

Surfactants Containing Imidazole Ligands. Spontaneous Formation of Vesicles by Addition of Metal Ions

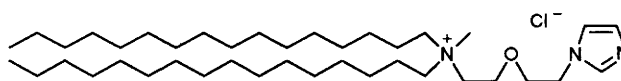
J. H. van Esch,^a A. L. H. Stols^b and R. J. M. Nolte*^a

^a Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

^b Department of Cell Biology and Histology, University of Nijmegen, Albertusplein 1, 6500 HB Nijmegen, The Netherlands

Metal ions increase the headgroup size of the ligand-surfactant dihexadecyl[5-(1-imidazolyl)-3-oxapentyl]-methylammonium chloride and trigger the conversion of open to closed bilayer structures.

Recent interest in the use of synthetic surfactant aggregates as supports for catalytic functions,¹⁻³ has prompted us to synthesize the imidazole ligand-surfactant **1** and to study its self-organizing properties in water. In this Communication, we report that aqueous dispersions of **1** form planar bilayer



1

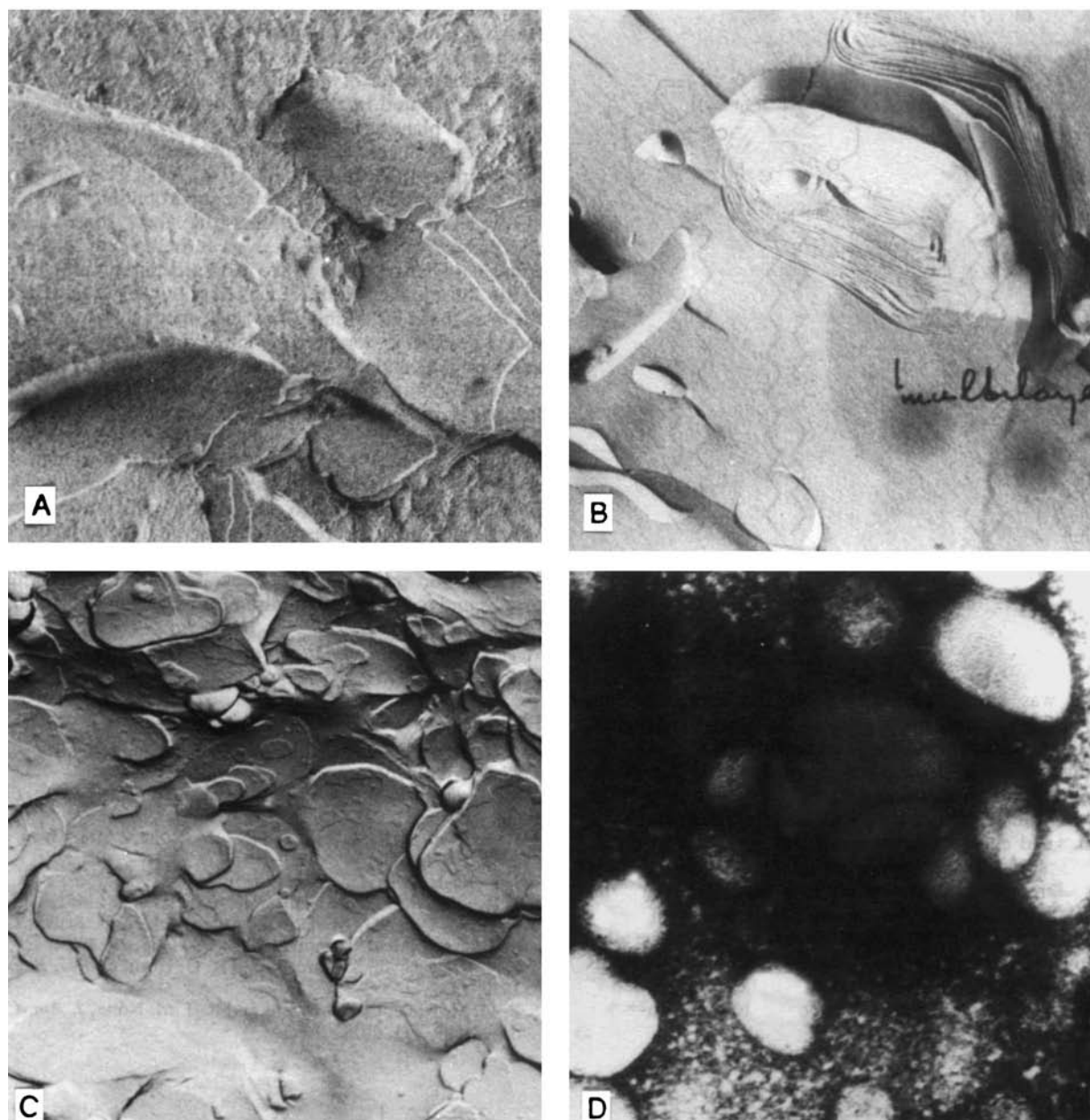


Fig. 1 Electron micrographs of 0.05 mol dm^{-3} dispersions of **1** (freeze-fracture method) in water (A, magn. $92\,000\times$), in $0.1 \text{ mol dm}^{-3} \text{ CuCl}_2$ (B, magn. $40\,000\times$), and in $0.1 \text{ mol dm}^{-3} \text{ ZnCl}_2$ (C, magn. $40\,000\times$). Electron micrograph of a 2 mol dm^{-3} dispersion of **1** in $0.1 \text{ mol dm}^{-3} \text{ CuCl}_2$ (D, negative staining with 1% uranylacetate, magn. $138\,000\times$).

structures, which spontaneously transform into closed vesicles when Cu^{2+} ions are added.

Compound **1** was synthesized starting from *N*-methyl-2-(2-aminoethoxy)ethanol by the following steps: (i) double alkylation with hexadecylbromide in ethanol in the presence of base (64%), (ii) treatment with SOCl_2 in CH_2Cl_2 (98%), and (iii) reaction with NaI and imidazole in acetonitrile (58%). The final product was converted into its chloride salt by ion exchange chromatography (Dowex 1X2-100).

Dispersion of **1** in water by vortexing at 50°C yielded a clear solution, which, after cooling to ambient temperature, became viscous but remained optically clear. Differential scanning calorimetry (DSC) showed a sharp phase transition at 33°C , which is indicative of the formation of an ordered bilayer structure.⁴ Electron microscopy revealed the presence

of large, stacked planar bilayer structures (Fig. 1). Vesicles or other curved bilayer structures are not observed.

Upon addition of CuCl_2 above the phase transition temperature a broad absorption band with a maximum at 620 nm is observed in the visible spectrum, characteristic of a $\text{Cu}^{\text{II}}\text{-(imidazole)}_4^{2+}$ complex.⁵ From a titration experiment, using the increase in absorbance at 620 nm, the stoichiometry of the complex was calculated to be 3.4 ± 0.2 . The apparent association constant amounted to $(6.5 \pm 1.2) \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$.⁶ Upon cooling, the solution became opalescent, which suggests that the metallo-aggregates have a morphology different from the metal-free dispersions. Electron microscopy showed the disappearance of the stacked bilayer structures and the formation of unilamellar and multilamellar vesicles (Fig. 1). Remarkably, the gel to liquid phase

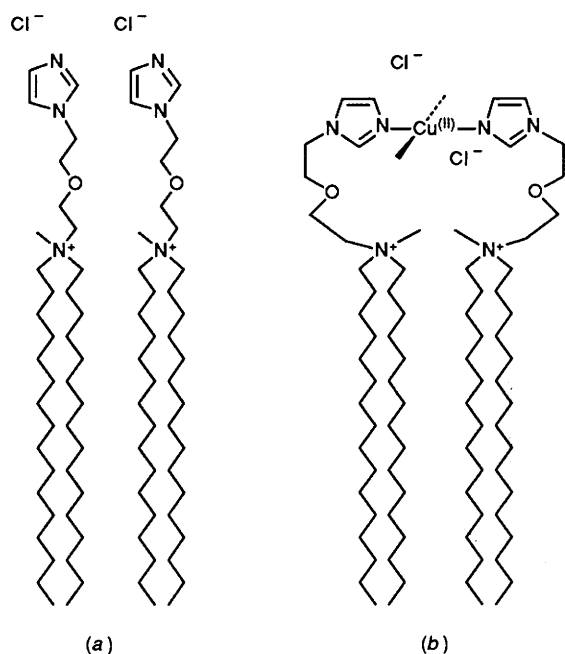


Fig. 2

transition was hardly affected (34°C), which means that binding of Cu²⁺ mainly takes place in the headgroup region, leaving the order of the alkyl chains undisturbed.

Binding of ZnCl₂ to dispersions of **1** above the phase transition temperature resulted in the formation of a white precipitate. Electron microscopy showed that this precipitate also contained curved bilayer structures, as opposed to the metal-free surfactant solutions (Fig. 1). However, these bilayers were strongly associated into very large globular aggregates. DSC did not detect any phase transition in the temperature range 5–60°C suggesting that melting of the alkyl chains in these aggregates is no longer cooperative. ¹H NMR titration experiments showed that complexes are formed in which four imidazole ligands are bound to one Zn²⁺ ion (experimentally 3.7 ± 0.3).

These results indicate that the aggregate morphology of **1** is strongly affected by binding of metal ions. The observed morphology changes can be explained from a decrease in the packing parameter of surfactant **1**.⁷ In the metal-free system the *N*-substituted imidazolyl functions will point away from the bilayer plane as is shown in Fig. 2(a). On coordination to a metal centre the imidazolyl functions are forced to become more parallel to the bilayer plane [Fig. 2(b)]. This will increase the headgroup size whereas the hydrophobic part is not affected. It is remarkable that the Cu²⁺ ions prefer to coordinate within the bilayers to form vesicles and do not coordinate between bilayers to form precipitates as in the case of the Zn²⁺ ions. This different behaviour might be related to the fact that Cu(II) and Zn(II) can form different types of metal-imidazole complexes. However, other factors like anion binding and hydration of the headgroup may also play a role. The nature of the dominant factors is currently under investigation. Interestingly, coordination of four ligand-surfactant molecules to a Cu²⁺ ion at the water-vesicle interface, as depicted in Fig. 2(b), leads to the formation of cavities of a type previously discussed by us.⁸ Such cavities, called metallohosts, may be expected to encapsulate substrate molecules, which could be of interest for further catalytic applications.

We are grateful to Dr José Leunissen (University of Utrecht) for recording the freeze-fracture electron micrographs and to Mr H. Duyghuisen for experimental assistance.

Received, 29th May 1990; Com. 0102381G

References

- 1 J. H. Fuhrhop, V. Koesling and G. Schönberger, *Liebigs Ann. Chem.*, 1984, 103.
- 2 R. Fornasier, P. Srimin, P. Tecilla and U. Tonellato, *J. Am. Chem. Soc.*, 1989, **111**, 224.
- 3 J. van Esch, M. F. M. Roks and R. J. M. Nolte, *J. Am. Chem. Soc.*, 1986, **108**, 6093.
- 4 J. F. Nagle, *Ann. Rev. Phys. Chem.*, 1980, **31**, 157.
- 5 J. Reedijk, *Recl. Trav. Chim. Pays-Bas*, 1969, **88**, 1451.
- 6 J. D. R. Hille, G. M. Donné-op den Kelder, P. Sauve, G. H. de Haas and M. R. Egmond, *Biochem.*, 1981, **20**, 4068.
- 7 J. N. Israelachvili, S. Marcelja and R. G. Horn, *Q. Rev. Biophys.*, 1980, **13**, 2.
- 8 F. G. M. Niele, C. F. Martens and R. J. M. Nolte, *J. Am. Chem. Soc.*, 1989, **111**, 2078.