

# Notes

## Coordinatively Polymerized Bilayer Membranes Prepared in Formamide

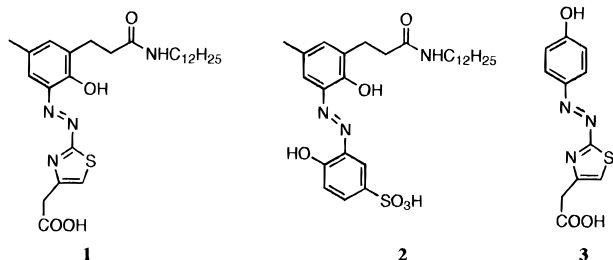
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Bilayer membranes formed by synthetic surfactants are receiving intense interest as biomembrane models and for their ability of drug delivery, solar energy conversion, and other biomimetic functions.<sup>1</sup> Emergence of a wholly new branch of organic chemistry is expected if stable molecular bilayers are produced in organic media,<sup>2</sup> but few examples of such bilayer membranes have been reported. Here, we wish to report a novel method of preparation of synthetic bilayer membranes in a polar organic solvent, based on coordinative polymerization of *N*-dodecyl-3-[2-hydroxy-3-((4-(carboxymethyl)-2-thiazolyl)azo)-5-methylphenyl]propanamide (**1**) in formamide (HCONH<sub>2</sub>).



Coordinative polymerization has been recently developed as a new method for stabilization of bilayer membranes.<sup>3</sup> Polymerization of bilayer membranes can eliminate the basic instability element of bilayer membranes while retaining the structure and physical characteristics of the parent bilayer membranes. Easier control of the degree of polymerization and, consequently, better balancing of the fluidity and rigidity of the polymerized bilayer membranes can be achieved through coordinative polymerization than through organic polymerization. Coordination polymers derived from bilayer membranes could provide additional advantages originating from electronic, magnetic, or catalytic properties of metal ions. A previous study with amphiphile **2** led to coordinatively polymerized bilayer membranes which manifested considerable enhancement in resistivity against disruption in aqueous ethanol.<sup>3</sup>

In the present study, we made a search for analogues of **2** which produce coordinatively polymerized bilayer membranes in polar organic solvents. Compound **1** (mp 178–180 °C dec) was prepared by coupling in 6 N NaOH at 4 °C of *N*-dodecyl-3-[2-hydroxy-5-methylphenyl]propanamide<sup>3</sup> with the diazonium ion derived from 2-amino-4-thiazoleacetic acid. When heated in formamide, **1** formed a scarlet solution. Bilayer membranes, however, were not formed with **1** in formamide. After 1 equiv of FeCl<sub>2</sub> (0.10 M, 0.050 mL) dissolved in formamide was added to the solution of **1** (0.010 M, 0.50 mL) in formamide kept at 80 °C and the mixture was sonicated for 15 min, a bluish black solution of bilayer membranes was obtained. The transmission electron micrographs of the self-assemblies of **1** prepared in formamide in the presence of FeCl<sub>2</sub>, FeCl<sub>3</sub>, or CoCl<sub>2</sub> are illustrated in Figure 1. Vesicular structure is strongly suggested by the micrographs of Figure 1.

When the self-assemblies obtained by sonication of **1** in the presence of the transition metal ions were subjected to gel filtration with Sepharose CL-2B in formamide, more than 80% of the metal ion and **1** were eluted in the void volume before the blue dextran marker. Thus, superstructures with very large molecular weights<sup>4</sup> were formed, in agreement with formation of bilayer membranes.

In addition, slow release of 5(6)-carboxyfluorescein entrapped within the superstructure obtained by sonication of **1** in formamide in the presence of FeCl<sub>2</sub> at 80 °C also supported formation of bilayer membranes. After the Fe(II)-containing self-assemblies of **1** were prepared in the presence of 10 equiv (0.10 M) of 5(6)-carboxyfluorescein and sodium bicarbonate in formamide, the superstructures containing entrapped 5(6)-carboxyfluorescein were separated by gel filtration with Sepharose CL-2B in formamide. It took about 10 h for half of the 5(6)-carboxyfluorescein entrapped within the vesicles to be released at room temperature as checked by the increase in fluorescence of 5(6)-carboxyfluorescein.<sup>5</sup> In formamide, 5(6)-carboxyfluorescein is not fluorescent at ≥0.02 M due to self-quenching but becomes strongly fluorescent upon dilution.

Precipitates were formed in a minor amount after sonication of **1** with FeCl<sub>2</sub> in formamide. These were removed by centrifugation or filtration. When FeCl<sub>3</sub> or CoCl<sub>2</sub> was used instead of FeCl<sub>2</sub>, dark brown solutions of bilayer membranes were obtained with formation of greater amounts of precipitates. Even greater amounts of precipitates were formed when NiCl<sub>2</sub> or CuCl<sub>2</sub> was used, and the materials obtained therein were not examined further.

The IR peak for the azo group of **1** appeared at 1480 cm<sup>-1</sup>, whereas those of the coordinatively polymerized bilayer membranes of **1** prepared with 1 equiv of Fe(II), Fe(III), or Co(II) were located at 1456–1468 cm<sup>-1</sup>. This is consistent with coordination of azo nitrogens to metal ions.

Formation of the self-assemblies of **1** in the presence of FeCl<sub>2</sub>, FeCl<sub>3</sub>, or CoCl<sub>2</sub> was accompanied by an increase in

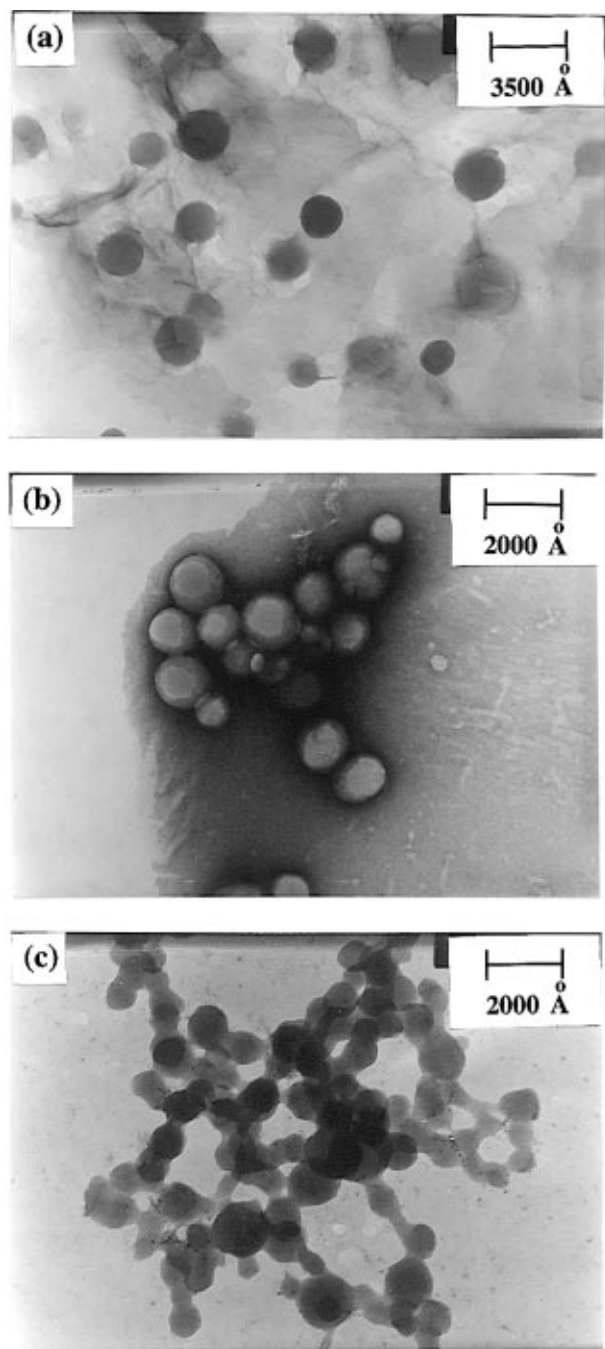
(1) (a) Calvin, M. *Acc. Chem. Res.* **1978**, *11*, 369. (b) Fendler, J. H. *Acc. Chem. Res.* **1980**, *13*, 7. (c) Gros, L.; Ringsdorf, H.; Schupp, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 305. (d) Fendler, J. H. *Membrane Mimetic Chemistry*; Wiley-Interscience: New York, 1982. (e) Fendler, J. H.; Tundo, P. *Acc. Chem. Res.* **1984**, *17*, 3. (f) Fuhrhop, J. -H.; Mathiew, J. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 100. (g) Fuhrhop, J. -H.; Frisch, D. *Acc. Chem. Res.* **1986**, *19*, 130. (h) Fendler, J. H. *Chem. Rev.* **1987**, *87*, 877. (i) Ringsdorf, H.; Schlab, B.; Venzmer, J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 113. (j) Robinson, J. N.; Cole-Hamilton, D. *Chem. Soc. Rev.* **1991**, *20*, 49. (k) Lockhoff, O. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1611.

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(4) Sepharose CL-2B is generally employed in separation of globular proteins with molecular weights of 7 × 10<sup>4</sup> to 4 × 10<sup>7</sup> or dextrans with molecular weights of 1 × 10<sup>5</sup> to 2 × 10<sup>7</sup>.

(5) Under these conditions, vesicular structure was retained, as checked by transmission electron microscopy.

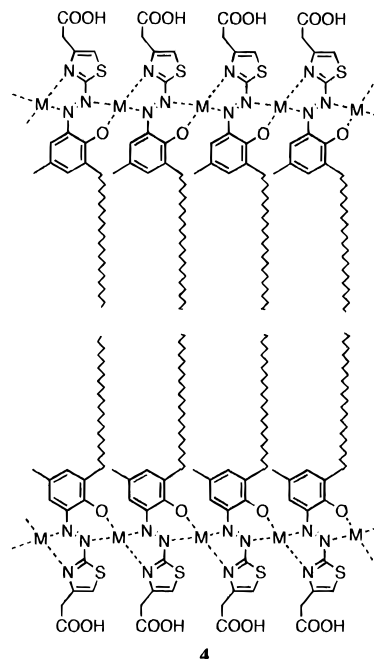


**Figure 1.** Transmission electron micrographs of assemblies of various bilayer membranes of **1** prepared in formamide in the presence of 1 equiv of Fe(II) (a), Fe(III) (b), or Co(II) (c) ion.

absorbance in the visible region, as was observed previously in the formation of coordinatively polymerized bilayer membranes of **2** in water.<sup>3</sup> When more than 1 equiv of the metal ion was added, the absorbance was not affected further, indicating that up to 1 equiv of the metal ion was incorporated into the superstructure.

Appreciable color changes were not observed when transition metal ions were mixed with **3**, which is not capable of coordinative polymerization. Thus, the appearance of intense colors upon coordination of transition metal ions to **1** also supports the formation of coordinative polymers. Since azothiazole rings coordinate to transition

metal ions through the aromatic nitrogen atom instead of the sulfur atom,<sup>6</sup> the coordinatively polymerized vesicles obtained with **1** can be schematically illustrated as **4**.



Bilayer membranes have been prepared in organic solvents of low polarity such as cyclohexane, chloroform, or toluene. For example, fluorocarbon chains were employed as the solvophobic part in cyclohexane.<sup>2</sup> Calcium phosphate salt was used as the solvophobic part to form a bilayer with fiber-like morphology in chloroform or toluene.<sup>7</sup> Reversed vesicles have been obtained by adding a small amount of water to a solution of tetra-ethyleneglycol dodecyl ether in dodecane, where the hydrophilic group of the surfactant was the solvophobic part.<sup>8</sup>

The results obtained in the present study support formation of coordinatively polymerized bilayer membranes of **1** in the presence of FeCl<sub>2</sub>, FeCl<sub>3</sub>, or CoCl<sub>2</sub> in formamide. Amphiphile **1** forms vesicles in formamide only in the presence of the transition metal ions. Transition metal ions bound to **1** would further interact with formamide, increasing the solvophilicity of the polar head of the amphiphile. In addition, coordinative polymerization of the polar heads would facilitate self-assembly of the amphiphiles. Induction of formation of vesicles of **1** in formamide by the transition metal ions may be attributed to the increased solvophilicity of the polar heads and/or the assemblage of polar heads. The hydrogen bonding between the propanamide groups in the solvophobic region and that between carboxyl groups and formamide in the solvophilic region may provide additional factors for stabilization of the vesicles in formamide.

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