Self-Organization of Bilayer Membranes from Amphiphilic Networks of Complementary Hydrogen Bonds[1]

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We describe herein self-assembly of ordered bilayer membranes from amphiphilic complexes of complementary hydrogen bond pairs as an aqueous dispersion and as a cast film.

Synthetic bilayer membranes are two-dimensionally organized molecular assemblies. The mode of packing of component amphiphiles plays a crucial role in determining physical properties of these bilayers and consequently their functions.[2] In addition to alignment of hydrophobic alkyl chains, the intermolecular stacking of rigid segments[3] and multiple hydrogen bonds among neighboring amphiphiles[4] promote ordered bilayer assemblies.

Molecular recognition and self-assembling processes directed by complementary hydrogen bonding have received a great deal of attention.[5-7] Construction of bilayer membranes via complementary hydrogen bonding would provide a new class of self-assembly in which novel molecular control is achieved. In general, hydrogen bonding in artificial molecular systems is most effective in solid states or in noncompetitive (aprotic) organic media. However, our recent finding that molecular recognition via hydrogen bonding is effective at the air–water interface[8] prompted us to investigate molecular recognition-directed bilayer assembly in bulk water.

Substituted melamines **1** and **2** and isocyanuric acid derivatives **3** and **4**[9] (shown in Chart I) were used as molecular components because they form extended arrays of complementary hydrogen bonds.[6,7]

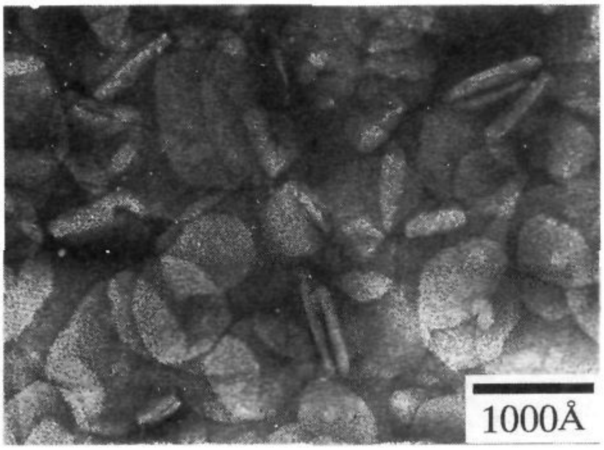
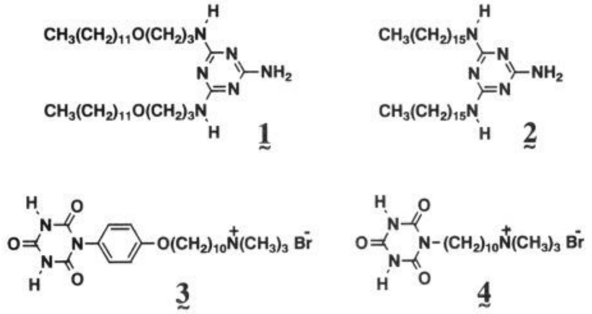


Figure 1. Electron micrograph of an aqueous dispersion of **1–3** (1.5 mM). Stained by uranyl acetate.

Chart I



Molecular complexes of **1**, **2** and **3**, **4** were prepared by mixing equimolar amounts of each component in ethanol and removing the solvent under reduced pressure. This procedure was repeated 3 times, and the resultant complexes were finally dried at 60 °C in vacuo. Among the prepared equimolar complexes of **1–3**, **1–4**, **2–3**, and **2–4**, only **1–3** gave a transparent dispersion in water (ca. 30 mM) upon ultrasonication (Branson Sonifier Model 185, sonic power 45 W, 10 min at 0 °C). The aqueous dispersion was stable over a period of 1 month. In contrast, the other complexes and components **1**, **2**, and **3** displayed poor solubilities in water even at a lower concentration of 5 mM. From comparisons of the component structures, we suggest that improved molecular orientation by the phenyl group in **3** and facilitated alkyl chain alignment by the ether linkage in **1** are crucial to give an ordered, stable assembly. Similar effects have been noticed in conventional bilayer assemblies.[11,12] The equimolar composition was essential for producing a stable dispersion, since nonequimolar mixtures (**1**:**3** = 1:2 or 2:1 (mol/mol), [**1**] = 20 mM) did not give homogeneous dispersions.

Figure 1 shows a transmission electron micrograph (Hitachi H600) of **1–3** dispersed in water. Disklike aggregates with diameters of several 100 Å and a thickness of ca. 100 Å are found. Differential scanning calorimetry of aqueous **1–3** (5 mM) displayed a reproducible endothermic peak in the range of 55–75 °C with ΔH of 40 kJ mol^{-1}. This ΔH value lies within the range of typical aqueous bilayers.[13]

A self-supporting film was obtainable by casting the aqueous dispersion on a glass plate, as is the case with other bilayer membranes.[14] An IR spectrum (KBr) of the film contained a group of the C=O stretching bands at 1761, 1738, and 1692 cm^{-1} which were altered from those observed for **3** alone (1754 and 1696 cm^{-1}). In addition, the triazine ring vibration[15] observed at 812 cm^{-1} in **1** alone was weakened significantly in the equimolar cast film. These IR changes suggest that complementary hydrogen bonds are formed between **1** and **3**.[16]

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[1] Contribution No. 973 from the Department of Chemical Science and Technology.

[2] Kunitake, T. *Angew. Chem., Int. Ed. Engl.* **1992,** *31,* 709 and references therein.

[3] Kunitake, T.; Okahata, Y.; Shimomura, M.; Takarabe, K. *J. Am. Chem. Soc.* **1981**, *103*, 5401.

[4] Kunitake, T.; Yamada, N.; Fukunaga, N. *Chem. Lett.* **1984**, 1089.

[5] For example, see: Rebek, J., Jr. *Acc. Chem. Res.* **1990,** *23,* 399. Rebeck, J., Jr. *Science (Washington, DC)* **1987**, *235*, 1478. Hamilton, A. D.; Van Engen, D. *J. Am. Chem. Soc.* **1987**, *109*, 5035. Chang, S.-K.; Hamilton, A. D. *ibid.* **1988**, *110*, 1318. Chang, S.-K.; Van Engen, D.; Fan, Erkang.; Hamilton, A. D. *Ibid.* **1991**, *113*, 7640. Garcia-Tellado, F.; Geib, S. J.; Goswami, S.; Hamilton, A. D. *Ibid.* **1991**, *113*, 9265.

[6] Lehn, J.-M.; Mascal, M.; Decian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1990**, 479. Lehn, J.-M.; Mascal, M.; Decian, A.; Fischer, J. *J. Chem. Soc., Perkin Trans. 2* **1992**, 461.

[7] Seto, C. T.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 6409; **1991**, *113*, 712. Zerkowski, J. A.; Seto, C. T.; Whitesides, G. M. *Ibid.* **1992**, *114*, 5473.

[8] Sasaki, D. Y.; Kurihara, K.; Kunitake, T. *J. Am. Chem. Soc.* **1991**, *113*, 9685 and references cited therein.

[9] Substituted melamines **1** and **2** were synthesized by aminoalkylation of 2-amino-4,6-dichlorotriazine. Isocyanuric acid derivatives **3** and **4** were prepared according to the modified method of Hagemann.[10] All new compounds gave satisfactory ^{1}H NMR data (60 MHz) and elemental analysis. Detailed description of the synthetic procedures will be reported elsewhere.

[10] Hagemann, H. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 743.

[11] (a) Nakashima, N.; Kunitake, T. *J. Am. Chem. Soc.* **1982,** *104,* 4261. (b) Kato, S.; Kunitake, T. *Polym. J.* **1991**, *23*, 135.

[12] Kimizuka, N.; Takasaki, T.; Kunitake, T. *Chem. Lett.* **1988**, 1911.

[13] Kunitake, T.; Ando, R.; Ishikawa, Y. *Mem. Fac. Eng., Kyushu Univ.* **1986**, *46*, 221.

[14] For example, see: Asakuma, S.; Okada, H.; Kunitake, T. *J. Am. Chem. Soc.* **1991**, *113*, 1749 and references cited therein.

[15] Padgett, W. M., II; Hamner, W. F. *J. Am. Chem. Soc.* **1958,** *80,* 803.

[16] Bellamy, L. J. *Advances in Infrared Group Frequencies*; Methuen & Co. Ltd.: Great Britain, 1968.

0002-7863/93/1515-4387$04.00/0

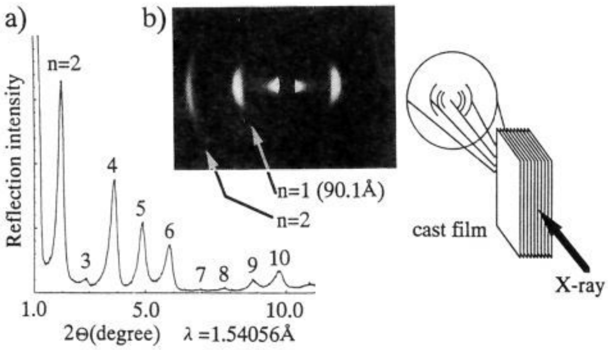

Figure 2. X-ray diffraction patterns of a **1–3** cast film: (a) reflection diffraction; (b) edge-view, small-angle, transmission diffraction.

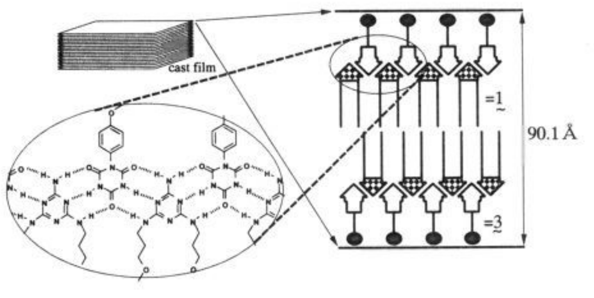

Figure 3. Schematic illustration of the bilayer structure of the **1–3** complex.

X-ray diffraction patterns of the cast film are shown in Figure 2. In the transmission method, the X-ray beam was irradiated parallel to the vertically-set film plane (edge view). Equatorial diffractions are observed up to 10th order with a long period of 90.1 Å. This spacing corresponds to the bilayer thickness of the hydrogen-bonded array of **1–3**, as estimated from a molecular model. It is clear that regular multibilayers exist parallel to the film plane.

IR and X-ray diffraction data indicate that a hydrogen-bonded molecular array as schematically illustrated in Figure 3 is formed in the cast film. The identical network structure is probably present in the aqueous dispersion. The presence of the single bilayer dispersion (90–100-Å thickness) is suggested by electron microscopy. The ordered structure is formed by self-organization of two molecular units via complementary hydrogen bonding and hydrophobic association. Remarkable stabilization of the complementary hydrogen bonds in the aqueous environment can be ascribed to the ordered stacking of the extended array of hydrogen bonding units in the bilayer.

Recently, association of adenine and hydrophilic Kemp's acid derivatives was observed in water.[17] Base-pairing of adenine and thymine derivatives in an aqueous micelle was also reported.[18] However, hydrogen-bond-mediated formation of an amphiphilic unit in water as an indispensable process to produce ordered assemblies has never be reported. The combination of bilayer assembly and hydrogen-bond network provides a unique structural feature and offers a wide range of novel functions.

Supplementary Material Available: Brief synthetic outlines of **1–4**, IR spectra of **1**, **3**, and **1–3** mentioned in the text (2 pages). Ordering information is given on any current masthead page.

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[17] Rotello, V. M.; Viani, E. A.; Deslongchamps, G.; Murray, B. A.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1993**, *115*, 797.

[18] Nowick, J. S.; Chen, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 1107.