Amphiphilic behavior of an apparently non-polar calixarene†

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The self-assembly properties of a non-polar calixarene have been investigated at the air–water interface, in water and in the solid state showing that this molecule behaves as an amphiphilic molecule.

Amphiphilicity may be defined by the presence, in the same molecule or supramolecular system, of a hydrophilic head group and a lipophilic moiety. This duality of affinity for water confers on these molecules self-organizing properties at interfaces.[1] In nature, lipids are the main "representatives" of this class of molecules; they are the building blocks of biological membranes.

As an exception to the rules of amphiphilic self-assembly, in spite of the absence of a polar head-group, per-[2] or semi-fluorinated[3] alkanes are able to self-assemble at the air–water interface to form ordered Langmuir monolayers. This behavior has been ascribed to the particular physico-chemical properties of the fluorinated molecules.

The calix[*n*]arenes,[4] and in particular calix[4]arene in its cone conformation, represent excellent molecular scaffolds for the construction of novel amphiphilic systems.[5] The self-organizational properties of a wide range of calix[*n*]arene derivatives, ranging from the parent systems,[6] *para*-acyl-derivatives,[7] *para*-sulfonato-*O*-alkyl,[8] to phosphonato-*O*-alkyl[9] calixarenes have been reported.

Herein we demonstrate that the seemingly apolar molecule, *para-H*-tetra-*O*-dodecyl-calix[4]arene, **1**, forms stable Langmuir monolayers. Brewster angle microscopy imaging indicates that the phase behavior of the film shows typical phase changes. The solid-state packing, determined by single crystal X-ray crystallography, shows a centrosymmetric arrangement of head-to-tail stacked molecular layers. Finally, we demonstrate the formation of colloidal suspensions by **1**. The above evidence indicates that **1**, in spite of the absence of hydrophilic functions in the molecular structure, possesses true amphiphilic properties.

para-H-tetra-*O*-dodecyl-calix[4]arene, **1**, was synthesized from the parent *para-H*-calix[4]arene, by reaction of sodium hydride and bromododecane in dimethylformamide.[10] The molecular structure is given in Fig. 1.

The amphiphilic character of the parent calix[4]arene is lost when the phenolic functions are etherified and **1** can be classified as a non-amphiphilic, apolar molecule. **1** is soluble in typical non-polar solvents, including hexane, chloroform, dichloromethane and toluene but it is insoluble in polar solvents including water, methanol, and ethanol. The solution-state cone conformation is supported by ^{1}H NMR, where the signals for the methylene bridging protons show $\Delta\delta > 0.8$ ppm.[4]

The first evidence for the amphiphilic nature of **1** arises from the formation of stable monomolecular films at the air–water interface, the Langmuir isotherm of **1** is shown in Fig. 1. It should be stated that the building unit, dodecyloxy-benzene, does not self-assemble at the air–water interface under the same conditions.

The apparent molecular area of 93 Å^2 is in agreement with that predicted for the calix[4]arene head group. A clear shoulder at $\pi = 2.7$ mN m^{-1} implies that even an expanded-liquid to a condensed liquid phase change exists. The collapse pressure of $\pi = 6.6$ mN m^{-1} (at an apparent molecular area of 73 Å^2), while lower than the *para*-dodecanoylcalix[4]arene, is still in agreement with stable monolayer formation. The expansion curve shows only slight hysteresis in the apparent molecular area, the compression–decompression experiment can be repeated at least five times without any change in the observed isotherm.

Further evidence is garnered from Brewster angle microscopy (BAM) imaging of a monolayer of **1**, images are given in Fig. 2. At 0 mN m^{-1} the presence of typical rounded expanded-liquid domains on the surface is observed. As the pressure increases the gas phase domains are laterally compressed with formation of a homogeneous liquid phase. The collapse of the monolayer is observed at 6.6 mN m^{-1}, but no domains corresponding to a crystalline multilayer appear. Decompression leads to the instantaneous reformation of the expanded liquid phase domains at 0 mN m^{-1}. Again, the cycles can be repeated at least five times with no changes in the appearance of the BAM images.

The amphiphilic behavior of **1** at the air–water interface seems established from the above results, however, the mechanism of the interactions between **1** and water requires clarification. We propose that in addition to the van der Waals interactions between the alkyl chains, water molecules form O–H···π hydrogen bonds with the aromatic units of **1**. Aromatic–water interactions have been previously shown in the form of weak hydrogen bonding between water and benzene molecules[11] (1.78 kcal mol^{-1}). In the

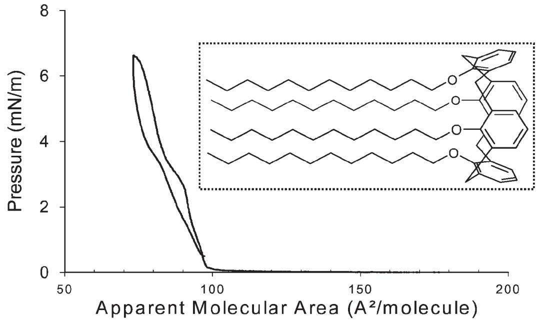

Fig. 1 Molecular formula of *para-H*-tetra-*O*-dodecyl-calix[4]arene and compression–decompression Langmuir isotherm of **1** on a pure water surface.

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† Electronic supplementary information (ESI) available: crystallographic data, experimental procedure for synthesis, AFM, BAM and Langmuir experiments. See http://www.rsc.org/suppdata/cc/b4/b412925n/

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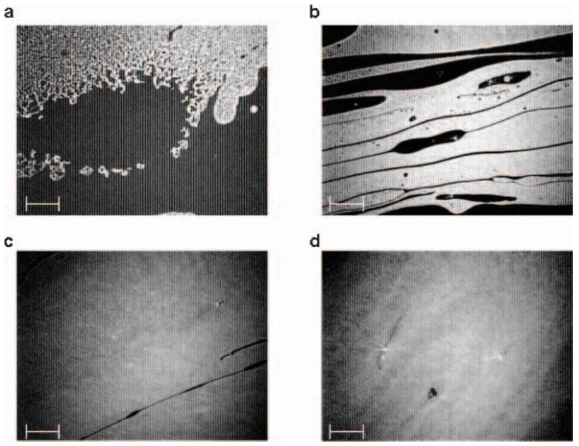

Fig. 2 Brewster angle microscope images of a monolayer of **1** at surface tensions of (a) 0; (b) 0.2; (c) 0.6 and (d) 5 mN m^{-1}. (scale bars indicate: 800 μm).

solid-state, Atwood observed a water molecule deeply embedded in a calixarene cavity, bonding to two aromatic rings.[12]

It would appear that the presence of several aromatic rings arranged in close spatial proximity, leads to cooperative stabilization of water–aromatic interactions.[13] The requirement of such cooperative behavior is confirmed by the fact that dodecyloxybenzene does not form a monolayer on a pure water interface.

We can further extend our postulate by the observation of the formation of colloidal aqueous dispersions of **1** using the solvent displacement method. Injection of a tetrahydrofuran solution of **1** into water leads to the spontaneous formation of a colloidal suspension which presents, as measured by photon correlation spectroscopy, a hydrodynamic diameter of 235 nm. These suspensions are stable over 45 days in the absence of a co-surfactant. The nanoparticles have been imaged by non-contact AFM (Fig. 3). The particles were shown to have a diameter of 400 nm and a height of 130 nm.

The crystal structure‡ of **1** has been determined and a packing diagram view down the *y*-axis is shown in Fig. 4. No solvent is present in the crystal structure. The symmetry of the molecule is forced out of C_4 to give a conformationally chiral molecule. The lowering of symmetry may be due to the tight packing of the hydrophobic alkyl chains. The calixarene head group is in the flattened cone conformation, with plane cone axis angles of 44.9°, 58.3°, −14.0° and −9.4°. Down the *x*-axis the molecules are arranged in head-to-tail layers, in an arrangement that shows no intermolecular interactions. The arrangement is that of an X or Z type Langmuir–Blodgett layer structure. Down the *y*-axis, the head-to-tail layers are seen to be arranged in a centrosymmetric, up–down manner. The hydrophobic chains are in an alternate arrangement and yield a planar lipid layer of width 18.3 Å. Between these lipid monolayers alternately oriented calix[4]arene head groups fill the void.

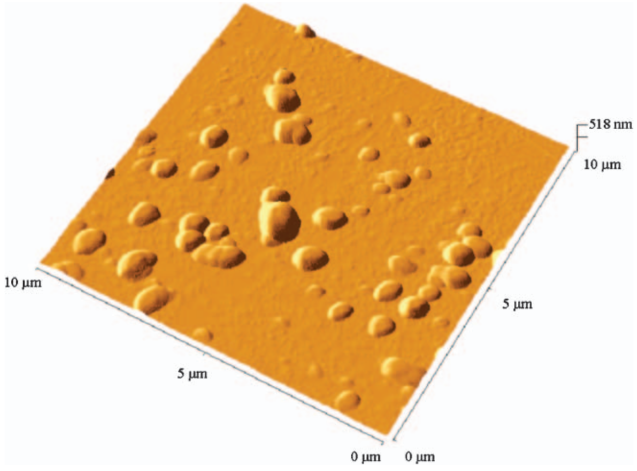

Fig. 3 Non-contact mode AFM image of **1**-based nanoparticles.

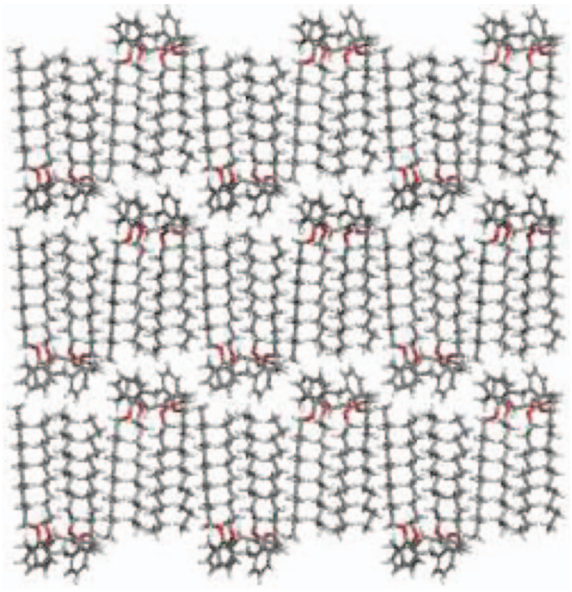

Fig. 4 Packing diagram of **1** down the *y*-axis, showing an anti-parallel centrosymmetric head-to-tail arrangement of the calixarene molecules.

The auto-organizing properties of **1** arise from a combination of oriented aromatic head groups capable of cooperatively interacting with water molecules and the presence of alkyl chains capable of forming a tightly packed non-permeable hydrophobic layer. The amphiphilic behavior of this apparently non-polar calixarene may open new lines of approach to the conception of novel supramolecular amphiphilic systems.

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Notes and references

‡ Intensity data for **1** were collected at 175 K on a Bruker SMART-APEX diffractometer using Mo-Kα radiation (λ = 0.7107 Å). The data were corrected for Lorentz and polarization effects and for absorption using the SADABS program. The structure was solved using direct methods and refined by full-matrix least-squares on |*F*|2. All non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed in geometrically calculated positions and refined with temperature factors 1.2 times those of their bonded atoms. Crystal data for **1**: Orthorhombic, *Pbca*, a = 18.760(1), b = 19.969(3), c = 36.601(6) Å, volume = 13711(4) Å^3, Z = 8, ρ_{cal} = 1.064 g cm^{-3}, μ = 0.063 mm^{-1}, $F(000)$ = 4864, $2\theta_{max}$ = 56.72°

($-24 \leqslant h \leqslant 24$, $-26 \leqslant k \leqslant -26$, $-48 \leqslant l \leqslant 44$). Final residuals (for 722 parameters) were $R^1 = 0.985$ for 16731 reflections with $I > 2\sigma I$, and $R^1 = 0.2121$, $wR^2 = 0.1870$, GooF = 0.875 for all 118361 data. Residual electron density was 0.402 and −0.330 e Å^{-3}. CCDC 249102. See http://www.rsc.org/suppdata/cc/b4/b412925n/ for crystallographic data in .cif or other electronic format.

1 G. L. Gaines, *Insoluble Monolayers at Liquid-Gas Interfaces*, Interscience, New York, 1966.
2 M. Li, A. A. Acero, Z. Huang and S. A. Rice, *Nature*, 1994, **367**, 151.
3 Z. Huang, A. A. Acero, N. Lei, S. A. Rice, Z. Zhang and M. L. Schlossman, *J. Chem. Soc., Faraday Trans.*, 1996, **92**, 545.
4 C. D. Gutsche, *Calixarenes Revisited*, The Royal Society of Chemistry, Cambridge, 1998.
5 A. Lucke, C. J. M. Stirling and V. Böhmer; in *Calixarenes 2001*, ed. Z. Asfari, Kluwer, Dordrecht, 2001; pp. 612–626.
6 Y. Ishikawa, T. Kunitake, T. Matsuda, T. Otsuka and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1989, 736.
7 P. Shahgaldian, M. Cesario, P. Goreloff and A. W. Coleman, *J. Chem. Soc., Chem. Commun.*, 2002, 326.
8 S. Shinkai, H. Kawabata, T. Arimura, T. Matsuda, H. Satoh and O. Manabe, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1073.
9 E. Houel, A. Lazar, E. Da Silva and A. W. Coleman, *Langmuir*, 2002, **18**, 1374.
10 A. Arduini and A. Casnati, *Macrocycle Synthesis, A Practical Approach*, ed. D. Parker, Oxford University Press, New York, 1996.
11 S. Suzuki, P. G. Green, R. E. Bumgarner, S. Dasgupta, W. A. Goddard III and G. A. Blake, *Science*, 1992, **257**, 942.
12 J. L. Atwood, F. Hamada, K. D. Robinson, G. W. Orr and R. L. Vincent, *Nature*, 1991, **113**, 2760.
13 B.-H. Hong, J.-Y. Lee, C.-H. Lee, J. C. Kim, S.-C. Bae and K. S. Kim, *J. Am. Chem. Soc.*, 2001, **123**, 10748.