Boomerang shaped aggregates from a histidine surfactant

Nico A. J. M. Sommerdijk, Mark H. L. Lambermon, Martinus C. Feiters, Roeland J. M. Nolte* and Binne Zwanenburg*

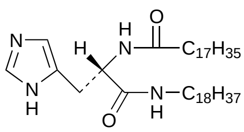
Department of Organic Chemistry, NSR-Institute for Molecular Structure, Design and Synthesis, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

Complexation of copper(II) ions to a long-chain histidine derivative leads to the formation of a new type of chiral architecture having the shape of a boomerang.

Following the discovery that phospholipid molecules can form vesicular, rod-like, and even helical aggregates,[1] many researchers have shown that similar supramolecular structures can be obtained from synthetic surfactants.[2–5] Here, we report that the synthetic histidine derivative **1** in aqueous solution in the presence of copper(ii) triflate forms boomerang-like scrolls. This novel architecture may be an intermediate state in the transformation of closed bilayers to helical structures.

Compound **1** was synthesized from Boc-protected L-histidine following a standard procedure;† **1** was not soluble in water at neutral pH, even at elevated temperatures. Protonation of **1** by dispersion in water adjusted to pH 2.5, led to the formation of very long thin fibres [Fig. 1(*a*)] which assembled side-by-side to yield bundles. Some of them showed a tendency to curl up into a right-handed, twisted structure [Fig. 1(*b*)].

Monolayer experiments indicated that **1** forms stable monolayers. The isotherm recorded at pH 6.5 displayed a sharp increase of the surface pressure at a molecular area of 60 Å^2 indicative of a non-compressible state (Fig. 2). When **1** was spread on a subphase adjusted to pH 2.5, the isotherm revealed an increase of the compressibility of the monolayer, as well as an increase in the area per molecule. The formation of a rigid monolayer at pH 6.5 is attributed to the presence of a high degree of preorganisation in the molecules, probably caused by strong intermolecular hydrogen bonds between the imidazole groups and by the formation of so-called amide polymers, *i.e.* linear arrays of hydrogen-bonded amide groups. Protonation of the imidazole groups at pH 2.5 apparently alters this hydrogen-bonding pattern, breaking up the preorganisation in the monolayer. It seems likely that the same strong intermolecular forces prevent the molecules of **1** from dissolving at neutral pH. Here also protonation is required to allow the head-groups of **1** to become hydrated and to form fibres.



1

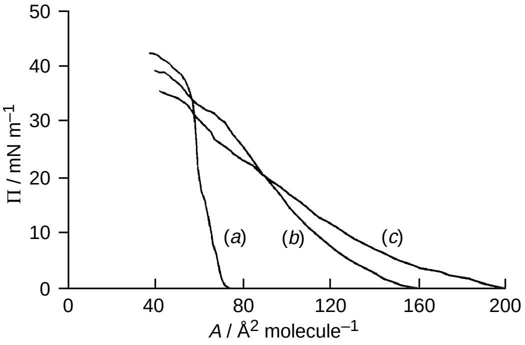


Fig. 2 Monolayer isotherms of **1** recorded at 20 °C on subphases containing (*a*) water of pH 6.5, (*b*) water adjusted to pH 2.5, and (*c*) 10 mM aqueous copper(ii) triflate

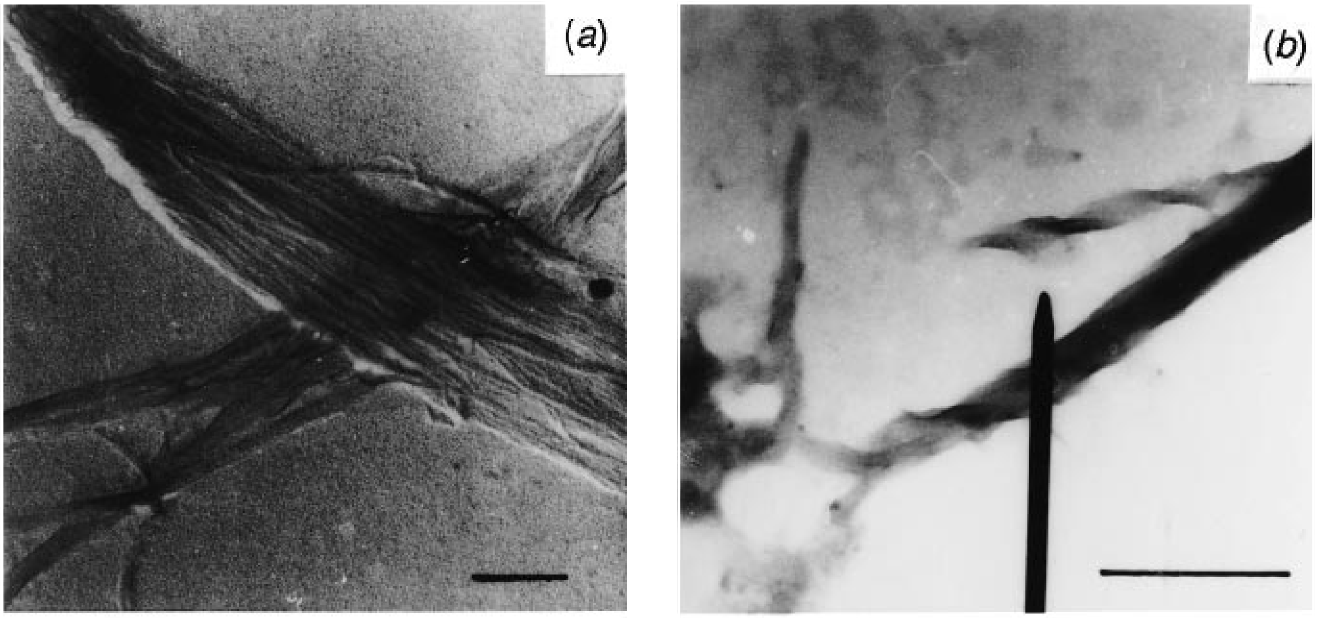


Fig. 1 Electron micrographs of aqueous 0.1% (m/m) dispersion of **1** adjusted to pH 2.5; bars represent 250 nm

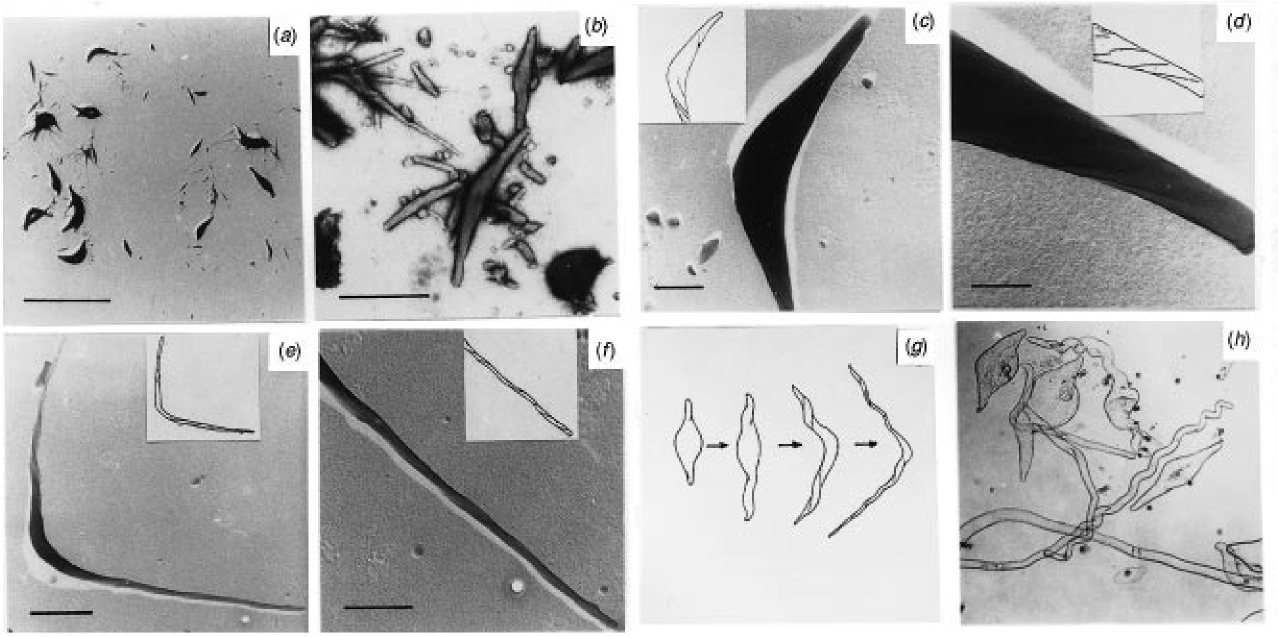


Fig. 3 (*a*)–(*f*) Transmission electron micrographs of a 0.1% (m/m) dispersions of **1** containing 0.25 molar equivalents of copper(ii) triflate. (*a*) Pt shadowing, bar 5 μm, (*b*) negative staining, bar 1 μm, (*c*) Pt shadowing, bar 250 nm, (*d*) Pt shadowing, bar 500 nm, (*e*) Pt shadowing, bar 500 nm, (*f*) Pt shadowing, bar 200 nm. Insets: graphic representations of the observed structures. (*g*) Schematic representation of the process of boomerang formation is deduced from the different observed structures, (*h*) optical micrograph of protoplasts at different stages of growth after addition of fusicoccin, kindly provided by Dr A. N. M. van Amstel.[6]

When copper triflate was added to **1** in a 1:4 ratio,‡ boomerang-like scrolls were generated [Fig. 3(*a*), (*b*)]. These had different thicknesses, but all showed a left-handed turn [Fig. 3(*d*), (*f*)]. Electron micrographs taken of samples stained with 2% uranyl acetate indicated that these scrolls were not massive, but contained an aqueous interior [Fig. 3(*b*)]. The different stages of scroll formation shown in Fig. 3 suggest that these boomerangs are formed by stretching and twisting of the vesicle membranes in a stereospecific manner. According to the overall shape of the scrolls, this twisting starts initially at opposite sides of the vesicle [Fig. 3(*g*)], resulting in a structure with a thickened centre and thin twisted ends [Fig. 3(*c*)], and eventually in thinner species which are also helical in the central part of the aggregate [Fig. 3(*e*)]. The aggregate structures in Fig. 3 show features that strongly resemble the spiral growth of protoplasts induced by the action of fusicoccin as reported by van Amstel [Fig. 3(*h*)].[6]

Remarkably, complexation of copper triflate leads to a monolayer which displays an even higher degree of compressibility, as compared to the monolayers formed on subphases of pure water adjusted to pH 6.5 and 2.5 (Fig. 2). This implies that addition of copper triflate leads to a lower degree of pre-organisation in the two-dimensional surfactant layer. This is most likely due to a preference of hydrogen-bond formation between molecules within the same complex, as opposed to the formation of long linear arrays of intermolecular hydrogen bonds. A similar situation may be present in the three-dimensional aggregates allowing the molecules to pack in such a way that their chirality is expressed at the supramolecular level. The boomerang shaped aggregates may be considered as being metastable states in the transformation of closed bilayer structures of helical ribbons. Further studies are in progress.

The authors thank H. P. M. Geurts for his assistance in performing electron microscopy experiments, W. Wong for providing artwork and Professor G. I. Tesser and P. J. H. M. Adams for the kind donation of Boc-protected l-histidine and helpful discussions.

Footnotes

† Surfactant **1** was conveniently prepared from Boc-protected l-histidine. One alkyl chain was introduced by a DCC coupling with octadecylamine (yield 60%). Deprotection of this Boc–amide with trifluoroacetic acid and subsequent acylation with *N*-stearoyloxy–succinimide resulted in the introduction of the second alkyl chain (yield 75%). Anal. **1** Calc. C, 74.9; H, 12.0; N, 8.3. Found: C, 74.2; H, 11.5; N, 8.4%.

‡ Comparable ligand systems have been shown to form copper complexes of the type [Cu(Him)$_4$] (Him = imidazole), see ref. 4*b*.

References

1 A. D. Bangham and R. W. Horne, *J. Mol. Biol.*, 1964, **8**, 660; D. Papahadjopoulos, W. J. Vail, K. Jacobson and G. Poste, *Biochim. Biophys. Acta*, 1975, **394**, 483; K. Inoue, K. Suzuki and S. Nojima, *J. Biochem.*, 1977, **81**, 1097.
2 J. H. Fuhrhop and W. Helfrich, *Chem. Rev.*, 1993, **9**, 1565 and references therein.
3 J. M. Schnur, *Science*, 1993, **262**, 1669 and references therein.
4 N. A. J. M. Sommerdijk, P. J. J. A. Buynsters, A. M. A. Pistorius, M. Wang, M. C. Feiters, R. J. M. Nolte and B. Zwanenburg, *J. Chem. Soc., Chem. Commun.*, 1994, 1941; (*b*) R. J. H. Hafkamp, M. C. Feiters and R. J. M. Nolte, *Angew Chem.*, 1994, **106**, 1054.
5 J.-H. Fuhrhop and J. Mathieu, *Angew. Chem.*, 1984, **96**, 124; T. Kunitake and S. Shinkai, *Adv. Phys. Org. Chem.*, 1980, **17**, 435.
6 A. N. M. van Amstel, Ph.D. Thesis, University of Nijmegen, 1994.

Received, 19th December 1996; Com. 6/08500H