

## Self-Organization of Bilayer Assemblies in a Fluorocarbon Medium<sup>1</sup>

Hiroaki Kuwahara, Mitsuo Hamada, Yuichi Ishikawa, and Toyoki Kunitake\*

Department of Chemical Science and Technology  
Faculty of Engineering, Kyushu University  
Fukuoka 812, Japan

Received October 14, 1992

We report herein a new class of bilayer assemblies that are unique to fluorocarbon media.

Self-assembling aqueous bilayers have been prepared from a variety of synthetic amphiphilic compounds.<sup>2</sup> These molecules are comprised of polar head groups and hydrophobic alkyl chains, and this amphiphilic property is essential to their self-organization into bilayers in water. The self-assembly concept was recently extended to novel "amphiphiles", represented by **1**, which contain a "solvophilic" hydrocarbon unit and a "solvophobic" fluorocarbon unit.<sup>3,4</sup> These compounds undergo bilayer formation in some hydrocarbon solvents due to aggregation and alignment of the fluorocarbon chains. The limited miscibility of hydrocarbons and fluorocarbons<sup>5</sup> is crucial in this case.

Yet another class of amphiphile is conceivable by reversing the roles of hydrocarbon and fluorocarbon units. Turberg and Brady reported formation of micellar aggregates in fluorocarbon solvents

### Chart I

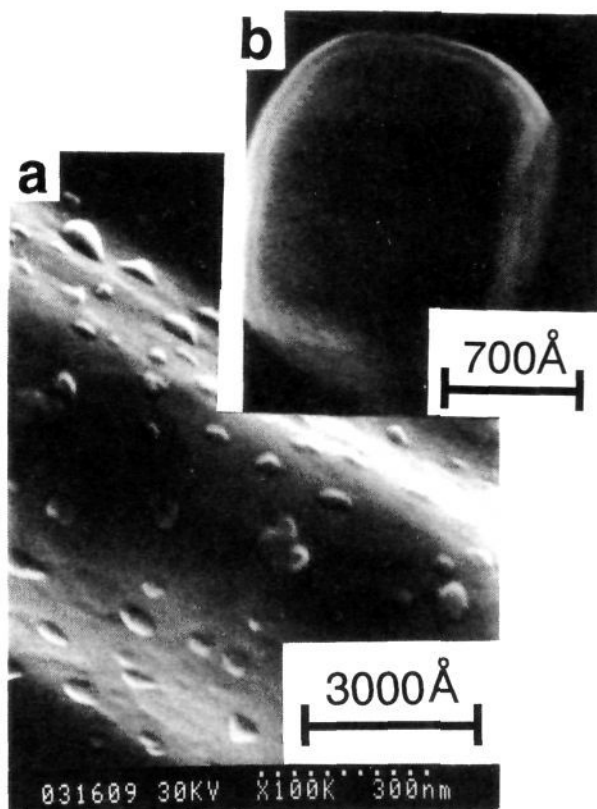
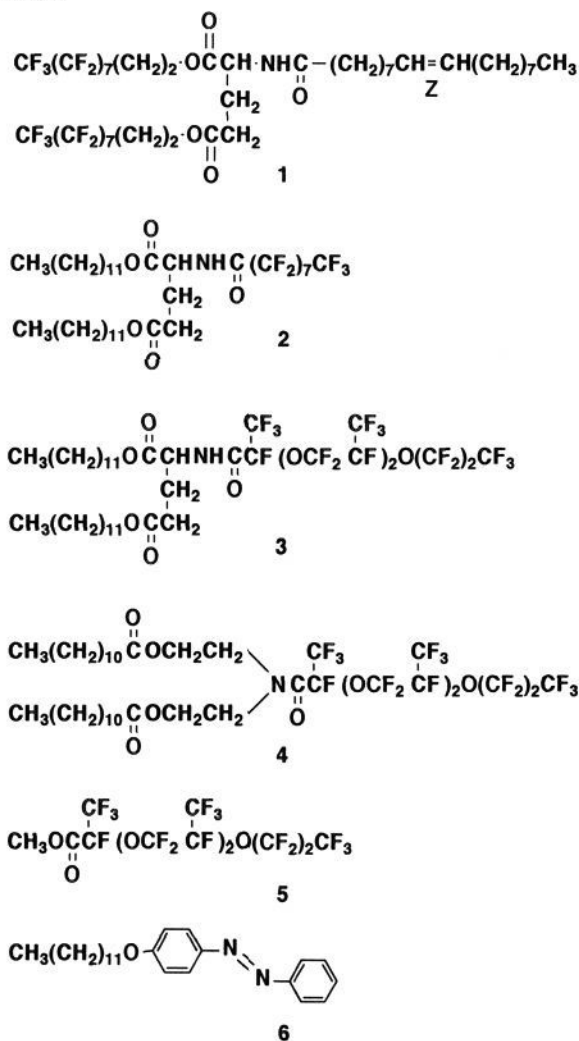


Figure 1. Scanning electron micrographs of **3** in solvent **5**, [**3**] = 10mM, at ca. 15 °C. (a) Overview, (b) expanded view.

by semifluorocarbon compounds.<sup>6</sup> We decided to explore formation of stable bilayer dispersions in fluorocarbon media. For this purpose, we synthesized novel amphiphiles **2**, **3**, and **4**.<sup>7</sup> Their molecular design is based on the following characteristics that are conceptually common to those of the above-mentioned bilayer-forming amphiphiles: (1) double hydrocarbon chains as the solvophobic unit; (2) glutamate or diethanolamine connectors which give rise to satisfactory alignment of the hydrocarbon chain; and (3) a highly solvophilic unit in fluorocarbon media.

Compound **2** was either insoluble or prone to precipitate in all the fluorocarbon solvents we examined.<sup>8</sup> Compounds **3** and **4** were dispersible in these solvents by sonication (Branson cell disrupter 185), but precipitates were formed in less than 24 h except for solvent **5**. The dispersions in **5** were stable for more than 1 month at room temperature. The structural similarity of the fluorocarbon portion between amphiphile and solvent was

(1) Contribution No. 967 from the Department of Chemical Science and Technology.

(2) For a review, see: Kunitake, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 709.

(3) Ishikawa, Y.; Kuwahara, H.; Kunitake, T. *J. Am. Chem. Soc.* **1989**, *111*, 8530.

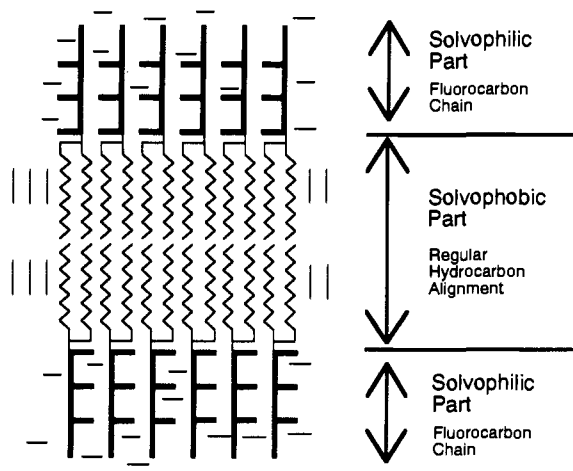
(4) Ishikawa, Y.; Kuwahara, H.; Kunitake, T. *Chem. Lett.* **1989**, *10*, 1737.

(5) Mukerjee, P.; Handa, T. *J. Phys. Chem.* **1981**, *85*, 2298.

(6) Turberg, M. P.; Brady, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 7797.

(7) Compound **2** was prepared from *O,O*-bis(didodecyl) L-glutamate and perfluoro(nonanoyl) chloride: colorless powder, mp 55–58 °C. Anal. Calcd for C<sub>38</sub>H<sub>56</sub>O<sub>5</sub>N<sub>1</sub>F<sub>17</sub>: C, 49.04; H, 6.07; N, 1.51. Found: C, 49.08; H, 6.08; N, 1.45. Compounds **3** and **4** were prepared by condensation of perfluoro(2,5,8-trimethyl-3,6,9-trioxadodecanoyl) chloride (PCR) with didodecyl glutamate and with bis(undecanoyl)diethanolamine, respectively: **3**: colorless oil, mp 9.2 °C. Anal. Calcd for C<sub>41</sub>H<sub>88</sub>O<sub>8</sub>N<sub>1</sub>F<sub>23</sub>: C, 43.66; H, 5.00; N, 1.24. Found: C, 43.90; H, 5.00; N, 1.22. **4**: colorless oil, mp –7.0 °C. Anal. Calcd for C<sub>40</sub>H<sub>84</sub>O<sub>8</sub>NF<sub>28</sub>: C, 43.13; H, 4.88; N, 1.25. Found: C, 43.70; H, 4.99; N, 1.44. IR and <sup>1</sup>H-NMR data are consistent with the respective structures.

(8) Fluorocarbon solvents examined: tris(perfluorobutyl)amine, tris(perfluoropentyl)amine, perfluoro(hexane), perfluoro(decane), perfluoro(1,3-dimethylcyclohexane), perfluoro(2-butyltetrahydrofuran), and methyl perfluoro(2,5,8-trimethyl-3,6,9-trioxadodecanoate) (**5**).



**Figure 2.** Schematic illustration of the bilayer structure of **3** and **4** in fluorocarbon media.

apparently responsible for the observed stability. Dark field optical microscopy (Olympus, BH2) of a 10 mM solution of **3** at 15 °C showed the presence of uniformly dispersed small particles with Brownian motion. The subsequent scanning electron microscopy (Hitachi, H-900) showed the presence of spherical particles with diameters of 1000–1500 Å, as given in Figure 1. Its expanded view displays the surrounding layer of the particle with 70-Å thickness. This value is close to two times the extended molecular length of **3**. Fibrous aggregates with diameters of 400–1000 Å were also found. Compound **4** gave similar electron microscopic results.

Differential scanning calorimetry (Seiko Instruments, SSC-2500) of the dispersion of **3** gives an endothermic peak at 2.3 °C (peak top) with  $\Delta H = 42$  kJ/mol. This enthalpy change is close to that of the gel-to-liquid crystal-phase transition of aqueous bilayers of double-chain hydrocarbon amphiphiles.<sup>9</sup> In addition, <sup>1</sup>H-NMR spectroscopy (JEOL, M-GSX 400N) of the dispersion

showed considerable sharpening of the methyl and methylene peaks as the measurement temperature is raised from –10 to 8 °C. Thus, the observed peak must be related to the chain melting process similar to that of the aqueous bilayer. A dispersion of **4** in **5** also gave a reproducible DSC peak at –12.6 °C with  $\Delta H = 19.5$  kJ/mol.

Aqueous hydrocarbon bilayers of glutamate-based amphiphiles often display enhanced circular dichroism (CD) in the crystalline state.<sup>10</sup> Induced CD of bound guest molecules has been also observed.<sup>11</sup> These CD data are indications of the regular molecular arrangement in bilayer assemblies. Thus, we conducted a similar examination of a dispersion of **3** in **5** by using *p*-dodecyloxybenzeneazobenzene (**6**) as a guest chromophore. A broad CD peak ( $[\theta]_{\max} = 2 \times 10^5$  deg cm<sup>2</sup> dmol<sup>-1</sup> at 310 nm) was found at –4 °C. The peak is gradually lessened with increasing temperature beyond the phase transition to 9 °C and totally lost at room temperature. Clearly, probe **6** is immobilized at –4 °C in a strongly chiral microenvironment of the regular bilayer.

In conclusion, all the available data point to the formation of stable bilayer aggregates in a fluorocarbon medium, as schematically illustrated in Figure 2. This endorses our previous presumption that bilayer formation can be observed for generalized amphiphilic molecules with proper molecular design. Combinations of fluorocarbon and hydrocarbon chains produce amphiphilic molecules because of their limited miscibility. Thus, normal fluorocarbon chains tend to align in hydrocarbon solvents, and vice versa. The solvophilic moiety in these cases should be composed of flexible hydrocarbon units in hydrocarbon media (as in **1**) and flexible fluorocarbon units in fluorocarbon media (as in **3** and **4**).

(9) Kunitake, T.; Ando, R.; Ishikawa, Y. *Mem. Fac. Eng., Kyushu Univ.* **1986**, *46*, 221.

(10) For example, see: Kunitake, T.; Nakashima, T.; Shimomura, M.; Okahata, Y.; Kano, K.; Ogawa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6642.

(11) (a) Kunitake, T.; Nakashima, N.; Shimomura, M.; Okahata, Y. *J. Am. Chem. Soc.* **1980**, *102*, 6644. (b) Hachisako, H.; Yamada, K.; Ihara, H.; Hirayama, C. *Polym. Prep. Jpn.* **1992**, *41*, 1145.