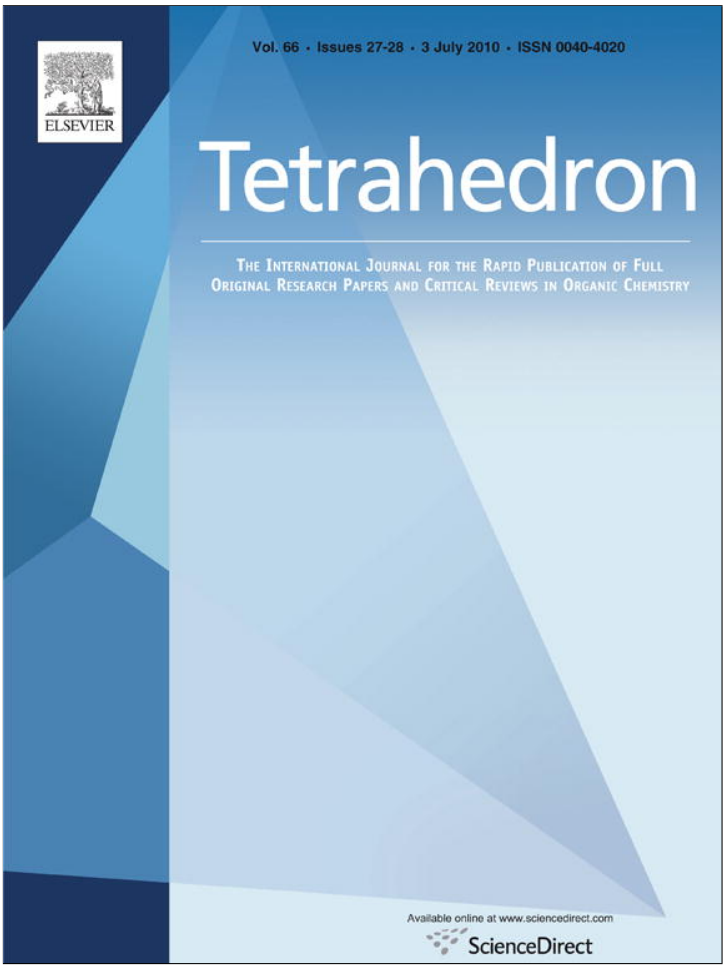

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Fluorous gallic acid derivatives as versatile gelators. Self-assembly into nanosized fibers or balls

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ABSTRACT

A new class of low molecular mass organogelators, the fluorous derivatives of gallic acid **1**–**3**, is described. The gelation properties have been examined in a large variety of organic liquids. The corresponding analogs possessing alkyl instead of semiperfluoroalkyl chains (**4**–**6**) do not display any gelation properties, thus revealing the key role of perfluorinated chains in the aggregation/gelation process. Gels have been studied by scanning electron microscopy, revealing the presence of three-dimensional networks of nanosized fibers. In the case of an instable gel, SEM images showed that these elongated fibers curl up into nanoballs, failing to create the entangled network responsible for solvent entrapment.

1. Introduction

Low mass organogelators (LMOGs, molecules whose molecular mass is <3000) are a growing class of compounds able to form gels with organic solvents at low concentrations (typically 10–50 mg/ml).[1] Solvent entrapment is the result of the ability to self-assemble into a wide variety of modes (rods, long fibers, tubules, strands, spheres, etc.).[2] Organogels have received increasing attention due to their potential useful applications: oil recovery systems,[3] toxicity remediation devices,[4] scaffolds for tissue repair,[5] drug delivery systems,[6] or templates for inorganic superstructures.[7] Less common are compounds able to gelate pure perfluorocarbons (PFCs);[8] however PFC gels have received special attention due to their potential use as delivery barrier creams.[9]

The supramolecular self-assembly of gelators is achieved by a combination of non-covalent interactions. For most known gelators such as amides, ureas, carbamates, peptides or sugars, H-bond is the driving force for molecular aggregation.[10] Gelators that are able to self-assemble without H-bonds and only via weaker interactions are not common. Among them, alkoxyaromatics,[11] azobenzene derivatives,[12] semiperfluoroalkanes,[13] and even simple alkanes[14] should be mentioned. In particular, molecules containing fluoroponytails display unusual chemical behavior due to the geometrical characteristics and the extreme hydrophobic and lipophobic nature of the fluorinated linkage, providing unique organizing forces based on repulsion by the solvent or by other different parts of the same molecule.[8c,d] On the other hand, some gallic acid derivatives possessing long alkyl chains were found to gelate alcohols and water.[15] Herein we report on the synthesis and gelation abilities of three new structurally simple organogelators **1**–**3** (Scheme 1). They are based on the gallic acid skeleton and are comprised by a polar group (ester, acid, or amide), an aromatic ring and three long semiperfluorinated chains. In principle, each of these elements may set up intermolecular interactions leading to aggregation. By comparison with their analogs **4**–**6** (Scheme 1, all fluorine atoms are replaced by hydrogens) that show no gelation properties, we demonstrate that the presence of semiperfluorinated chains is essential for the aggregation/gelation process.

2. Results and discussion

2.1. Synthesis

Esters **1** and **4** were easily prepared by alkylation of commercial propyl gallate with 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl iodide (98% yield) and undecyl bromide (50% yield), respectively, in refluxing acetone and in presence of potassium carbonate. Notably, our initial attempts to react propyl gallate with 1*H*,1*H*,2*H*,2*H*-perfluoroundecyl iodide in a variety of conditions (solvents: acetone, DMF; bases: K_2CO_3, Cs_2CO_3, NaH) were unsuccessful, probably due to elimination side-reactions. The esters were hydrolized with lithium hydroxide in aqueous ethanol, to afford in good yields (64% and 76%, respectively) the corresponding free acids **2** and **5**. The

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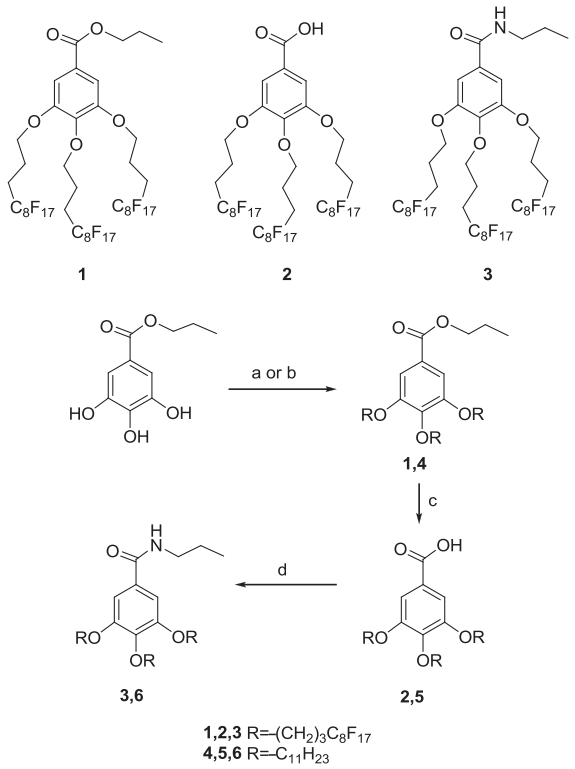

Scheme 1. Structures of organogelators **1**–**3** and synthesis of compounds **1**–**6**. Conditions: (a) $C_8F_{17}(CH_2)_3I$, K_2CO_3, acetone, reflux, overnight. (b) $C_{11}H_{23}Br$, KI, K_2CO_3, acetone, reflux, 3 days. (c) LiOH, EtOH/H_2O, reflux, overnight. (d) carbonyldiimidazole, dichloromethane, reflux, 2 h; then propylamine, reflux, overnight.

amides **3** and **6** were obtained in 70% and 80% yields by activation of the acids with carbonyldiimidazole followed by reaction with propylamine (Scheme 1).

The three semiperfluorinated compounds **1**–**3** were solid and their solubility in organic solvent was rather low at room temperature; however it significantly increased at higher temperatures. On the other hand, while the ester **4** was a liquid, acid **5** and amide **6** were both solids with a good solubility in organic solvents at room temperature.

2.2. Gelation studies

The gelation abilities of fluorous compounds **1**–**3** were investigated in various organic solvents and the results are summarized in Table 1. Gelation tests were carried out following a previously reported procedure:[17] 25 mg of the compound were weighted in a vial, then 1 ml of the chosen solvent was added and the mixture warmed until a clear solution was obtained. Upon cooling down to room temperature and inversion of the vial, if the solution did not flow, the compound was judged to be a gelator of the corresponding solvent (Fig. 1). If a gel was formed, it was evaluated quantitatively by determining the minimum gelator concentration (MGC, expressed in mg/ml) needed to fully gelate the solvent at 25 °C. The MGC varied in the range 8–25 mg/ml (5–15 mM), depending on the solvent and the gelator.

Gel formation occurred typically in 5–20 min. However, some exceptions were observed: acid **2** gelated chloroform almost instantly while ester **1** needed at least 1 h to gelate mineral oil. Gel-to-sol phase transition temperatures (T_{gel}) were determined by the 'inverse-flow method'.[18] A sealed vial containing the gel was immersed upside-down in a thermostated water-bath. The temperature of the bath was raised at a rate of 2 °C/min. T_{gel} was defined as the temperature at which the gel started to flow.

Table 1
Gelation abilities of fluorous compounds **1**–**3** in different organic solvents[a]

Solvent	Gelator		
	1	**2**	**3**
Silicone oil	CG (10; 78 °C)	P	P
Cyclohexane	OG (10; 46 °C)	I	OG[b]
Mineral oil	OG (11; 79 °C)	P	P
Undecane	VS	P	VS
Hexane	OG (9; 41 °C)	I	VS
CFC113[c]	S	S	S
Perfluorooctane	VS[d]	I	OG (22; 55 °C)
CCl_4	S	OG (13, 45 °C)	P
Toluene	S	OG (17; 63 °C)	OG (10; 57 °C)
Dioxane	CG (18; 56 °C)	CG (20; 56 °C)	CG (10; 54 °C)
Chloroform	S	OG (8; 54 °C)	CG (25; 44 °C)
Dichloromethane	S	OG (19; 53 °C)	OG (20; 47 °C)
Acetone	S	S	S
DMF	VS	CG (10; 48 °C)	CG (10; 48 °C)
tert-Butanol	OG (10; 43 °C)	OG (9; 42 °C)	CG (15; 45 °C)
Propionitrile	OG (18; 58 °C)	CG (20; 60 °C)	CG (12; 46 °C)
DMSO	P	I	I
Acetonitrile	P	P	P
Isopropanol	OG (8; 49 °C)	OG (10; 47 °C)	CG (20; 45 °C)
Ethanol	VS	P	CG (12; 44 °C)

[a] CG: clear gel, OG: opaque gel, VS: viscous solution, P: precipitate, S: solution, I: insoluble even at boiling temperature. Parentheses contain the MGC at 25 °C (in mg/ml) and the T_{gel}.
[b] Separates quickly in a precipitate and a viscous solution.
[c] 1,1,2-Trichloro-1,2,2-trifluoroethane.
[d] OG at 4 °C. Solvents are ordered by increasing Reichardt's normalized empirical parameter of solvent polarity (E_T^N);[16] polyfluorinated solvents were considered as CCl_4.

In this work we present three new simple compounds that are able to gelate a wide range of solvents (see Table 1). Ester **1** is the most convenient for gelating apolar solvents such as cyclohexane, hexane and also silicone and mineral oil. Less general behavior was observed with polar solvents; however, ester **1** could also gelate dioxane, propionitrile, and alcohols, such as *tert*-butanol and isopropanol. For solvents with a normalized empirical parameter of polarity higher than that of toluene (E_T^N = 0.099) (dioxane, chloroform, dichloromethane, and DMF), compounds **2** and **3**, containing acid and amide moieties in their structures, are more suitable. For all three compounds, gelation was prevented in

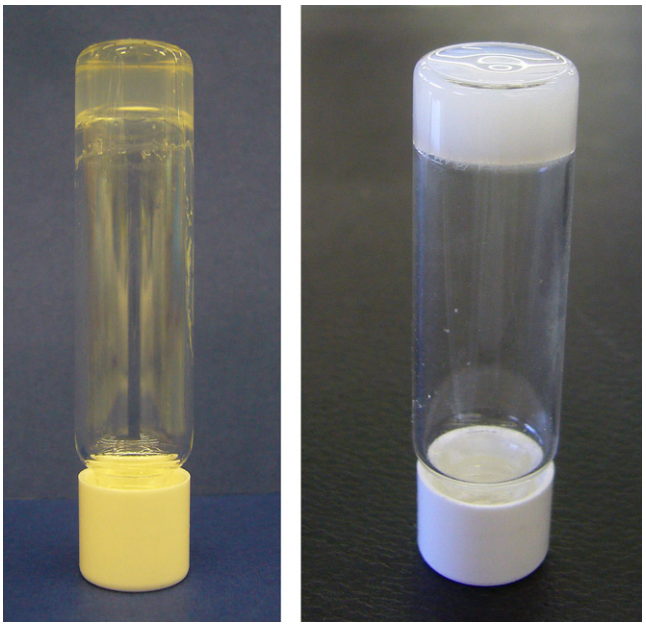

Figure 1. Gel obtained from **1** in silicone oil (left) and from **3** in perfluorooctane (right).

acetone (due to the high solubility) and in highly polar aprotic solvents such as DMSO or acetonitrile (E_T^N = 0.444 and 0.460, respectively), due to lack of solubility. However, highly polar protic solvents, able to set up hydrogen bonds with the polar moieties contained in **1**–**3** molecules, could be gelated in some cases, being amide **3** the best gelator. It is noteworthy that fluorous amide **3** gelates also neat perfluorooctane, as perfluorocarbons (PFCs) are probably the most difficult solvents to gelate, due to their low surface tension, and only a few compounds were shown to gelate pure PFCs.[8] Fluorocarbon gels could be of great interest for topical use to protect the skin or a wound while keeping it permeable to gases.[9a]

All the obtained gels were thermally reversible and stable for weeks when stored at room temperature in closed vials in contact with air. They were also thermally stable up to 40 °C, being their gel-to-sol transition temperature comprised between 42 °C and 63 °C. Exceptions are represented by the mineral oil and silicone oil gels of **1**, which exhibit superior thermal stabilities (T_{gel} 79 °C and 78 °C, respectively).

Once we had determined the gelation properties of **1**–**3**, in order to get insight into the nature of the interactions involved in the gelation process, we studied their anologues **4**–**6**, in which the fluoroponytails were replaced by aliphatic chains of the same length. These new compounds were tested for gel formation in the same solvents following the same procedure, but none displayed gelation properties, not even with the concentration raised up to 50 mg/ml. This result clearly demonstrates that the semiperfluorinated chains play a key role in imparting the gelation ability upon these molecules. In fact, organogelators **1**–**3** contains two markedly different segments: a solvophilic polar head (ester, acid, or amide group) and a solvophobic fluorous tail, joined by an aromatic ring. In our case, it is probable that the organized molecular assembly is driven by the solvophobic property of the semiperfluorinated chains that result in a molecular bilayer as the fundamental building unit of the aggregate, as schematically illustrated in Figure 2.

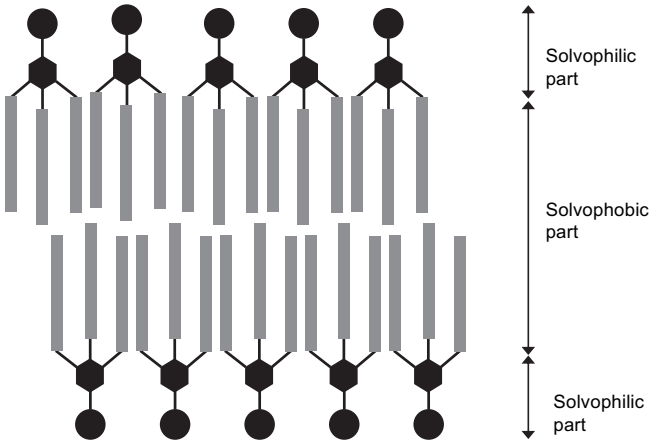

Figure 2. Schematic illustration of the bilayer structure of **1**–**3** in organic media.

In fact, 'amphiphiles' containing one or more perfluorinated chains are known to self-assemble in microstructures in water or organic media.[19a,b] Moreover, perfluoroalkyl fragments promote the formation of fibers.[19c] Polar heads may interact further through hydrogen bonding (in the case of **2** and **3**) and/or dipolar interactions; anyway, the fact that the non fluorous analogs **4**–**6** do not display gelation abilities clearly shows that these interactions represent a minor contribution. However, it is likely that in the perfluorooctane gelation, the hydrogen-bond formation between amide groups is an important driving force for aggregation, and an opposite bilayer structure could be proposed as illustrated in Figure 3.[8c]

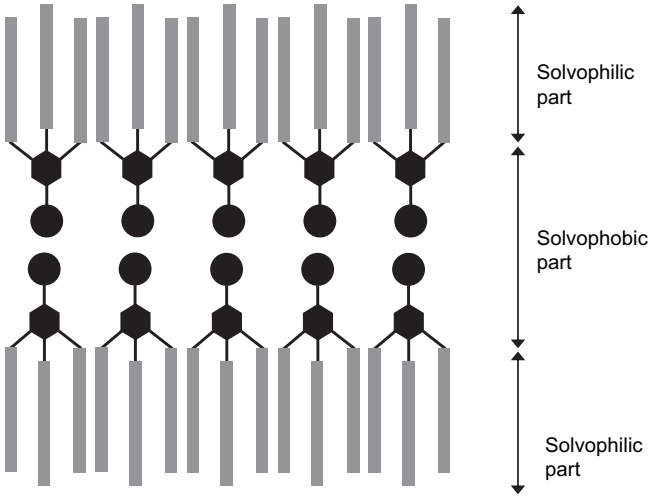

Figure 3. Schematic illustration of the bilayer structure of **3** in fluorous media.

The presence of hydrogen-bonding interactions was investigated with NMR and IR studies. Among the three gelators, secondary amide **3** was selected as its NH signal is easy to be studied by both of these techniques and can provide useful information. Firstly, the IR peak characteristic of the amino moiety of the chloroform xerogel of **3** (obtained by slow evaporation of the solvent) falls within the expected ranges of H-bonded ones[20] (3286 cm^{-1} in chloroform and 3326 cm^{-1} in perfluorooctane, NH stretching band, see ESI). This observation suggests that hydrogen bonding is involved in the organogel formation, as previously described.[8d] Secondly, a variable temperature ^1H NMR study of the $CDCl_3$ gel of **3** was carried out. At 60 °C, when the system is a clear solution, the signals are sharp (Fig. 4a), while when the temperature is lowered down, below the T_{gel}, the system gelates and a significant line broadening of all the signals is observed (Fig. 4b). This line broadening effect is common for gels and in some cases may lead to unobservable (NMR silent) samples.[21] All of the signals present almost identical chemical shifts in both spectra and only a small downfield shift ($\Delta\delta$=0.07 ppm) for the signal of the NH proton was observed. This result is similar to those found for other

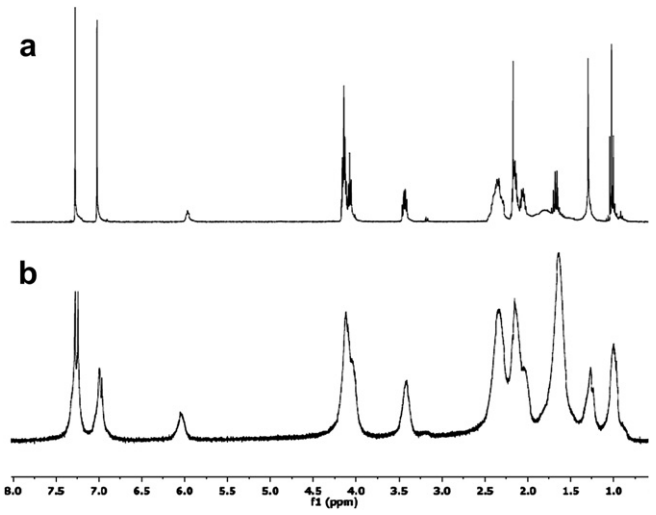

Figure 4. ^1H NMR spectra of **3** in $CDCl_3$ at 60 °C (a) and at room temperature (b); [**3**]= 0.04 M.

amide-based organogelators [22] and confirms the presence of weak hydrogen-bonding interactions.

2.3. Morphological characterization of the organogels

The morphologies of the obtained gels of **1**–**3** in various solvents were determined by scanning electron microscopy (SEM). SEM images of the gels formed by compound **1** in hexane (Fig. 5) and in isopropanol (see ESI) showed three-dimensional networks, consisting of entangled bundles of fibers. These fibers were ribbon-shaped and had an average width of 0.5 μm. In Figure 4 twists of these ribbons and junction zones are clearly visible. This assembly is closely packed and able to trap solvent molecules into its interstices.

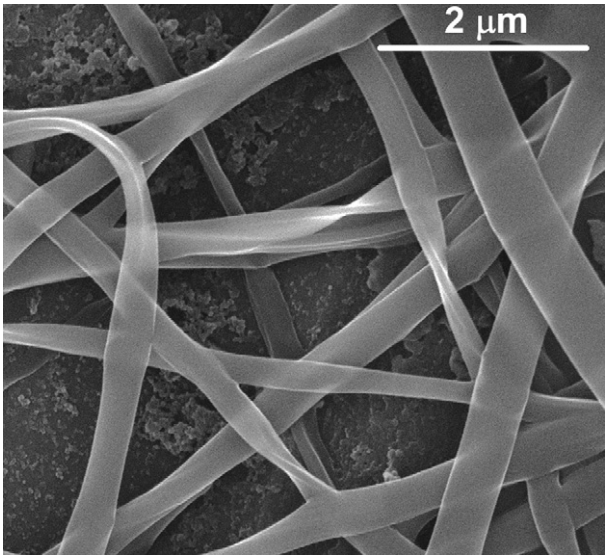

Figure 5. SEM image of the gel formed by compound **1** in hexane.

SEM images of the gel of compound **2** in chloroform (see ESI) showed the same structures observed in the case of ester **1**: long, ribbon-like fibers of about 1–1.5 μm width and more than 100 μm length. Zoom images (Fig. 6) showed that these ribbon-like fibers are made of tinier fibers of about 100 nm width, thus revealing a hierarchically organized assembly.

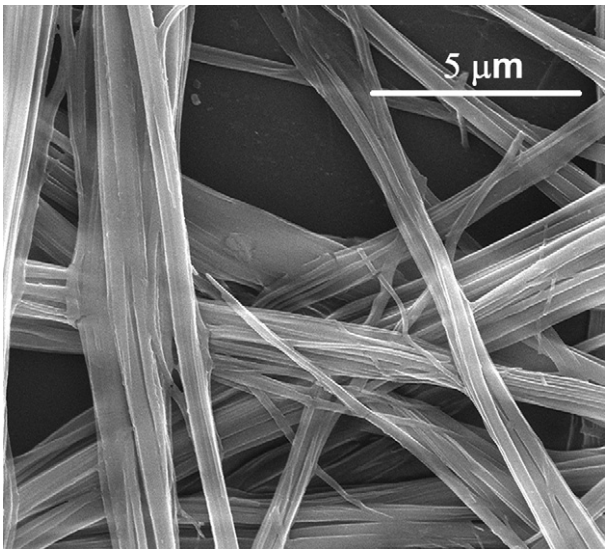

Figure 6. SEM image of chloroform gel of **2**.

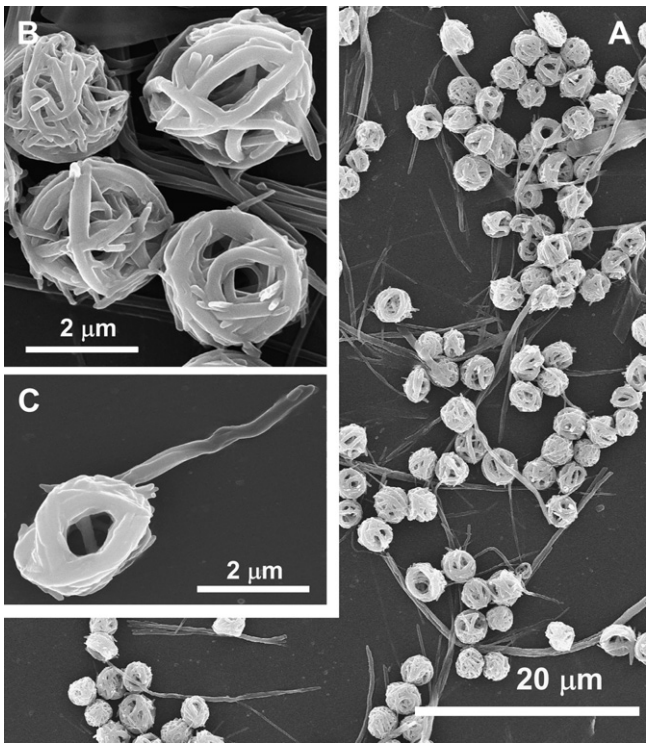

Figure 7. SEM images of the viscous solution of **3** in cyclohexane.

As shown in Table 1, amide **3** formed stable gels in chloroform and propionitrile, and the SEM images for these gels revealed the already seen fibrillar structures (see ESI). On the other hand, **3** formed a very instable gel in cyclohexane, that separated quickly in a colloidal precipitate and a viscous solution. SEM images of the viscous solution revealed compact, globular aggregates of fibers, resembling balls of wool. At the best of our knowledge, this kind of assembly has never been reported before. The balls have an average diameter of 2–3 μm and are made of long, cylindrical fibers with an average diameter of 200–300 nm. As we can see in Figure 6A, these globular assemblies co-exist with a small amount of elongated fibers. The analysis of these images prompted us to propose a pathway for different evolution of the assemblies formed. As presented schematically in Figure 8,

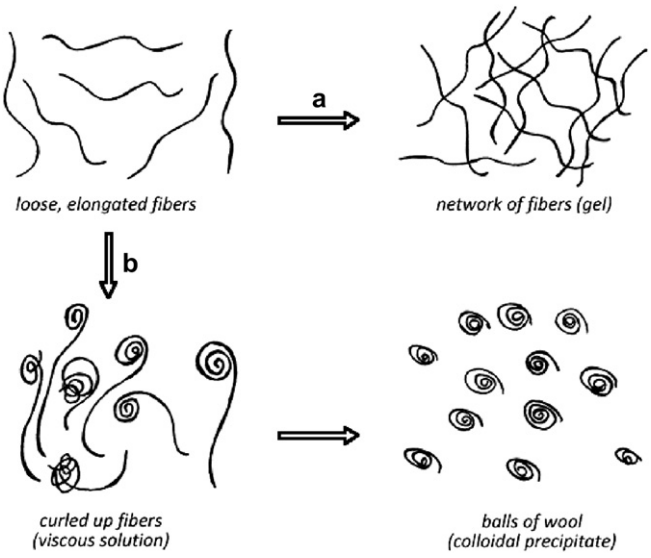

Figure 8. Schematic representation of the possible evolution pathways of the organogelator assemblies. (a) Common gel formation. (b) Behavior of **3** in cyclohexane.

polyfluorinated molecules promote the formation of loose fibers that can assemble in three-dimensional networks, trapping solvent molecules and allowing the formation of a stable gel (as observed in Figs. 5 and 6). However, in the case of amide **3** in cyclohexane, this network does not form, and the fibers start to curl up (See Fig. 7C; a globular aggregate, that is, almost fully formed, but still presents an elongated tail) and this process lead to nanosized balls of wool (Fig. 7A,B). These aggregates are unable to entrap the solvent and result in a viscous solution that evolves into a colloidal precipitate.

A tentative explanation for the formation of globular aggregates is proposed: in a very apolar solvent such as cyclohexane, H-bonds are strong enough to become the main driving force for the supramolecular assembly. So in the case of amide **3** in cyclohexane, probably the organization of gelator molecules is the same as in perfluorooctane (amide groups in the inner part and perfluorinated tails in the outer part of the bilayer). However in the case of cyclohexane the tails are solvophobic, and the fibers would be forced to curl up in order to minimize the contact surface with the solvent.

2.4. Concluding remarks

The fluorous gallic acid derivatives **1**–**3**, a new class of structurally simple LMOGs, have been synthesized. These molecules have shown the ability to gelate a wide range of different organic solvents, from alkanes to alcohols, in 8–25 mg/ml concentration. Compound **1** is the best gelator for apolar solvents, while **2** and **3** are more suitable to gelate polar protic and aprotic solvents. Notably, compound **3** is one of the few known molecules able to gelate neat perfluorooctane. The analog compounds **4**–**6**, in which all fluorine atoms are replaced by hydrogens, were tested for gelation, giving negative results and revealing that the driving force for the aggregation/gelification process is the solvophobic effect displayed by semiperfluorinated chains. Gelation process is likely to be an equilibrium between the solubility of compounds and their ability to organize themselves in different media.

Scanning electron microscopy showed that in all cases the aggregates that lead to gelification have a fibrillar nature. The SEM study of the **3**/cyclohexane system revealed that the long fibers curl up into globular assemblies resembling balls of wool, instead of forming the entangled network responsible for gelification. As the best of our knowledge, it is the first time that this kind of structure has been described. Further studies will be performed to establish if this behavior is observed in other cases. A bilayer structure was proposed for the organization of gelator molecules in fibers: semiperfluorinated chains are oriented inward or outward the bilayer depending on the polarity of solvents and the force of the intermolecular hydrogen bonds formed.

3. Experimental

3.1. Apparatus

Scanning electron microscopy (SEM) observations were carried out on an Hitachi S-570 electron microscope. The samples for these measurements were prepared as follows: 1 mM solutions of the organogelators were casted on silicon wafers, dried at room temperature and finally coated with gold vapor. FT-IR spectra were recorded on a Bruker Tensor 27 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV400 spectrometer. High resolution mass spectra (HR-ESI-MS) were recorded on a Bruker Daltonics microTOF instrument, equipped with an electrospray source.

3.2. Materials

All reagents were obtained from commercial suppliers and used without further purification. Acetone was distilled under nitrogen from calcium chloride prior to use.

3.3. Synthesis

*3.3.1. Propyl 3,4,5-tris(1H,1H,2H,2H,3H,3H-perfluoroundecan-1-yloxy)benzoate (**1**).* To a solution of propyl gallate (60 mg, 0.28 mmol) in dry acetone (5 ml) were added 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoroundecyl iodide (600 mg, 1.02 mmol) and K_2CO_3 (464 mg, 3.36 mmol) and the reaction mixture was stirred under nitrogen at reflux overnight. Reaction was monitored via TLC (SiO_2, hexane/AcOEt 2:1) and then stopped. The reaction mixture was filtered on Celite and the solid washed several times with acetone. The solution was concentrated to dryness, and the crude product was digested in tetrahydrofuran. The solid filtered off and the filtrate concentrated in vacuo, affording the desired product as a white solid (500 mg, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 2H), 4.30 (t, J=6.7 Hz, 2H), 4.15 (t, J=5.8 Hz, 4H), 4.09 (t, J=5.8 Hz, 2H), 2.50–2.25 (m, 6H), 2.21–2.13 (m, 4H), 2.11–2.00 (m, 2H), 1.82 (sext, J=7.3 Hz, 2H), 1.05 (t, J=7.4 Hz, 3H). ^{13}C{^{1}H}-NMR (100.6 MHz, $CDCl_3$) δ 166.0, 152.6, 141.9, 126.2, 108.9, 71.9, 67.9, 66.5, 28.0, 22.2, 20.7, 10.2. Mp=92–94 °C. IR (ATR): 2966, 1711, 1588, 1430, 1371, 1197, 1145, 1113, 687. HR-ESI-MS: 1615.0890 $(M+Na)^+$; calcd for $C_{43}H_{27}F_{51}O_5Na$ 1615.0936.

*3.3.2. 3,4,5-Tris(1H,1H,2H,2H,3H,3H-perfluoroundecan-1-yloxy)benzoic acid (**2**).* To a suspension of the ester **2** (1.7 g, 1.1 mmol) in ethanol (45 ml) was added a solution of $LiOH\cdot H_2O$ (260 mg, 6.2 mmol) in water (5 ml) and the reaction mixture stirred at reflux overnight. Reaction mixture was cooled down to room temperature, diluted HCl was added until pH 2 was reached and a white solid formed. Additional 20 ml of water were added and more solid formed. This was filtered, washed with more water and dried, affording the desired product as a white powder (1.06 g, 64% yield). ^{1}H NMR (400 MHz, acetone-d_6, 40 °C) δ 7.40 (s, 2H), 4.28 (t, J=5.8 Hz, 4H), 4.21 (t, J=5.8 Hz, 2H), 2.62–2.48 (m, 6H), 2.21–2.17 (m, 6H). ^{13}C{^{1}H}-NMR (100.6 MHz, acetone-d_6, 40 °C) δ 166.9, 152.9, 142.4, 126.4, 109.1, 72.1, 68.1, 28.0, 21.8, 20.9. Mp=128–130 °C. IR (ATR): 2960, 2360, 1686, 1588, 1434, 1371, 1196, 1145, 703. HR-ESI-MS: 1573.0426 $(M+Na)^+$; calcd for $C_{40}H_{21}F_{51}O_5Na$ 1573.0467.

*3.3.3. 3,4,5-Tris(1H,1H,2H,2H,3H,3H -perfluoroundecan-1-yloxy) benzoic acid propyl amide (**3**).* To a solution of the acid **2** (600 mg, 0.39 mmol) in dichloromethane (12 ml) and CFC113 (8 ml) was added carbonyldiimidazole (75 mg, 0.46 mmol) and the mixture was stirred under reflux for 2 h. Propylamine (42 μl, 0.51 mmol) was added and the reaction mixture stirred at reflux overnight under nitrogen. The reaction mixture was cooled down to room temperature and washed three times with a diluted solution of HCl (pH 2); the organic fraction was dried over Na_2SO_4 and concentrated to dryness. The crude product was washed with ethanol and dried in vacuo, affording the desired product as a white powder (437 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$ and CFC113, 40 °C) δ 7.05 (s, 2H), 6.11 (t, J=5.3 Hz, 1H), 4.15 (t, J=5.8 Hz, 4H), 4.09 (t, J=5.8 Hz, 2H), 3.46 (m, 2H), 2.52–2.25 (m, 6H), 2.22–2.02 (m, 6H), 1.70 (sext, J=7.3 Hz, 2H), 1.03 (t, J=7.4 Hz, 3H). ^{13}C{^{1}H}-NMR (100.6 MHz, $CDCl_3$, 40 °C) δ 167.8, 153.2, 141.7, 131.3, 107.0, 72.5, 68.8, 42.7, 30.0, 28.3, 23.3, 21.9, 21.1, 11.6. IR (ATR): 3318, 2962, 2875, 1687, 1629, 1578, 1550, 1497, 1438. Mp=100–102 °C. HR-ESI-MS: 1614.1060 $(M+Na)^+$; calcd for $C_{43}H_{28}F_{51}O_4NNa$ 1614.1096.

*3.3.4. Propyl 3,4,5-tris(undecyloxy)benzoate (**4**).* To a solution of propyl gallate (2.6 g, 12.4 mmol) in dry acetone (140 ml) were

added undecyl bromide (10.0 ml, 44.6 mmol), K_2CO_3 (15.4 g, 111 mmol), and KI (920 mg, 5.6 mmol) and the reaction mixture was stirred under nitrogen at reflux for 3 days. Reaction was monitored via TLC (SiO_2, hexane/AcOEt 5:1) and then stopped. The reaction mixture was filtered on Celite and the solid washed several times with acetone. The filtrate was concentrated to dryness, and the crude product was purified via column flash chromathography (SiO_2, hexane/AcOEt, 15:1), affording the desired product as a pale yellow liquid (4.2 g, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 4.28 (t, J=6.7 Hz, 2H), 4.04 (t, J=6.5 Hz, 6H), 1.89–1.71 (m, 6H), 1.55–1.44 (m, 2H), 1.29 (m, 48H), 1.04 (t, J=7.4 Hz, 3H), 0.91 (t, J=6.5 Hz, 9H). ^{13}C{^{1}H}-NMR (100.6 MHz, $CDCl_3$) δ 166.9, 153.4, 143.1, 125.7, 108.7, 73.9, 69.6, 66.8, 32.3, 30.7, 30.1, 30.0, 29.8, 26.5, 23.1, 22.6, 14.4, 10.9. IR: 2921, 2852, 2361, 1716, 1585, 1331, 1210, 1111. HR-ESI-MS: 697.5719 $(M+Na)^+$; calcd for $C_{43}H_{78}O_5Na$ 697.5741.

*3.3.5. 3,4,5-Tris(undecyloxy)benzoic acid (**5**).* To a solution of the ester **4** (3.0 g, 4.44 mmol) in ethanol (95 ml) was added a solution of $LiOH\cdot H_2O$ (1.12 g, 26.6 mmol) in water (5 ml) and the reaction mixture stirred at reflux overnight. Reaction mixture was cooled down to room temperature, diluted HCl was added until pH 2 was reached and a white solid formed. Additional 50 ml of water were added and more solid formed. This was filtered and dried. The crude product was recrystallized from ethanol, affording the desired product as a white powder (2.15 g, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 2H), 4.09–4.02 (m, 6H), 1.90–1.72 (m, 6H), 1.56–1.45 (m, 6H), 1.40–1.25 (m, 42H), 0.90 (t, J=7.1 Hz, 9H). ^{13}C{^{1}H}-NMR (100.6 MHz, $CDCl_3$) δ 172.2, 153.0, 143.4, 123.8, 108.8, 73.7, 69.4, 32.1, 30.5, 29.9, 29.8, 29.7, 29.5, 26.2, 22.8, 14.2. Mp=53–54 °C. IR (ATR): 2918, 2849, 1681, 1585, 1430, 1331, 1225, 1118. HR-ESI-MS: 655.5247 $(M+Na)^+$; calcd for $C_{40}H_{72}O_5Na$ 655.5272.

*3.3.6. 3,4,5-Tris(undecyloxy)benzoic acid propyl amide (**6**).* To a solution of the acid **5** (1.0 g, 1.58 mmol) in dichloromethane (8 ml) was added carbonyldiimidazole (282 mg, 1.7 mmol) and the mixture was stirred at reflux for 2 h. Propylamine (160 μl, 1.9 mmol) was added and the reaction mixture stirred at reflux overnight under nitrogen. The reaction mixture was cooled down to room temperature and washed three times with a diluted solution of HCl (pH 2); the organic fraction was dried over Na_2SO_4 and concentrated to dryness. The crude product was washed with a little amount of acetone and dried in vacuo, affording the desired product as a white powder (852 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (s, 2H), 6.26 (t, J=5.6 Hz, 1H), 3.99 (t, J=6.4 Hz, 6H), 3.39 (q, J=6.7 Hz, 2H), 1.83–1.72 (m, 6H), 1.63 (sext, J=7.3 Hz, 2H), 1.50–1.42 (m, 6H), 1.38–1.20 (m, 42H), 0.97 (t, J=7.4 Hz, 3H), 0.89 (t, J=6.9 Hz, 9H). ^{13}C{^{1}H}-NMR (100.6 MHz, $CDCl_3$) δ 167.5, 153.0, 141.1, 129.8, 105.8, 73.5, 69.4, 41.8, 31.9, 30.3, 29.7, 29.6, 29.3, 26.1, 22.7, 14.0, 11.4. Mp=52–53 °C. IR (ATR): 3270. 2918, 2850, 1629, 1580, 1550, 1499, 1335, 1112. HR-ESI-MS: 696.5878 $(M+Na)^+$; calcd for $C_{43}H_{79}O_4NNa$ 696.5901.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2010.04.086.

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