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A fluoroponytails containing organogelator: gelation of perfluorotributylamine and isopropopanol

Julien Loiseau,[a] Marion Lescanne,[b] Annie Colin,[b] Frédéric Fages,[a] Jean-Baptiste Verlhac[a] and Jean-Marc Vincent[a,*]

[a]*Laboratoire de Chimie Organique et Organométallique (UMR 5802 CNRS), Universite Bordeaux 1, 351 cours de la Libération, 33405 Talence Cedex, France*

[b]*Centre de Recherche Paul Pascal, Avenue Albert Schweitzer, 33600 Pessac, France*

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Abstract—A highly fluorinated bis-benzamide is readily prepared from a carboxylic acid bearing two perfluoalkyl-alkyl chains and a phenylendiamine. The bis-benzamide **2** gelates isopropanol at low concentration providing a thixotropic gel resulting from the formation of a network of highly rigid fibers. A gel of perfluorotributylamine stable at 4°C was also obtained using **2** at 10 mM concentration.

Trapping solvent molecules into a three-dimensional network of fibers leads, at the macroscopic level, to the formation of a gel. The network structure resulting from the self-assembling of a low molecular weight gelling agent is generally held together by attractive non-covalent forces, such as hydrogen bonding, π-stacking and van der Waals interactions.[1] The organogelators discovered to date can be classified into two broad families whether they have hydrogen bonding functionality,[2] or not.[3] Molecules bearing 'fluoroponytails' such as $(CH_2)_y(CF_2)_xCF_3$ groups, 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 dissimilar parts of the same molecule. These unique properties have already been successfully exploited in the colloid chemistry with the design of ionic fluorinated amphiphiles that form higher organized and more stable structures than their hydrogenated analogues.[4] Fluorinated surfactants have also been developed to prepare highly stable reverse water-in-fluorocarbon emulsion,[5] and stable highly concentrated perfluorocarbon gels requiring a water content as low as 1% (v/v).[6] Rather surprisingly there are only a few examples of gelation of an organic solvent by a gelling agent bearing fluoroponytails. A challenging and successful strategy for the gelation of CO_2 was reported recently by Beckman, Hamilton, and co-workers using a non-ionic organogelators with ureas as hydrogen bonding functional group and perfluoroalkyl chains to increase the 'CO_2-philicity'.[7] Upon drying of the gels, microcellular organic material with a bulk density reduction >95% relative to the parent material were obtained. Gelation of formamide with a neutral long chain fluoroalkyl glycolipid was also reported by Rico-Lattes and co-workers.[8] It was also shown by Rabolt and co-workers that binary mixtures of semifluorinated *n*-alkanes with hydrocarbon liquids exhibit gel-like characteristics.[9a] Interestingly, these simple semifluorinated *n*-alkanes possess the unique property of gelifying fluorocarbon solvents.[9a]

We have recently described the preparation of the carboxylic acid **1** bearing two long perfluoroalkyl–alkyl chains that renders it highly soluble in perfluorocarbons.[10] In the course of our study to use **1** as a precursor for the synthesis of fluorophilic molecules we have discovered the diamide organogelator **2**.[11] Herein we describe the synthesis of the bis-benzamide organogelator **2** and its preliminary gelation properties for both an organic solvent, isopropanol, and a perfluorocarbon, the perfluorotributylamine.

The diamide **2** (Scheme 1) was synthesized by treatment of the acyl chloride with the diamine in THF in the presence of triethylamine.[11] The acyl chloride was prepared by reacting **1**, that is soluble in THF, with oxalyl chloride (10 equiv.) at ambient temperature for 20 h. After evaporation of the solvent and the unreacted oxalylchloride the raw acyl chloride was used without further purification.

As expected, the diamide **2** that has a fluorine content of 62.7% did not dissolve at ambient temperature in organic solvents. It thus appeared that the amphiphilic compound **2**

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* Corresponding author. Tel.: +33-556-84-8942; fax: +33-556-84-6994; e-mail: jm.vincent@lcoo.u-bordeaux.fr

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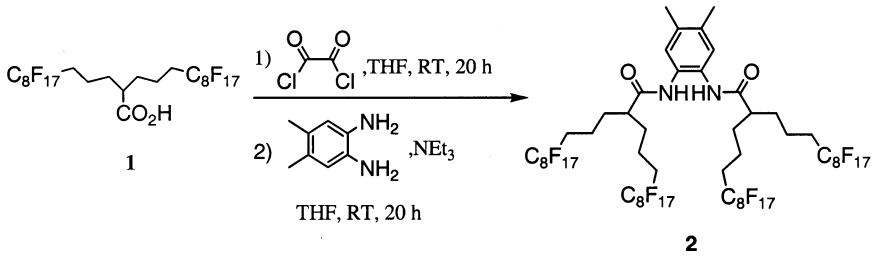

Scheme 1.

that has structural analogies with the orthophenylenediureas developed by Feringa, Kellogg and co-workers[2f] but formed of benzamide functions with strong hydrogen bonding character[12] and bulky non-polar fluoro ponytails could be a good candidate as a gel forming molecule. The gelation ability of **2** for non-fluorinated solvents was studied by heating 10 mM (20.6 mg/mL) heterogeneous mixture until the solid dissolved completely and then let the solution cooling down to 20°C. In DMF, THF, $CHCl_3$, *n*-butanol, *n*-octanol, toluene, *n*-hexane **2** dissolved when heated but precipitation was observed upon cooling. By contrast, a thermoreversible transparent gel was obtained in isopropanol within a few minutes at ambient temperature. The TEM images of a gel of **2** shown in Fig. 1 revealed that the gel network consisted of straight fibers bundles of highly regular shape, the aggregates having a length of typically 5–15 μm and a diameter of 0.05–0.25 μm.

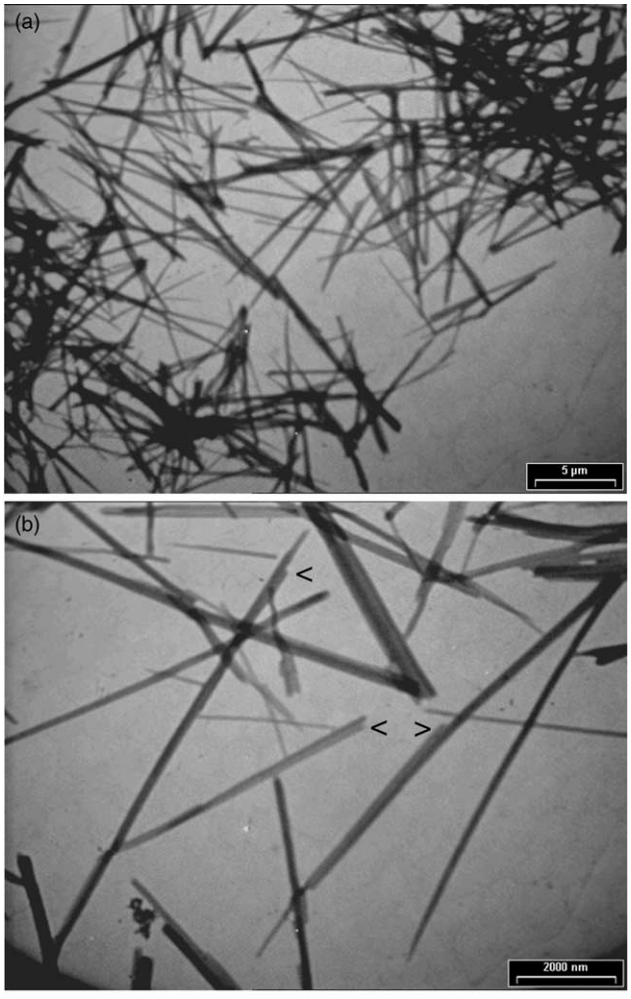

Figure 1. TEM images of a 10 mM isopropanol gel of **2** (a) bar=5 μm, (b) bar=2 μm). The sample was prepared by picking up the gel on a carbon grid.

The straight aggregates formed in isopropanol displayed striking analogies in shape and size when compared to the hollow tubules that were formed in water from single-chain perfluoroalkylated amphiphiles as described previously by Riess and co-workers.[4b] Whether these aggregates are hollow tubules or scrolls is under investigation. Interestingly, the isopropanol gel displays a thixotropic behavior. Upon hand shaking, a 20 mM gel flows as a viscous solution, setting instantaneously to gel again when the disturbance stops and then maintaining a shape on its own. No apparent deterioration of the gel structure leading to segregation between the solvent and the fibers was observed. Thixotropy is usually associated with systems whose molecular bonds are disrupted by movement. This physical property has already been observed for cyclic bis-urea gelators developed by Kellog, Feringa, and co-workers.[2f,g] It was proposed that the presence of intertwined and fused fibers that were observed in the network could explain this property. Such twin fibers were also observed in the isopropanol gel network (indicated by arrows in Fig. 1b). Preliminary rheological measurements confirmed the thixotropic character of the gel.[13] A frequency sweep experiment shows that the elastic modulus G' (a parameter that represents the ability of the material to 'snap back' to its original geometry) and the loss modulus G'' are fairly independent of frequency over more than three decades. The G' value (5×10^3 Pa) was observed to be one order of magnitude higher than that of G'' (4×10^2 Pa) indicating that the system still exhibits a solid-like behavior. Flow curves showed a shear thinning behavior (the viscosity decreasing with time at constant shear stress) and a 'yield stress' value at which the gel 'breaks', the G' value becoming very small (about 20 Pa). After a rest of several minutes without shear stress, frequency sweep experiment shows that G' is restored to 5×10^3 Pa. The gel has recovered its initial structure in agreement with a thixotropic behavior.

Fluorocarbon gels could be of great interest for topical use to protect the skin or a wound while remaining permeable to gasses. However, perfluorocarbons are probably the most difficult solvents to gelify due to their low surface tension and the difficulty to solubilize organic molecules in a lipophobic media. To the best of our knowledge, the only example of gelation of perfluorocarbons without addition of water has been reported by Möller and co-workers with

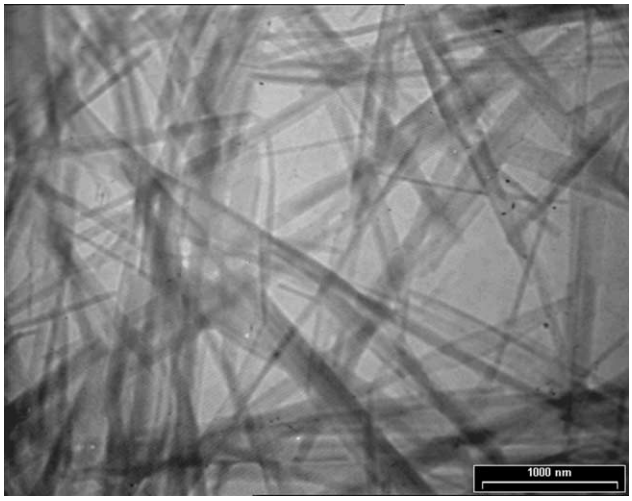

Figure 2. TEM images of a 10 mM perfluorotributylamine gel of **2** (bar=1 μm). The sample was prepared by picking up the gel on a carbon grid.

the semifluorinated *n*-alkanes as gelling agents[9b]. In light of the gelation ability of **2** and its high fluorine content we then wondered if it could gelate perfluorocarbons. The more promising results were obtained for the gelation of perfluorotributylamine (FC40). When a 10 mM heterogeneous solution of **2** in perfluorotributylamine was heated, **2** dissolved rapidly and, upon standing at ambient temperature, a limpid, slightly viscous solution was obtained. Gelation of the solution was achieved upon cooling the sample at −18°C for 24 h. The gel formed was then stable at 4°C but melted at 20°C. Electron microscopy (Fig. 2) revealed that the formation of a network of fibers, looking more like ribbons, was responsible of the gelation.

As a summary, the bis-benzamide **2** bearing four fluoroponytails possesses the unique property of gelifying either a polar and protic solvent that is isopropanol or a lipophobic and hydrophobic solvent that is perfluorotributylamine. Further studies will attempt to get insights into the mechanism of the network formation and the structure of the fibers. It is likely that the solvophobic interactions are dominant for the isopropanol gelation whereas in perfluorotributylamine the hydrogen-bond formation between amide groups is the primary driving force for aggregation.

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solvent was removed under reduced pressure. The raw acyl chloride is dissolved in anhydrous THF (1.5 mL) and added slowly to a THF solution (1 mL) containing the 4,5-dimethyl-1,2-phenylendiamine (17.05 mg, 0.125 mmol) and the triethylamine (38.3 μL, 0.275 mmol). Rapidly **2** precipitates, the mixture being stirred for 20 h and then filtered. The precipitate is washed with THF and MeOH leading to the isolation of **2** as a white powder in 74% yield. Analytical data for **2**: ^{1}H NMR (250 MHz, THF d_8, 40°C): δ (ppm) 9.06 (s, 2H, N–H), 7.06 (s, 2H, Ar–H), 2.23 (s, 6H, Ar–CH_3), 2.10–1.88 (m, 10H), 1.58–1.40 (m, 16H). ^{13}C NMR (100 MHz, THF d_8, 35°C): δ (ppm) 171.6 (–CO), 132.0 (Ar–C), 126.9 (Ar–C), 123.5 (Ar–CH), 45.9 (CHCO), 30.6 (CH_2CH), 29.1 (CH_2CF_2), 16.9 ($CH_2CH_2CH_2$ and CH_3); LSIMS-MS *m/z*: 2061 (M+1).

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