Solution self-assembly and solid state properties of fluorinated amphiphilic calix[4]arenes†

Oana M. Martin,[a] Lian Yu[a] and Sandro Mecozzi*[ab]

A novel amphiphilic semifluorinated calix[4]arene has been shown to exhibit liquid crystalline character and to self-assemble in solvents of varying polarity.

Self-assembly is the process by which monomeric molecules recognize each other in solution and form aggregates of complexity ranging from dimers to mesoscopic-size structures.[1] The inter-molecular forces that make molecular recognition possible are very often dependent on the solvent. For instance, an assembly held together by hydrogen bonds may not be stable in hydrogen bonding solvents such as water and alcohols. On the other hand, complexes using the hydrophobic effect as their driving force usually dissociate in hydrophobic organic solvents. It is known that the addition of perfluorinated chains to organic molecules radically changes the physical and chemical properties of those molecules.[2] The tendency of highly fluorinated molecules to segregate into a fluorous phase that is both hydrophobic and lipophobic is known as the fluorophobic effect. In analogy to its hydrophobic counterpart, the fluorophobic effect can be used as a driving force in molecular[3] and biomolecular[4] recognition. Furthermore, our results suggest that the fluorophobic effect can be used as an element of recognition to direct the formation of regular self-assembly patterns that are dependent on solvent polarity.

For our studies we have used a semifluorinated amphiphilic molecule based on the calix[4]arene scaffold. A variety of self-assembled systems based on the versatile calix[4]arene scaffold have been reported in the literature,[5] from dimeric capsules, to mono- and multilayers. More specifically, the hydrophobic effect was used to drive the self-assembly of various amphiphilic calix[4]arenes and resorcinarenes functionalized with *n*-alkyl chains.[6] In aqueous solutions these amphiphiles tend to aggregate in order to reduce the surface area in contact with the bulk water phase. Perfluoroalkyl groups add a new dimension to the amphiphilic character of a molecule due to their unique com-bination of properties, thereby promoting the formation of stable colloids. Recently, a new series of amphiphilic perfluoroalkylthio-β-cyclodextrins was synthesized and self-assembled into nano-spheres, combining the inclusion properties of cyclodextrins

with the unusual amphiphilicity of fluorous chains.[6] We have attached perfluoroalkyl chains on the upper rim and polar water-solubilizing groups on the lower rim of a calix[4]arene.[7] The resulting semifluorinated molecule **1** combines the structural characteristics of amphiphiles and thermotropic liquid crystals: polar head, hydrophobic tails and mesogenic unit (Fig. 1). We show here that such fluorinated amphiphiles self-assemble in solvents of varying polarity and form a diversity of nanostructures. This phenomenon is entirely governed by the formation of a microscopic super-hydrophobic fluorous phase.

The self-assembly properties of molecule **1** were investigated in four solvents: water, methanol, chloroform and perfluorohexanes (FC-72). The aggregate structures were studied by transmission electron microscopy (TEM) and were found to be strongly dependent on the polarity of the solvent. Bilayer vesicles are formed in polar protic solvents, like water and methanol. TEM of an aqueous solution of **1** shows formation of spherical particles with diameters of 50–70 nm (Fig. 2a). The morphology of these particles suggests that they are vesicles and can further aggregate into larger assemblies with diameters around 200 nm. Further evidence that **1** forms cationic vesicles in water was obtained by encapsulation of the hydrophilic fluorescent dye Rhodamine B inside the vesicles. Coincidence of the elution of entrapped Rhodamine B with the vesicles confirms the existence of an aqueous interior.[8] Addition of F8P6, a perfluorooctyl and poly-ethyleneglycol-based surfactant,[9] breaks the vesicles and leads to a marked increase in Rhodamine B fluorescence, indicating the disappearance of self-quenching upon dilution of the dye into the bulk solution. In methanol both lamellar-like aggregates (Fig. 2b) and vesicles (Fig. 2c) are observed. The spherical vesicles with sizes ranging from 50 nm to 1 μm can be consistently formed and are the most stable structures. The self-assembling behavior of
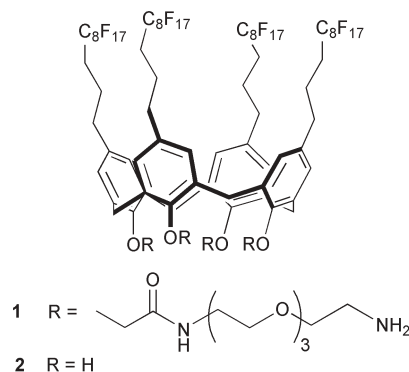
[a]School of Pharmacy, University of Wisconsin-Madison, 777 Highland Ave., Madison, WI 53705, USA. E-mail: smecozzi@pharmacy.wisc.edu; Fax: 608-262-5345; Tel: 608-262-7810
[b]Department of Chemistry, University of Wisconsin-Madison, 777 Highland Ave., Madison, WI 53705, USA
† Electronic supplementary information (ESI) available: Encapsulation of Rhodamine B in vesicles of **1**, DSC thermograms of **1** and **2**, powder X-ray diffraction of **2** quenched at 60 °C and 140 °C, polarized optical microscopy of **1** and **2**, and conditions and procedures for transmission electron microscopy. See http://dx.doi.org/10.1039/b506781b
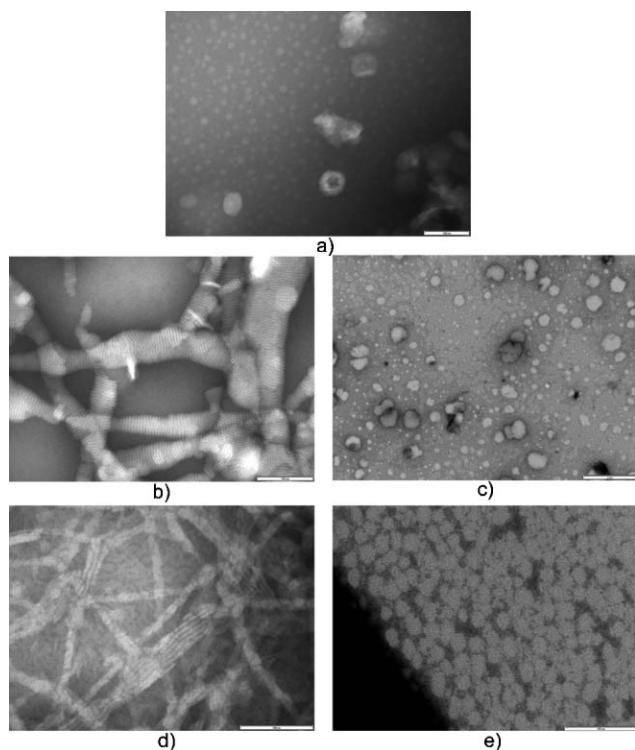

Fig. 1 Chemical structures of the mesogenic fluorinated calix[4]arenes.

Fig. 2 Transmission electron micrographs of **1** in (a) water ([**1**] = 200 μM, bar is 100 nm), (b) methanol ([**1**] = 200 μM, bar is 100 nm), (c) methanol, ([**1**] = 200 μM, bar is 2 μm), (d) chloroform ([**1**] = 200 μM, bar is 100 nm), (e) FC-72 ([**1**] = 20 μM, bar is 100 nm).
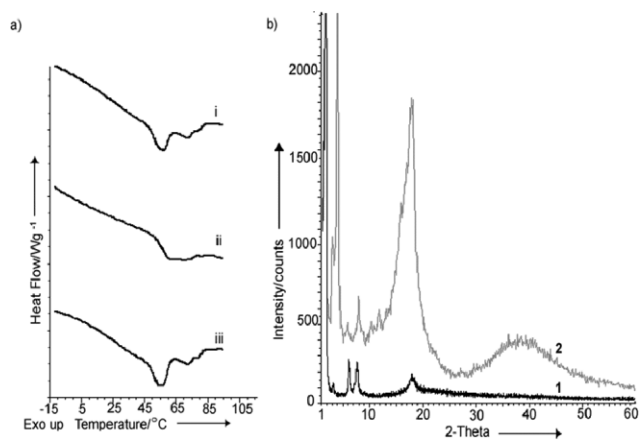

Fig. 3 (a) TMDSC profile of **1**. Heat flow scale from: (i) (total heat flow) −0.21 to −0.06 W g^{-1}. (ii) (reversible heat flow) −0.08 to −0.02 W g^{-1}. (iii) (irreversible heat flow) −0.02 to 0.04 W g^{-1}. (b) Powder X-ray diffraction patterns of **1** (bottom) and **2** (top).

molecule **1** is radically different in hydrophobic solvents. Bundles of fibers are observed in chloroform, presumably formed by head-to-head and tail-to-tail assembly of the amphiphile **1** (Fig. 2d). Finally, in perfluorohexane, calix[4]arene **1** forms inverted micelles characterized by an average diameter of 25 nm (Fig. 2e).

The phase behavior of the semifluorinated calix[4]arenes **1** and **2** was determined by a combination of differential scanning calorimetry (DSC), thermal optical polarized microscopy and powder X-ray diffraction (XRD).‡ Both materials were studied between glass slides using polarized optical microscopy and were found to be birefringent even at room temperature. As temperature was increased at 10 °C min^{-1} liquid crystalline mesophases were observed under crossed polarized light. The DSC thermograms of these two calix[4]arene derivatives exhibit several broad transitions, characteristic of materials with high molecular weight, such as polymers. The DSC profile of **1** shows multiple endothermic phase transformations occurring between 52 °C (T_g) and 85 °C, which are associated with the reorganization of the linear chains. A broad crystallization event is observed in the cooling scan at 50 °C. Calix[4]arene **1** exhibits a glassy liquid crystalline state at room temperature and then transforms into a liquid crystalline mesophase above T_g, followed by an isotropic liquid phase at temperatures higher than 125 °C. A temperature dependence XRD study of polyfluorinated derivative **2** proved that quenching the material at a temperature above the melting point leads to a significant reduction in the number of low-angle peaks, associated with long-range order in the lattice.

Temperature modulated DSC of **1** (Fig. 3a) demonstrates the occurrence of a glass transition at 52 °C. The nonreversible heat

flow profile exhibits a peak value of 56.6 °C and an enthalpy of 2.2 J g^{-1}, while the inflection point for the second order transition in the reversible heat flow profile was found to be 57.6 °C. This material exhibits a long-range order characteristic of liquid crystals that are frozen in the solid state. In this respect, compound **1** can be defined as glassy liquid crystal[10] at room temperature. This behavior is not completely unexpected as the introduction of rigid fluorinated substituents in organic molecules has been shown to favor the appearance of liquid crystalline states.[11] At higher temperatures the material undergoes several phase transitions. The liquid crystalline character of **1** is confirmed by the occurrence of sharp Bragg peaks at low angles (d = 55, 28, 14, 11 and 4.9 Å) in the powder XRD pattern and the absence of peaks at higher angles (Fig. 3b). The tetraphenol **2** retains most of the liquid crystalline properties of **1**, exhibiting a broad exothermic transition at 75 °C, followed by an endothermic pretransition at 114 °C and melting at 120 °C, as shown by the DSC profile. The powder XRD pattern of **2** shown in Fig. 3b is similar to that of the larger derivative **1**, exhibiting only sharp diffraction peaks at low angles and no peaks at high angles (d = 22, 11, 5 and 2 Å). The liquid crystalline properties of these semifluorinated calix[4]arenes are presumably imparted by the combination of the bulky and stiff perfluorooctyl chains and the rigid calix[4]arene core. The d values of 55 Å for compound **1** and 22 Å for **2** are associated in both cases with the bilayer thickness. Calix[4]arene compounds similar to **2**, but functionalized with long alkyl chains on the upper rim, have been shown to form bowlic columnar liquid crystalline phases.[12] However, amphiphile **1** cannot stack in a similar manner due to the large substituents at the lower rim.

In conclusion, we have shown that the novel amphiphile **1** has the ability to form microscopic fluorous domains that drive the formation of polarity-dependent self-assembly patterns. Furthermore, this is the only molecule, to our knowledge, that is able to self-assemble in regularly ordered patterns in solvents as different as water, chloroform and perfluorohexane. The self-assembly properties of compound **1** are an example of the variety of structures and possibilities offered by fluorous-phase driven recognition. It is conceivable that the solvent dependence of fluorous-phase driven self-assembly could be used in sensing

devices and as a molecular tool to organize complex self-assembling structures.

Notes and references

‡ DSC and temperature modulated DSC experiments were performed on DSC Q1000, TA instruments. For POM OptiphotoT2-POL, Nikon, was linked to a hot stage (TMS92, Linkam). Powder XRD patterns were recorded on a D8 Advance, Bruker Inc. instrument.

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