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Self-assembly of a silylated steroid-based organogelator and its use as template for the in situ sol–gel polymerization of tetraethyl orthosilicate

Valeria C. Edelsztein, Gerardo Burton, Pablo H. Di Chenna *

Departamento de Química Orgánica and UMYMFOR (CONICET-FCEN), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pabellón 2, C1428EGA Buenos Aires, Argentina

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ABSTRACT

In this paper we report the synthesis of a new steroid-based low-molecular weight organogelator, the analysis of the self-assembled fibrilar network (SAFIN) and its use as template for the preparation of SiO_2 nanotubes. This novel steroidal organogelator has a unique structure among the well known family of steroid-based organogelators, the most important characteristic of this molecule is the presence of a silyl ether group at C-3 together with a 6β,19-oxo bridge. It was capable to gelate hydrocarbons and tetraethyl orthosilicate at very low concentrations (<1 wt %). An insight into the aggregation mechanism is provided revealing that complementary interaction between an α-oriented hydrogen bond donor and a β-oriented acceptor on the steroid skeleton is the driving force for the primary 1D self-assembly. The SAFIN was successfully used as template to grow silica nanotubes (external diameter: 40–60 nm, internal diameter: 7 nm and several micrometers length) through a catalyst-free in situ co-assembly polymerization process. Hydrogen bond or electrostatic interactions between the anionic silicate intermediate species and the SAFIN are proposed to be the driving force for templating.

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1. Introduction

The design, preparation, and study of properties of low-molecular mass organogelators (LMOGs) have attracted considerable attention during the last decades due to their potential application in materials science.[1] In particular, the use of LMOGs as templates to direct the growth of a wealth of inorganic and also hybrid nanofibrous materials exhibiting different morphologies has been successfully developed, with many potential applications.[2] A wide variety of molecules have the ability to gelate a broad spectra of organic solvents to form physical, thermoreversible gels, among them steroids are a well known example of LMOGs. Although they have been used and investigated as naturally occurring molecules for many years, the discovery that some are LMOGs was made serendipitously and only a few decades ago.[3] Since then, many steroid derivatives with gelating properties have been developed and the gels transformed into functional materials (fluorescent gels,[4] chemical-responsive gels,[5] templates for materials transcription,[2,6] etc.). Cholesterol derivatives (prepared from commercially available cholesterol) are considered among the most versatile in order to design functional LMOGs. On the other hand, there are very few examples in the literature of synthetic variations at the steroidal skeleton. Cholesterol-based LMOGs tend to form mesophases in which steroid–steroid stacking is governed by van der Waals forces. These interactions together with the extra intermolecular contacts from the pending moieties linked at C-3, result in long range primary one-dimensional growth that finally lead to the 3D self-assembled fibrillar network (SAFIN).[7,8]

Here we report the synthesis of a novel non-cholesteryl steroid LMOG (**1**) and the study of the SAFIN of its gels (Fig. 1). The main characteristic of this new organogelating pregnane steroid is the rigid and inherently asymmetric architecture due to the presence of a 6β,19 oxygen bridge (acting as a hydrogen bond acceptor) and a complementary hydrogen bond donor hydroxyl at position 5α. These functionalities together with the presence of a 3β-*tert*-butyldimethylsilyl ether moiety covalently linked at C-3 make the structure unique among the steroidal LMOGs.

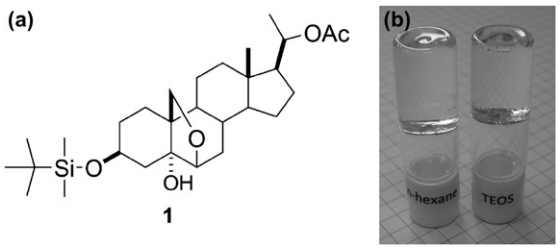

Figure 1. (a) Structure of LMOG **1**. (b) Gels of **1** in *n*-hexane and TEOS (inverted tubes).

* Corresponding author. Tel./fax: +54 11 4576 3346.
E-mail address: dichenna@qo.fcen.uba.ar (P.H. Di Chenna).

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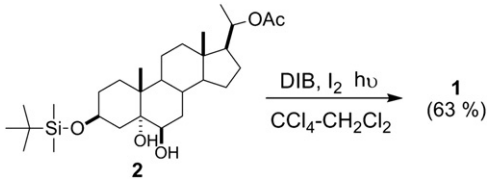
2. Results and discussion

2.1. Synthesis

Compound **1** was first detected by us as a low yield by-product, intermediate in the photochemical reaction of **2** with HgO and iodine, a reaction typically performed in our group for the preparation of secosteroids.[9] After isolation from a chromatography column, **1** showed to gelate *n*-hexane and other hydrocarbon solvents at very low concentration (<1 wt %). This interesting property focused our attention on the synthesis of **1**. Since the HgO/I_2 system oxidizes intermediate **1** to the corresponding secosteroid[10] we applied the photochemical method developed by Suarez et al. to steroid **2** using the iodobenzene diacetate (DIB)/iodine system (Scheme 1).[11] Under these conditions compound **1** was obtained with 63% yield.



Scheme 1. Synthesis of organogelating steroid **1**.

2.2. Gelation and self-assembly analysis

The gelation ability of **1** toward various organic solvents was examined using the simple inversion tube test with a wide range of solvents (Table 1). This compound formed stable, transparent, thermoreversible gels with hydrocarbons and tetraethyl orthosilicate (TEOS) at very low concentration. For example, a transparent gel was formed after a hot solution of **1** (0.2 wt %) in *n*-hexane was allowed to stand for 5 min at room temperature. Using a higher concentration and lower temperatures, **1** could also gelate acetone. Alcohols, even those with long hydrocarbon chains like 1-octanol and 1-dodecanol, cannot be gelated by **1** due to the high solubility observed.

To assess the behavior of **1** from a structural standpoint, T_g versus concentration plots were determined by DSC of gels formed with *n*-hexane and TEOS. Typically, as the concentration was increased, T_g increased until a plateau region was reached at about 0.4 wt % for *n*-hexane and 1.8 wt % for TEOS with a maximal thermal stability of 85 °C and 93 °C, respectively (Supplementary data (S3)). At higher concentrations the gels became turbid, accounting for saturation and precipitation. FTIR spectroscopy of **1** provided evidence that the self-assembly mechanism involved a hydrogen bond interaction of the 5α-hydroxyl, with the 6β,19 oxygen bridge being the most probable acceptor. In dichloromethane solution a broad band was observed at ν_{O-H} 3599.3 cm^{-1} for the O–H stretching, while in the *n*-hexane gel the band was shifted to 3426.9 cm^{-1}, typical of an intermolecular hydroxyl hydrogen bond. As already documented in the literature, not all LMOG molecules are incorporated into the solid-like fibrillar network of the gels,[12] in this case the FTIR spectrum of the gel showed two carbonyl bands for the acetate group, a weak one at $\nu_{C=O}$ 1722.1 cm^{-1} that matched the same band observed in dichloromethane solution and may be associated with **1** in the liquid-like solution phase and a second, more intense, at 1731.8 cm^{-1} corresponding to the solid-like phase of self-assembled molecules (Supplementary data (S4)). The addition of a small amount of methanol to the *n*-hexane gels destroys the SAFIN making it fluid in a few minutes, probably by breaking the intermolecular steroid–steroid hydrogen bond stacking interaction. Nevertheless, we observed that **1** can selectively gelate the organic phase of a mixture of hydrocarbons and water (for example, *n*-hexane or decane) after a heating–cooling process; this property has been also recently reported for some cholesterol-based LMOGs.[13]

To gain a better insight into the packing of the material, X-ray powder diffraction (XRPD) and circular dichroism spectroscopy (CD) were performed. The X-ray diagram of a xerogel of **1** from *n*-hexane showed a single broad peak at *d*=19.57 Å in the small angle region and a broader peak with a maximum between *d*=6.27 and 5.80 Å (Fig. 2). A computational optimized model (semi-empirical, AM1) for a proposed self-assembled structure based on an eight molecule system held together by hydrogen bonds between the 5α-hydroxyl group on one molecule and the bridge oxygen on the next one showed structural dimensions compatible with the XRD pattern. No bond or distance restrictions were imposed during the energy minimization that gave a stabilization energy of 6.49 kcal/mol for each molecule–molecule interaction (relative to a system with the same number of non interacting molecules) and an H···O distance of 2.13 Å for the intermolecular hydrogen bonds (Fig. 3). In the optimized structure steroid molecules packed themselves around the hydrogen bond axis in order to minimize the serious steric hindrance of the bulky *tert*-butyldimethylsilyl groups by forming a helical structure with spiral staircase shape. However, the broadness of the peaks in the large angle region of the XRD pattern indicated a poorly ordered stacking between molecules through the hydrogen bond axis of the 1D assembly. CD of a solution and gel of **1** showed no change after the self-assembly process, supporting a non-helical, disordered stacking around the hydrogen bond axis (Fig. 3c).

To correlate the main structural features present in compound **1** with its gelation ability we determined the gelation properties of

Table 1
Gelation tests of **1** and minimal concentration for gelation (MCG) in organic solvents

Solvent	Test[a]	MCG[b] of **1** (wt %)
n-Pentane	G	0.48
n-Hexane	G	0.20
Cyclohexane	G	0.56[c]
Decane	G	0.20
1-Octanol	S	—
Methanol	S	—
Dodecanol	S	—
Ethyl acetate	S	—
Toluene	S	—
Dichloromethane	S	—
TEOS	G	0.60
Acetone	G	3.10[c]
Acetonitrile	S	—
DMSO	P	—

[a] Inversion tube test: G: stable gel, S: solution, P: precipitate.
[b] At 25 °C.
[c] Gelates at 5 °C.

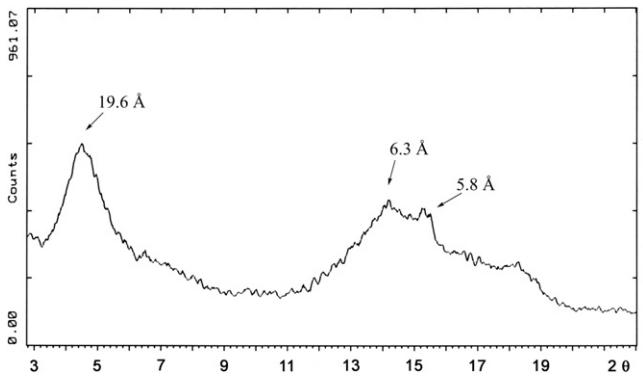


Figure 2. Powder X-ray diffraction pattern of the xerogel of **1** from *n*-hexane.

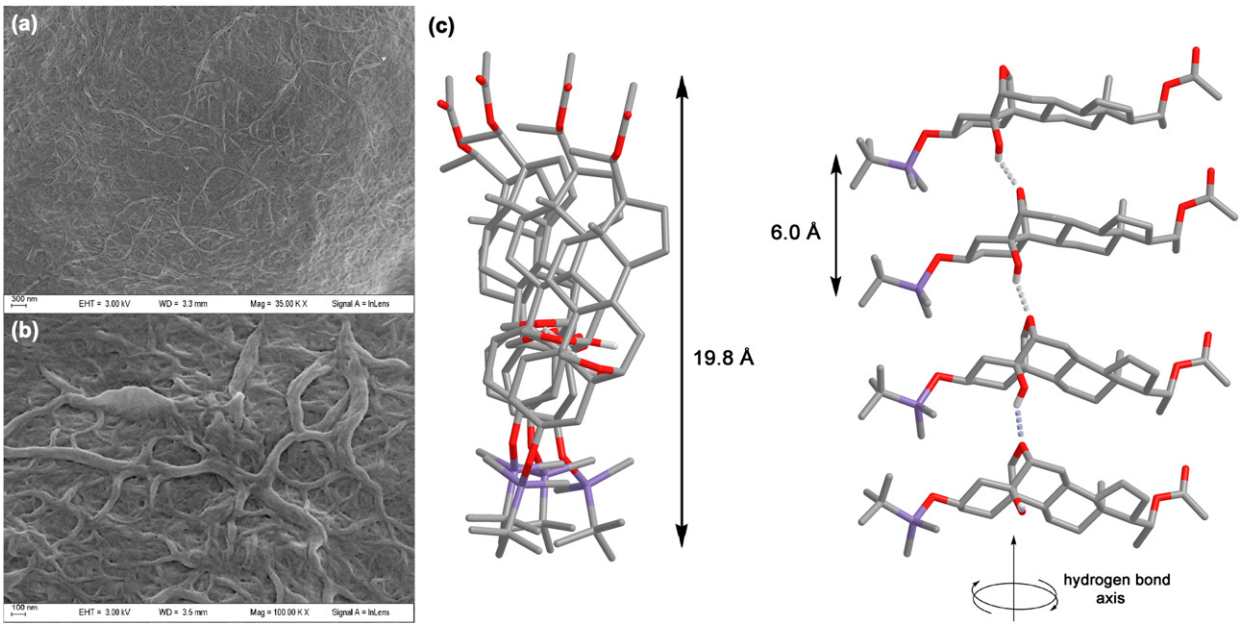
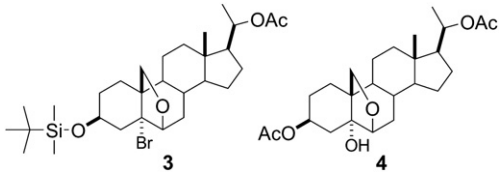


Figure 3. (a,b) SEM images of xerogel of **1** from *n*-hexane. (c) Proposed structure for the self-assembly of **1** (HyperChem 8.0.4, AM1), only four of the eight molecules of the system are shown for clarity, hydrogen atoms are not shown, except hydrogen bonds in dotted lines. The hydrogen bond axis of the 1D assembly is marked.

analogues **2**, **3**, and **4**. Compound **2**, the synthetic precursor of organogelator **1** (Scheme 1), has a complementary 5α,6β-dihydroxy functionality that could lead to intermolecular complementary hydrogen bonds in a 1D self-assembled structure. However, this compound did not gelate any solvent; this pointed to the importance of the alignment between the complementary groups involved in the hydrogen bond and the need for well differentiated H-bond donating and H-bond accepting faces (α and β faces of the steroid nucleus in **1**). Replacement of the 5α-hydroxy group of **1** by a bromine as in compound **3** (Scheme 2) resulted in the loss of gelation properties supporting the key role of the intermolecular hydrogen bond interaction in the 1D self-assembly of **1**. To evaluate the influence of the bulky *tert*-butyldimethylsilyl group, we determined the gelation properties of the 3β-acetoxy analogue **4**, previously prepared by us.[10] This compound did not gelate any solvent showing the important role of the bulky silyl group and its hydrophobic interaction in the gelation process. Thus, although the self-complementary hydrogen bond interaction is involved in the SAFIN structure and may be spatially directing the 1D self-assembly, the non-polar interactions between the alkylsilyl groups themselves and with the solvent appear as a determining factor to stabilize the self-assembled structure. A similar conclusion about the determining role of a bulky silyl group has been recently reported for a nucleoside-based alkylsilylated guanosine organogelator with multiple self-complementary hydrogen bond donors and acceptors.[14]



Scheme 2. Analogues of organogelator **1**.

Finally, the microscopic morphology of the xerogel of **1** was analyzed by SEM, TEM, and AFM. The SEM images showed an entangled fibrilar network, with a fiber width ranging from 14 to 40 nm and crosslinked zones up to 100 nm (Fig. 3a and b). Fibers with lengths up to several micrometers were clearly visible. TEM and AFM images are in agreement with the morphology observed (Supplementary data (S5)).

2.3. Template synthesis

As LMOG **1** is a very good gelator of TEOS, sol–gel polymerization experiments by the in situ co-assembly process were performed to investigate the templated synthesis of silica. Attempts to prepare templated silica with gels of TEOS and *n*-hexane/TEOS (70:30) using benzylamine and water as catalysts failed; after 5 days of polymerization at room temperature the SEM images of the product showed spherical particles of silica with a very homogeneous size (40–45 nm) but no templated fibers. However, the slow, catalyst-free, polymerization of a TEOS gel of **1** rendered fibers of SiO_2. The sample of the TEOS gel was stored at room temperature in a sealed flask for 6 months to study the stability of the gel, as time passed the gel turned semitransparent and when the sample was heated and liquified the silica precipitated. We observed the SEM images of this material before and after calcination. In the first case the images showed solid fibers with a very uniform diameter of 40–60 nm and several micrometers length (Fig. 4a–c). A mapping of the sample showed zones of straight ordered fibers between zones of entangled fibrilar network. After calcination, where organic compounds are removed by combustion, SEM pictures showed hollow, straight fibers with a uniform inner diameter of about 7 nm and external diameter comparable to those of the non calcinated material (Fig. 4d–f). It should be pointed out that the SiO_2 resulting from the calcination of the *tert*-butyldimethylsilyl ether moiety present in **1** remains inside the tubes and may form part of the inner wall and/or partially fill the tubes.

The above observations indicated that the organogel structure was successfully transcribed into the silica nanotubes by an exotemplating process. Since **1** is the only molecule that can catalyze the polymerization of TEOS in absence of added catalyst, hydrogen bonding or electrostatic interactions between the 5α-hydroxyl and silicate intermediates is the probable cause of the successful silica

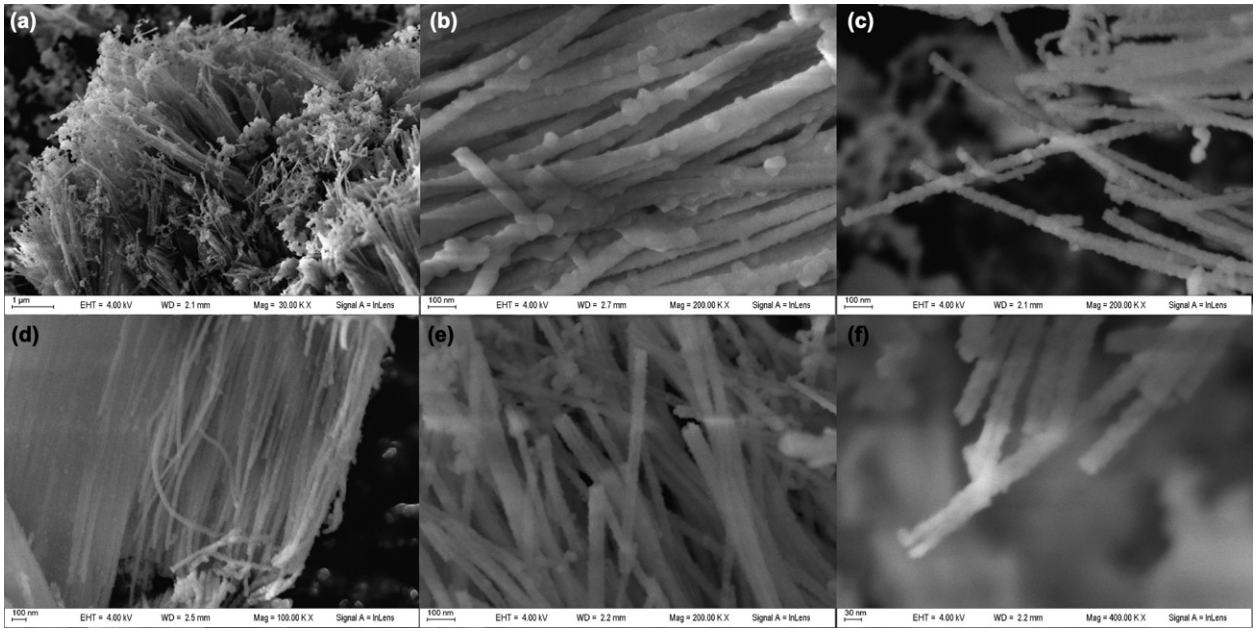


Figure 4. SEM images of templated silica fibers before calcination (a–c) and after calcination (d–f). In images (e) and (f) the hollow fibers are clearly visible.

templating. This is the only way by which the growing silicates may be held near the surface of the fibers and retain the nanoscopic structure of the SAFIN. The crosslinking zones between fibers observed in the xerogel were not found on the templated silica, this clearly indicates that the gel SAFIN collapsed in the drying process of xerogel preparation and so, the inner hollow space of the silica nanotubes shown in Figure 4d–e reflects more accurately the SAFIN structure of the gel. Based on the above results and the 1D hydrogen bond directed self-assembled structure shown in Figure 3, a tentative aggregation model may be proposed. In this model, the 1D stacked molecules further aggregate into a hexagonal column giving rise to fibers that finally form part of the SAFIN trapping the solvent molecules to give a gel (Fig. 5). The dimension of the inner diameter of the silica nanotubes matches with seven units of 1D self-assembled arrays aggregated into a hexagonal column.

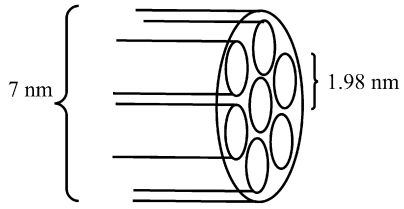


Figure 5. Schematic representation for the formation of the SAFIN based on the inner diameter of the silica nanotubes and the proposed self-assembled mechanism for the organogelator.

3. Conclusions

In summary, we synthesized and characterized the gels of a novel non-cholesteryl LMOG (**1**) possessing a unique structure among the members of the LMOG steroid family and developed a first approach to the preparation of silica nanotubes by the in situ co-assembly process. The self-assembly steroid–steroid stacking of **1** would be governed by intermolecular hydrogen bond interactions between the self-complementary 5α-hydroxyl and 6β,19-epoxy groups, with this functionalities are also directing the growing silicate species of the catalyst-free templated polymerization of TEOS. The presence of the bulky alkylsilyl group is a determining factor for the gelation ability of **1**, thus even though the self-complementary hydrogen bond interaction would direct the one-dimensional growth of the fibers, the non-polar, hydrophobic interactions between the *tert*-butyldimethylsilyl groups themselves and with the solvent appear to be crucial to stabilize the fibers and the SAFIN. The catalyst-free template silica experiment strongly suggests that the 5α-hydroxyl functionality of **1** must be accessible to the solvent molecules in order to direct the growth of the intermediate silica species. Thus, LMOG **1** may be used as a base structure for the design and preparation of new organogelation agents with potential applications in the synthesis of inorganic or hybrid templated materials.

4. Experimental

4.1. Materials

Melting points of crystalline solids were taken on a Fisher-Johns apparatus and are uncorrected. IR spectra of solid samples were recorded in thin films using KBr disks on a Nicolet Magna IR 550 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were measured in a Bruker Avance II 500 (500.13 and 125.72 MHz) NMR spectrometer in deuteriochloroform using TMS as internal standard. The electron impact mass spectra were measured in a Shimadzu QP-5000 mass spectrometer at 70 eV or in a VG-Trio 2 at 20 eV, by direct inlet. Exact mass spectra (ESI) were measured on an Agilent LCTOF, high resolution TOF analyzer with APCI/ESI ionization. Elemental analysis was performed on an EAI Exeter Analytical, Inc. CE-440 apparatus. Analytical thin layer chromatography (TLC) was performed on pre-coated silica plates (Merck F_{254}, 0.2 mm thickness); compounds were visualized by staining with cerium molybdate (Hannessiańs stain). Flash column chromatography was performed on silicagel Merck 9385 (0.0040–0.0063 mm). All solvents used were reagent grade. Solvents were evaporated at 45 °C under vacuum in a rotary evaporator. The homogeneity of all compounds was confirmed by TLC. Products obtained as solids or syrups were dried under high vacuum. Tetraethyl orthosilicate (TEOS, >99.0%, Fluka Analytical) was used as received. 3β,20β-Diacetyloxy-5α-bromo-

6β,19-epoxypregnane was prepared following a synthetic route previously developed by our group.[15]

*4.1.1. 3β-tert-Butyldimethylsilyloxy-5α,6β-dihydroxy-20β-acetoxypregnane (**2**).* Compound **2** was prepared following a synthetic route previously developed by our group.[9] A solution of 3β,20β-diacetyloxypregn-5-ene (5.6 g, 13.9 mmol) in formic acid 88% (50 mL) was stirred at 70–80 °C for 5 min. and then cooled to room temperature. The mixture was treated with 30% H_2O_2 (15 mL) and stirred vigorously overnight. The solution was poured into boiling water (100 mL) and stirred until it reached room temperature. The white solid was filtered, dried under vacuum, and dissolved in methanol (160 mL). The suspension was treated with NaOH 25% (15 mL) and stirred at 0 °C for 1 h. The reaction was quenched with HCl 1 N to pH 7. The methanol was evaporated and the white solid filtered to yield 20β-acetyloxy-3β,5α,6β-trihydroxypregnane (5.5 g). The crude product was dried at 70 °C under vacuum for 6 h, dissolved in anhydrous DMF (140 mL), and treated with imidazole (1.9 g, 27.9 mmol) and *tert*-butyldimethylsilyl chloride (4.2 g, 27.9 mmol) at 0 °C. The mixture was stirred at room temperature overnight. The reaction mixture was poured into brine (50 mL) and extracted with diethyl ether. The organic layer was washed with brine, water, dried over anhydrous Na_2SO_4, filtered, and the solvent evaporated. Purification by flash column chromatography on silicagel with *n*-hexane/ethyl acetate (7:3) gave compound **2** as a white, crystalline solid in 71% yield (5.0 g, 9.8 mmol). Mp 195–197 °C (hexane/ethyl acetate). FTIR (KBr, cm^{-1}) ν 3454 (O–H), 2935 (C–H), 2856, 1716 (C=O), 1376, 1255; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 4.83 (m, 1H, 20-H), 4.05 (1H, m, 3-H), 3.51 (s, 1H, 6-H), 2.01 (s, 3H, CH_3COO–), 1.17 (s, 3H, 19-H), 1.15 (d, 3H, *J*=6.0 Hz, 21-H), 0.88 (s, 9H, *t*-Bu-H), 0.64 (s, 3H, 18-H), 0.05 (s, 6H, $(CH_3)_2Si$–). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 170.4 (COO–), 76.2 (C-5), 76.0 (C-6), 72.8 (C-20), 68.1 (C-3), 55.0 (C-14), 54.9 (C-17), 45.8 (C-9), 42.5 (C-13), 41.2 (C-4), 39.1 (C-12), 38.2 (C-10), 34.3 (C-7), 32.4 (C-1), 31.1 (C-2), 30.5 (C-8), 25.9 ($C(CH_3)_3$), 24.1 (C-15), 24.1 (C-16), 20.8 (C-11), 21.5 (CH_3COO–), 19.9 (C-21), 18.1 ($C(CH_3)_3$), 16.9 (C-19), 12.6 (C-18), −4.5 ((CH_3)Si), −4.6 ((CH_3)Si). HRMS (ESI) calcd for $C_{29}H_{53}O_5Si$ (MH^+) 509.3662; found 509.3666.

*4.1.2. 3β-tert-Butyldimethylsilyloxy-20-acetyloxy-5α-hydroxy-6,19-epoxypregnane (**1**).* To a solution of 3β-*tert*-butyldimethylsilyloxy-20-acetyloxy-5α,6β-dihydroxypregnane **2** (2.9 g, 5.7 mmol) in freshly distilled carbon tetrachloride (100 mL) and dichloromethane (100 mL) were added DIB (2.2 g, 6.8 mmol) and iodine (1.7 g, 6.8 mmol). The solution was then irradiated with two 300 W tungsten lamps for 50 min while being vigorously stirred at room temperature. After the lamps were turned off the reaction was quenched by adding a saturated solution of sodium thiosulfate and stirred until discoloration. The organic layer was washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated to yield a crude product. Purification by flash column chromatography on silicagel with *n*-hexane/ethyl acetate (8:2) afforded **1** as a white crystalline solid in 63% yield (1.8 g, 3.6 mmol). After concentration of the column fractions on a rotary evaporator at 45 °C a gel is formed that needs to be dried for several hours under high vacuum in order to completely remove the solvent. Mp 186–189 °C (hexane/ethyl acetate). FTIR (KBr, cm^{-1}) ν 3599, 2929, 2883, 2859, 1722, 1377, 1078; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 4.84 (m, 1H, 20-H), 3.87 (m, 1H, 3-H), 3.87 (d, 1H, *J*=7.7 Hz, 19a-H), 3.76 (d, 1H, *J*=8.6 Hz, 19b-H), 3.70 (d, 1H, *J*=4.25 Hz, 6-H), 2.01 (s, 3H, CH_3COO–), 1.89 (dd, 1H, *J*=13.6, 11.8 Hz, 4β-H), 1.82 (dt, 1H, *J*=13.0, 3.1 Hz, 12β-H), 1.15 (d, 3H, *J*=6.0 Hz, 21-H), 0.88 (s, 9H, *t*-Bu-H), 0.67 (s, 3H, 18-H), 0.06 (s, 6H, $(CH_3)_2Si$–). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 170.4 (COO–), 81.2 (C-6), 77.6 (C-5), 72.8 (C-20), 69.1 (C-19), 67.2 (C-3), 55.0 (C-17), 54.3 (C-14), 45.0 (C-9), 44.0 (C-10), 43.4 (C-4), 43.1 (C-13), 39.4 (C-12), 33.0 (C-8), 31.5 (C-1), 31.1 (C-2), 25.9 ($C(CH_3)_3$), 25.5 (C-7), 24.0 (C-15), 23.6 (C-16), 22.2 (C-11), 21.5 (CH_3COO–), 19.9 (C-21), 18.1 ($C(CH_3)_3$), 12.9 (C-18), −4.5 ((CH_3)Si), −4.6 ((CH_3)Si). Anal. Calcd for $C_{29}H_{50}O_5Si$: C, 68.7; H, 9.9%. Found: C, 68.5; H, 9.8%; MS (EI) *m*/*z* 507 $(M)^+$, 450 $(M-t\text{-Bu})^+$, 357, 297, 279, 121, 75, 43 (100).

*4.1.3. 3β-tert-Butyldimethylsilyloxy-5α-bromo-20β-acetyloxy-6β,19-epoxypregnane (**3**).* To a solution of 3β,20β-diacetyloxy-5α-bromo-6β,19-epoxypregnane (100 mg, 0.20 mmol) in methanol (3.0 mL) was added 10% aqueous KOH (0.2 mL) at room temperature. The reaction mixture was stirred for 2 h and neutralized with HCl 1 N. The solvent was evaporated and the residue dissolved in dichloromethane. The resulting solution was washed with aqueous sodium bicarbonate, brine, and water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated to give the crude product (82 mg). The product was dissolved in anhydrous DMF (2 mL) without further purification and followed by addition of imidazole (27 mg, 0.40 mmol) and *tert*-butyldimethylsilyl chloride (60 mg, 0.40 mmol). The reaction mixture was stirred at room temperature under N_2 overnight and quenched by addition of brine. The mixture was extracted with diethyl ether and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated to yield the crude product. Purification by flash column chromatography on silicagel with *n*-hexane/ethyl acetate (9:1) afforded 3β-*tert*-butyldimethylsilyloxy-20β-acetyloxy-5α-bromo-6β,19-epoxypregnane (**3**) in 68% yield (80 mg, 0.14 mmol). Mp (hexane/ethyl acetate): 143–144 °C. IR ν_{max} (KBr, cm^{-1}) 2937 (C–H), 2855 (C–H), 1735 (C=O), 1476, 1459, 1377, 1244, 1081, 1022, 834, 780; ^{1}H NMR (ppm) 4.85 (m, 1H, 20-H), 4.11 (1H, m, 3-H), 4.04 (d, 1H, *J*=4.0 Hz, 6-H), 3.93 (d, 1H, *J*=8.5 Hz, 19a-H), 3.69 (d, 1H, *J*=8.5 Hz, 19b-H), 2.01 (s, 3H, CH_3COO–), 1.15 (d, 3H, *J*=6.0 Hz, 21-H), 0.89 (s, 9H, *t*-Bu–H), 0.66 (s, 3H, 18-H), 0.07 (s, 6H, Me_2Si–); ^{13}C NMR (ppm) 170.4 (COO–), 82.2 (C-6), 76.2 (C-5), 72.8 (C-20), 67.8 (C-19), 67.6 (C-3), 54.8 (C-17), 53.8 (C-14), 48.9 (C-9), 45.8 (C-10), 45.5 (C-4), 43.0 (C-13), 39.1 (C-12), 33.1 (C-8), 32.9 (C-1), 31.1 (C-2), 25.87 (*t*-Bu–), 25.5 (C-7), 23.7 (C-15), 23.5 (C-16), 22.6 (C-11), 21.5 (CH_3COO–), 19.9 (C-21), 18.1 (C–*t*-Bu), 12.9 (C-18), −4.6 (($CH_3)_2Si$). HRMS: calcd for $C_{29}H_{49}BrO_4SiNa$ (M+Na) 591.2481; found 591.2476.

4.2. Gelation test in organic solvents

A mixture of the gelator and the solvent in a closed flask were heated and shaken until the solid was dissolved and then cooled to room temperature. If a stable gel was observed after inversion of the flask, it was classified as G. When gelation was not observed at room temperature, the sample was cooled at 5 °C.

4.3. Phase-selective gelation experiment

Compound **1** (8 mg) was added to a flask with a mixture of 1 mL of *n*-hexane and 1 mL of water, the flask was closed, shaken, and heated until the solid was dissolved. Then, the solution was cooled and left at room temperature, after ca. 15 min the *n*-hexane phase became a gel and the water layer was still fluid. The same result was obtained with *n*-decane.

4.4. FTIR measurement

FTIR measurements of the solution and gel of **1** were performed on a Nicolet Magna IR 550 FT-IR spectrometer in a demountable liquid cell with two NaBr disks, 32 mm in diameter and a 0.5 mm thick Teflon spacer. For the *n*-hexane gel, a warm solution of **1** (0.25 wt %) was injected onto the cell and allowed to cool down for 10 min at room temperature before measuring the spectra.

4.5. X-ray powder diffraction measurements

Diffraction pattern was obtained in a Siemens D5000 diffractometer with Cu Kα X-ray (λ=1.54056 Å). Step size: 0.025°, time/step: 6 sec.

4.6. Sol–gel polymerization of TEOS with catalyst

Compound **1** (5 mg) was dissolved in *n*-hexane/TEOS (70:30) and TEOS (1 mL) with addition of benzylamine (5 μL) and water (5 μL) as catalysts by heating and shaking. The solution was cooled to room temperature until gelation was observed and then left at room temperature for 5 days. Subsequently, the sample was dissolved in dichloromethane, the solid was centrifugated, and washed once with dichloromethane. The silica was heated at 200 °C for 2 h and 600 °C for 4 h in air.

4.7. Sol–gel polymerization of TEOS without catalyst

Compound **1** (9 mg) was dissolved in TEOS (1 mL) by heating and shaking. The solution was cooled to room temperature until gelation was observed and then left at room temperature for 6 months. Subsequently, the sample was dissolved in dichloromethane, the solid centrifugated, and washed once with dichloromethane.

4.8. Calcination procedure

Silica nanoparticles were heated at 200 °C for 2 h and 600 °C for 4 h in air.

4.9. Preparation of xerogel of 1 from *n*-hexane

The xerogel was prepared by drying under high vacuum a frozen thin film of the gel (0.2 wt % **1** in *n*-hexane) over liquid nitrogen for 12 h and then allowed to reach slowly to room temperature.

4.10. SEM measurements

A Carl Zeiss NTS SUPRA 40 FEG-Scanning electron microscopy spectrometer was used for taking the SEM pictures. A small portion of the solid sample (xerogel or silica) was attached to the holder by using a conductive adhesive carbon tape. Prior to examination the xerogel was coated with a thin layer of gold.

4.11. Molecular modeling experiment

The computational experiments were performed with HyperChem 8.0.4, semiempirical optimization, AM1 method in vacuum. Algorithm: Fletcher–Reeves. Termination condition, rms gradient: 0.05 kcal/(Å mol). No bond restrictions were imposed. To have an insight in the stabilization energy of the 1D self-assembled model proposed we carried out two experiments:

4.11.1. Experiment A. Eight molecules of organogelator **1** with a separation of 45–50 Å between molecules were minimized using the above conditions.

4.11.2. Experiment B. The eight molecules from experiment A were placed in a 1D arrangement facing the alpha and beta faces of the steroid with a separation of about 6 Å and a rotation angle around the hydrogen bond axis of 12°. No bond or distance restrictions were imposed. Coordinates can be found in Supplementary data (S7). The interaction energy was estimated from the difference between the heats of formation of both arrangements of molecules divided by the number of molecule–molecule interfaces (7). For the eight molecules system the total stabilization energy (based on heats of formation) was 45.46 kcal/mol giving a net stabilization energy for the interactions in each molecule–molecule interface of 6.49 kcal/mol.

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Supplementary data

Supplementary data includes ^{1}H and ^{13}C NMR spectra; TEM, AFM, and extra SEM images of xerogel and SiO_2 fibers, T_g versus concentration plots, FTIR spectra, and computational analysis coordinates. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.01.065.

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