Supramolecular expression of chirality in assemblies of gemini surfactants

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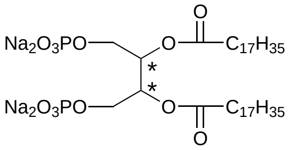
Supramolecular expression of chirality occurs in mixtures of an L-histidine derivative and the (*S*,*S*) isomer of a phosphatidic acid-based gemini surfactant, but not in mixtures of this histidine derivative and the (*R*,*R*)- or (*R*,*S*)-gemini surfactant.

Gemini surfactants are amphiphilic molecules containing two hydrophilic head groups and two long aliphatic chains, which are linked by a rigid[1,2] or flexible spacer,[3,4] and as such have potentially interesting properties.[1] Theoretical calculations[5] and recent experimental results[6,7] indeed indicate that 'geminis' behave differently from normal surfactants, which opens the way for new applications.



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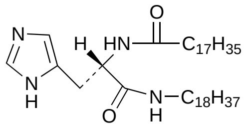

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In a previous paper we showed that gemini surfactants based on phosphatidic acid (see **1**) can undergo stereodependent fission or fusion in the presence of calcium ions.[8] Here we report that these surfactants are capable of recognising a long chain L-histidine derivative, leading to a stereodependent expression of molecular chirality at the supramolecular level.

The (*R*,*R*), (*S*,*S*) and (*R*,*S*) forms of compound **1** were synthesised as described elsewhere.[8] All three stereoisomers of **1** formed bilayer aggregates when they were dispersed in water. Histidine surfactant **2** alone could not be dispersed in water to form distinct aggregates due to its low solubility.‡ When **2** (25 or 50 mol%) was mixed with the (*R*,*S*) isomer of **1** and dispersed in water at pH 6.5, vesicles with diameters ranging from 150 to 750 nm were generated. Increasing the concentration of **2** to 75 mol% led to the formation of extended bilayers and multilayer structures. In contrast, at all concentrations aqueous dispersions of **2** and the (*R*,*R*) isomer of **1** yielded irregularly shaped, rod-like structures with an average diameter of 30 nm and a length of 0.2–2.0 μm [Fig. 1(*a*)]. When **2** and the (*S*,*S*) isomer of **1** were mixed, helical structures together with planar bilayer aggregates were found in samples containing 25 mol% of **2** [Fig. 1(*b*)]. In samples containing 50 and 75 mol% of **2**, the aggregates tended to form twisted structures [Fig. 1(*c*)], but no distinct morphologies could be detected in the bulk of the material.

Further experiments revealed that the helical structures were only generated when the concentration of **2** was between 25 and 35 mol%, with the optimum lying at 30 mol%. Right-handed helices with a pitch of approximately 90 nm and a thickness of *ca.* 40 nm were observed exclusively [Fig. 1(*d*)].§ When the concentration of **1** deviated from 30 mol%, the observed helices were shorter and many of them contained defects [Fig. 1(*c*)]. The fact that the pitch and the thickness of the helices were similar in all cases suggests that their formation occurred in a precise manner, requiring a distinct ratio of the two surfactants, rather than a variable one. Since a concentration of 30 mol% of **2** appeared to be optimal, 1 : 2 complexes of **2** and (*S*,*S*)-**1** are probably the building blocks from which the helices are constructed.

Monolayer experiments revealed that **2** forms stable monolayers at the air–water interface. The surface area–surface pressure isotherms displayed a transition to a non-compressible state at relatively low surface pressure (Fig. 2). This suggests

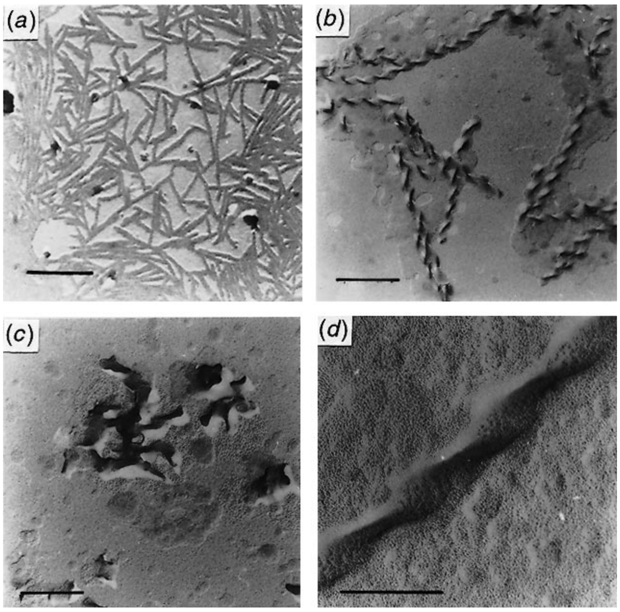

Fig. 1 Transmission electron micrographs [Pt shadowing, (*a*)–(*c*) bars represent 400 nm, (*d*) bar represents 100 nm] of mixtures of (*a*) (*R*,*R*)-**1** and **2** (75 mol%), (*b*) (*S*,*S*)-**1** and **2** (25 mol%), (*c*) (*S*,*S*)-**1** and **2** (50 mol%) and (*d*) (*S*,*S*)-**1** and **2** (30 mol%)

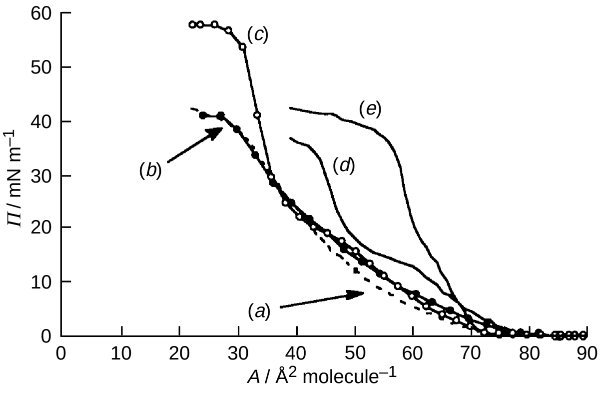

Fig. 2 Monolayer isotherms recorded at 20 °C of mixtures of (*S*,*S*)-**1** and **2** on a sub-phase of pH 6.5: (*a*) 25, (*b*) 33, (*c*) 50, (*d*) 75 and (*e*) 100 mol% **2**

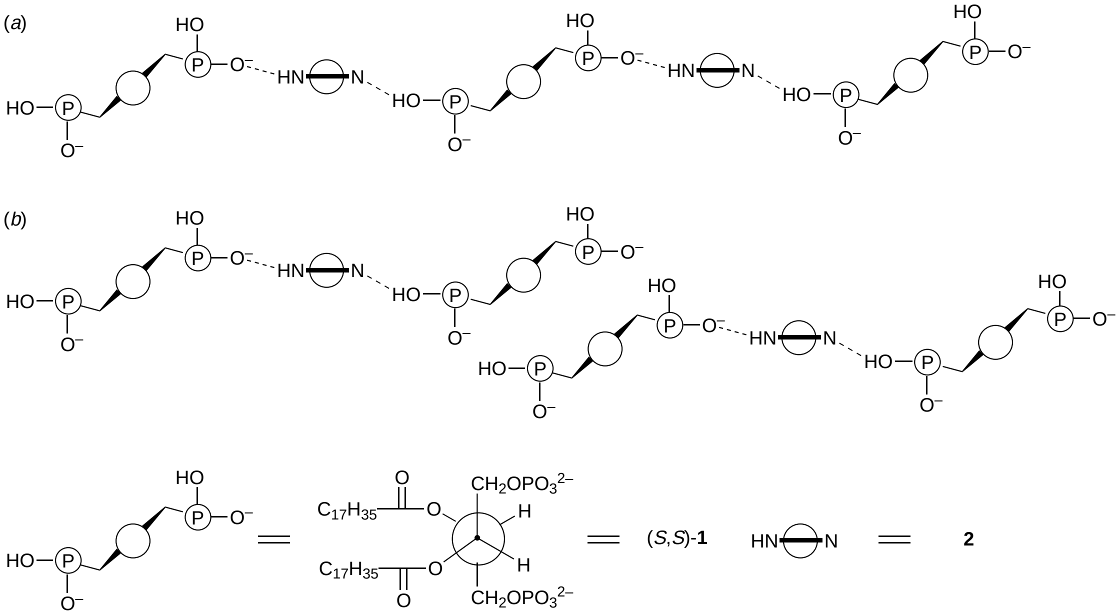

Fig. 3 Schematic representation of (*a*) a 1 : 1 complex and (*b*) a 1 : 2 complex of **2** and (*S*,*S*)-**1**

that in the monolayer the molecules of **2** have a high degree of organisation, probably because they are linked by strong intermolecular hydrogen bonds *via* their imidazole groups, assisted by the formation of so-called amide polymers, *i.e.* linear arrays of hydrogen bonds between the amide groups of **2**. Mixing **2** with an increasing amount of (*S*,*S*)-**1** led to a gradual increase in the compressibility of the monolayer and to a gradual change in the overall shape of the isotherm. At a concentration of 33 mol% of **2**—this is the concentration at which helices start to be observed—the isotherm did not change further and showed the highest degree of compressibility.¶ These results can be rationalised as follows: the (*S*,*S*) isomer of **1** preferentially adopts an extended conformation in which the phosphate groups have an *anti* orientation.[8]‖ It is likely therefore that in a 1 : 1 mixture highly ordered, linear arrays of pairs of (*S*,*S*)-**1** and **2** are present, interconnected by hydrogen bonds, both between the head groups and the neighbouring amide groups [Fig. 3(*a*)]. In this way the molecules will be confined to their positions in a two dimensional lattice. In a mixture containing 33 mol% of **2**, however, individual 2 : 1 complexes of (*S*,*S*)-**1** and **2** may be formed, allowing both translational and rotational freedom of the complexes with respect to each other [Fig. 3(*b*)]. The complexes are thus free to adopt orientations in which the average molecular area is minimised, and in which chirality is accumulated by close packing of the stereogenic centres. This asymmetric packing of the building blocks probably extends over long distances, leading to the formation of helical aggregates.

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Footnotes

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‡ Surfactant **2** was prepared from Boc-protected L-histidine. One alkyl chain was introduced by a DCC coupling with octadecylamine (yield 60%). Deprotection of the Boc-amide with trifluoroacetic acid and subsequent acylation with *N*-(stearoyloxy)succinimide resulted in the introduction of the second alkyl chain (yield 75%). Calc. for **2** ($C_{42}H_{80}O_2N_4$): C, 74.9; H, 12.0; N, 8.3. Found: C, 74.2; H, 11.5; N, 8.4%.

§ In mixtures containing 1–10 mol% of **2** planar bilayers and a small amount of fibres were observed, suggesting that only a small fraction of (*S*,*S*)-**1** is interacting with **2**, leading to the formation of these fibres.

¶ Monolayers of mixtures of **1** and **2** were inspected by Brewster angle microscopy. No chiral domains were detected.

‖ The pK_a values of (*S*,*S*)-**1** were determined to be 1.8 and 10.2, implying that at pH 6.5 the molecules are in the monoprotonated state (ref. 9).

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