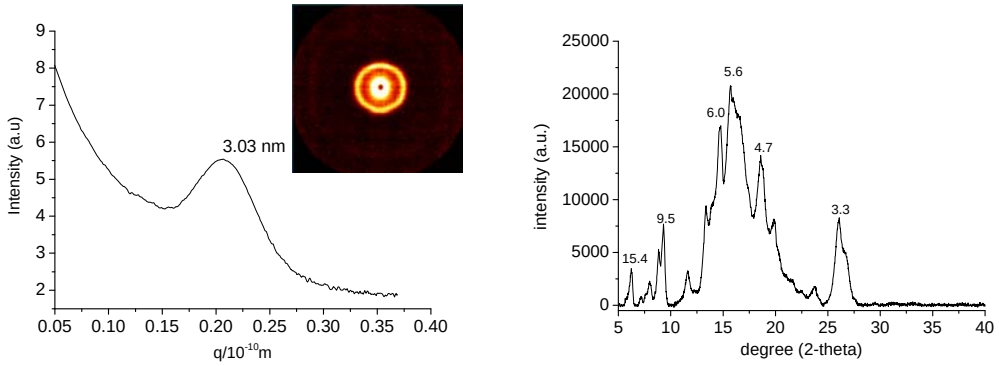


Fig. S6. X-ray diffraction patterns of **1** xerogel in CH_2Cl_2 at room temperature. d values are as follows: d = 30.3, 15.4, 12.8, 11.2, 10.0, 9.5, 7.6, 6.6, 6.0, 5.6, 4.7, 4.5, 3.7, 3.4 Å

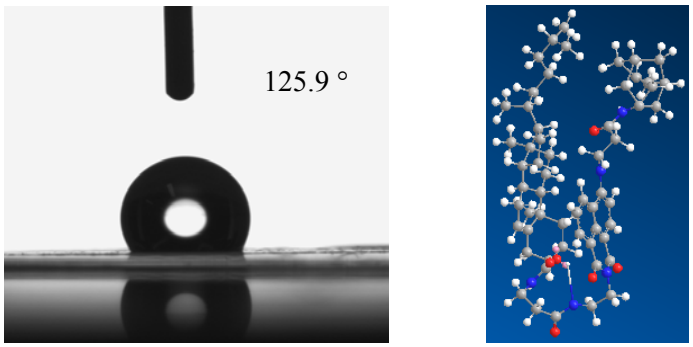


Fig. S7 Photographs of a water droplet on glass slices spin-coated with **1**

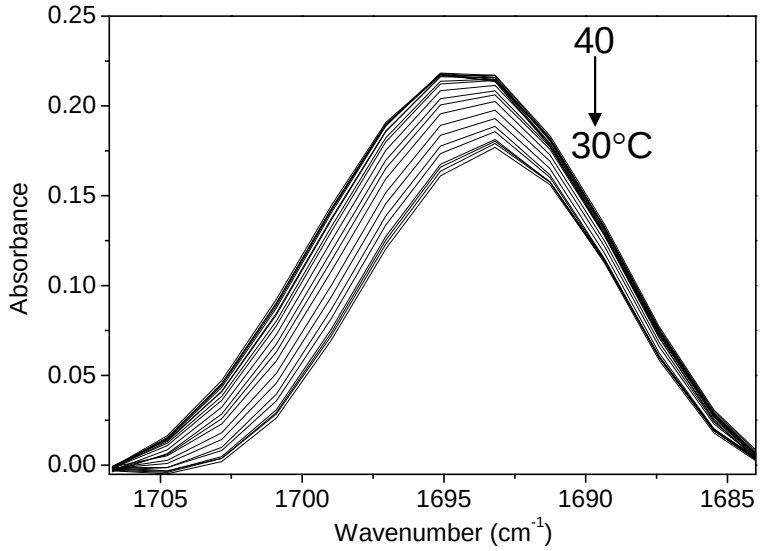


Fig. S8 Temperature-variable IR spectra in C=O stretching region in the temperature range of 40–30°C (temperature interval is 0.5°C)

Table S2 Tentative Spectra Assignment for 2D IR

Wave number/cm^{-1}	Assignment	Wave number/cm^{-1}	Assignment
3381	ν (N-H) (linking to naphthyl)	2964	2ν (C=O) (linking to naphthyl)
3363	ν (linking to adamantane)	2924	ν_{as} (CH_2) (adamantane)
3346	ν (H-bonding N-H) (-CO-CH_2-CH_2-NH-)	2914	ν_{as} (CH_2) (-CO-CH_2-CH_2-NH-)
3309	ν (H-bonding N-H) (-CO-CH_2-CH_2-NH-)	2889	ν (C-H) (cholesteryl)
3255	ν (H-bonding N-H) (-CO-CH_2-CH_2-NH-)	2879	ν_s (CH_3) (cholesteryl)
3221	ν (H-bonding N-H) (-CO-CH_2-CH_2-NH-)	2854	ν_s (CH_2) (-CO-CH_2-CH_2-NH-)
3070	2δ(N-H)	2846	ν_s (CH_2) (cholesteryl)
3055	ν_{as} (CH_2Cl_2)	2821	ν_s (CH_2) (cholesteryl)
3043	ν (C-H) (naphthyl)	1699	ν (C=O) (-$(CO)_2$-N<)
2987	ν_s (CH_2Cl_2)	1691	ν (C=O) (-CO-NH-)

2D IR can discern the sequence of group motions upon temperature perturbation. The synchronous and asynchronous patterns were generated from the temperature variable IR spectra in Fig. 4a. The red and yellow colors represent positive intensities while blue colors negative ones. According to Noda's rule, [4]

if the cross-peaks (v_1, v_2, and assume $v_1 > v_2$) in synchronous and asynchronous spectra have the same sign, the change at v_1 may occur prior to that of v_2, and vice versa. Combining the signs of cross peaks in synchrnous and asynchronous spectra in Fig. 4c and d, we deduced the sequence as follows: 3346 → 2821 → 3255 → 2879 → 3221 → 2846 → 3192 → 3309 → 3363 → 2889 → 3055 → 2987 → 3043 → 3381 → 3070 → 2964 → 2924 → 2914 → 2854 cm^{-1}. Based on the tentative spectra assignment in Table S2, this sequence can be interpreted as: -CO-CH_2-CH_2-NH- → cholesteryl → CH_2Cl_2 → naphthyl → adamantane.

References

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(2) L. Salmon-Chemin, E. Buisine, V. Yardley, S. Kohler, M. A. Debreu, V. Landry, C. Sergheraert, S. L. Croft, R. L. Krauth-Siegel, E. Davioud-Charvet, *J. Med. Chem.* 2001, **44**, 548.
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