

Self-Organization of Solvophobic, Double-Chained Fluorocarbon  
Derivatives in Organic Media<sup>1)</sup>Yuichi ISHIKAWA, Hiroaki KUWAHARA, and  
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A novel type of compounds which contain two fluorocarbon chains and one flexible hydrocarbon chain gave bilayer-based molecular assemblies in organic solvents. The regularity of the assemblage was supported by specific incorporation of benzene.

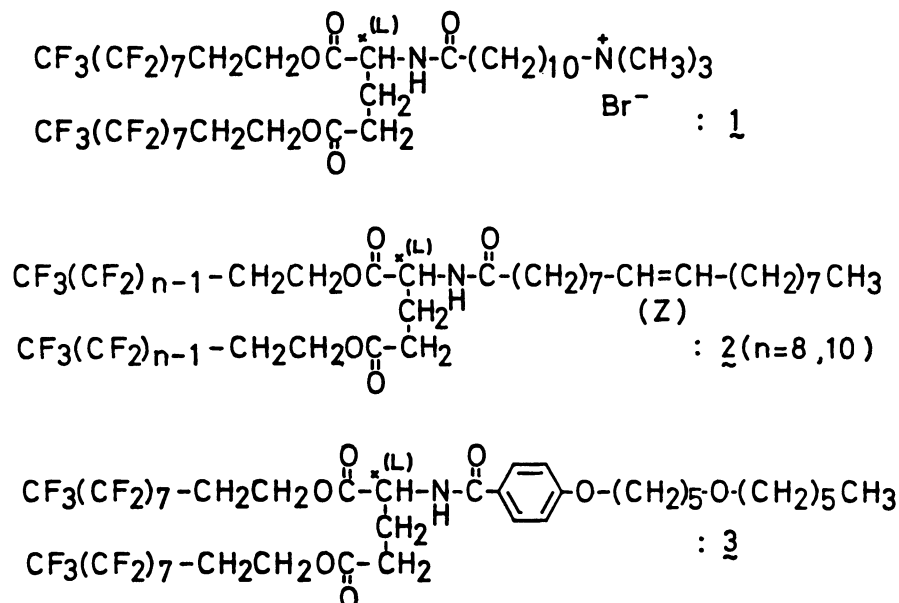
Stable bilayer membranes are formed from a large variety of synthetic amphiphiles.<sup>2)</sup> They are self-organized molecular assemblies with highly-ordered, two-dimensional structures, and their ordered assembly has been used advantageously for producing cooperative effects such as, for example, efficient energy transfer<sup>3)</sup> and enhanced magnetic coupling.<sup>4)</sup>

The conventional bilayer membrane uses the hydrophobic interaction in water as the major driving force of molecular assemblage. Therefore, applications of their structural advantages have been restricted to aqueous media. If, however, the concept of bilayer assemblage can be extended more generally so as to include organic media, we can compartmentalize organic media at the molecular level and a wholly new branch of chemistry will emerge. For this purpose, we have prepared a  $\text{Ca}^{++}$  complex of a phosphate molecular bilayer that is stable in  $\text{CHCl}_3$  and benzene.<sup>5)</sup> A two-dimensional polymer network provide a different approach.<sup>6)</sup> In this paper, we report molecular self-organization in some organic solvents which results from limited miscibilities of hydrocarbon and fluorocarbon moieties.<sup>7,8)</sup>

Semifluorinated n-alkanes,  $\text{F}(\text{CF}_2)_n(\text{CH}_2)_m\text{H}$  ( $n \geq 8$ ,  $m \geq 12$ ), assume crystal structures of the bilayer type<sup>9)</sup> and form micelles in organic solvents.<sup>10)</sup> These results were interpreted in terms of the "amphiphilic" nature of the semifluorinated alkanes. Ammonium amphiphiles with double fluorocarbon chains form stable bilayer vesicles in water.<sup>11)</sup> Compound **1** is a typical example, and its bilayer membrane tends to form separate domains in matrices of its hydrocarbon counterparts.<sup>12)</sup> Based on these previous experiences, we hypothesized that double-chained fluorocarbon compounds **2** which possess the flexible oleyl unit in place of the ammonium head of **1**, would produce organized molecular assemblies in hydrocarbon solvents.

Compound **2** ( $n = 8$ ) gave transparent, fluid dispersions in benzene (10 mM) and in cyclohexane (1 mM) by warming, but the dispersions became turbid and very viscous at room temperature. It dissolved readily as fluid solutions in  $\text{CHCl}_3$ ,

acetone, and 2-butanone. Compound 2 ( $n = 10$ ) was less soluble: it could not be dispersed in benzene and gave a viscous turbid dispersion at 10 mM in 2-butanone.



The aggregate morphology of these organic dispersions was examined by optical and electron microscopies. In dark-field optical microscopy,<sup>13)</sup> 2 ( $n = 8, 10$  mM) did not give any indication of aggregation in  $\text{CHCl}_3$ , but it produced fiber-like aggregates (diameter, ca.  $2.5 \mu\text{m}$ ; length, several hundred  $\mu\text{m}$ ) in benzene (10 mM). A transmission electron micrograph (Hitachi H600) of this dispersion given in Fig. 1a indicates the presence of the layer structure with thickness of ca  $120 \text{ \AA}$ . This thickness agrees approximately with twice the molecular length of 2 ( $n = 8$ ):  $59 \text{ \AA} \times 2$ , as estimated from the CPK molecular model.

Figure 1b shows the aggregate morphology of 2 ( $n = 10$ ) in 2-butanone. Partially twisted tapes are found and the layer thickness ( $100\text{--}150 \text{ \AA}$ ) is close to two times of the molecular length ( $63 \text{ \AA} \times 2$ ). This morphology is rather close to that observed for an aqueous dispersion of a double-chain ammonium amphiphile related to 1.<sup>14)</sup>

Subsequently, the regularity of these molecular assemblies was examined spectroscopically. As shown in Fig. 2, when a small amount (50 mM) of benzene was added to a cyclohexane dispersion of 2 ( $n = 8$ ), circular dichroism (CD) was induced at 250–350 nm. The CD peak was not observed in  $\text{CHCl}_3$  solvent. Induced circular dichroism has been frequently observed for dyes specifically bound onto regular bilayer membranes.<sup>15)</sup> Therefore, benzene molecules must be specifically bound at or near the chiral center of 2 ( $n = 8$ ).

Figure 3 displays partial NMR spectra of 2 ( $n = 8$ ) in  $\text{CDCl}_3$  and  $\text{C}_6\text{D}_6$ . The chemical shifts of the N-H doublet and the  $\text{C}^*\text{-H}$  sextet of the glutamate region and the oleyl  $-\text{CH}=\text{CH}-$  are virtually identical in  $\text{CDCl}_3$  with those of a related hydrocarbon compound.<sup>16)</sup> The peaks are broader in  $\text{C}_6\text{D}_6$  and the N-H proton alone is shifted to a higher magnetic field by 0.46 ppm. As is clear from the CD data, benzene molecules are specifically oriented near the glutamate chiral carbon. Therefore, the high-field shift of the N-H proton must be caused by the specific

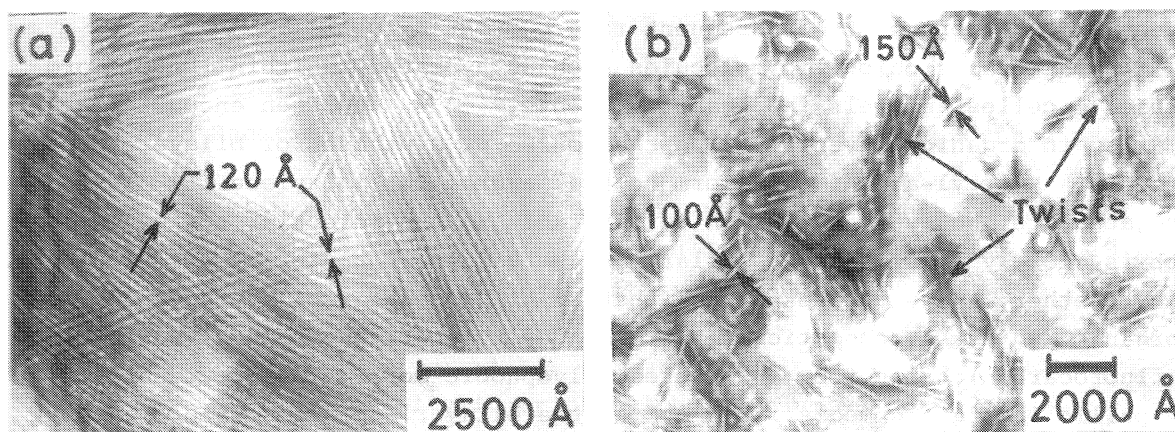


Fig. 1. Electron micrographs of **2** in organic solvents (17°C). Sample solutions (2 mM, ca. 60  $\mu$ l) were dropped on carbon-coated TEM grids and dried. A few drops of the staining agents were then added.  
 (a) **2** (n=8) in benzene, stained with phenyl mercury(II) acetate.  
 (b) **2** (n=10) in 2-butanone stained with Pb(acac)<sub>2</sub>.

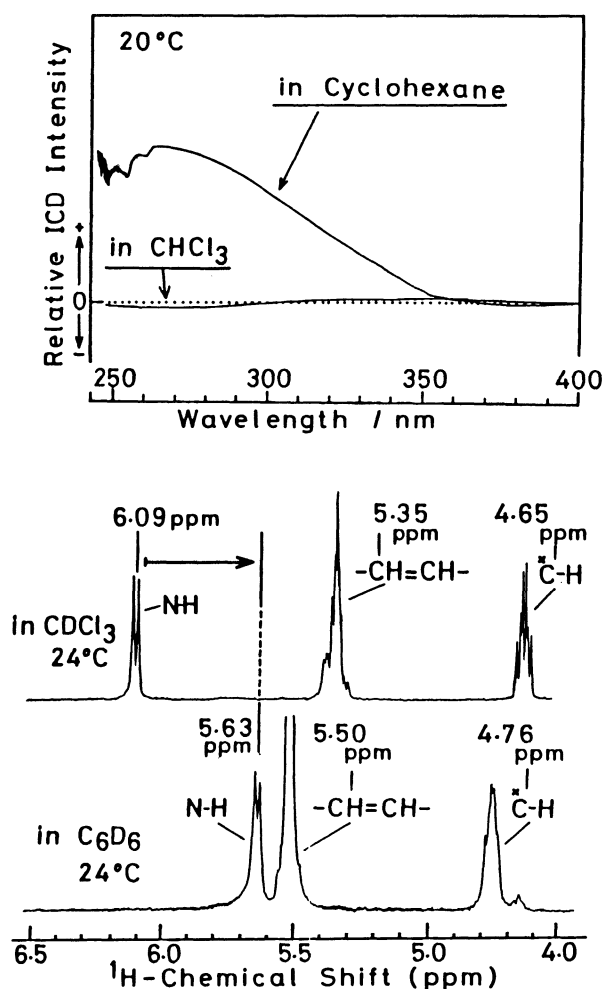


Fig. 3. Influence of solvent on <sup>1</sup>H-NMR spectra (400 MHz, TMS) of **2** (n=8). [**2** (n=8)] = 10 mM

Fig. 2. Induced circular dichroism of benzene mixed with **2** (n=8) in organic solvents. 20°C, [**2** (n=8)] =  $1.0 \times 10^{-4}$  M, [benzene] =  $5.0 \times 10^{-2}$  M.

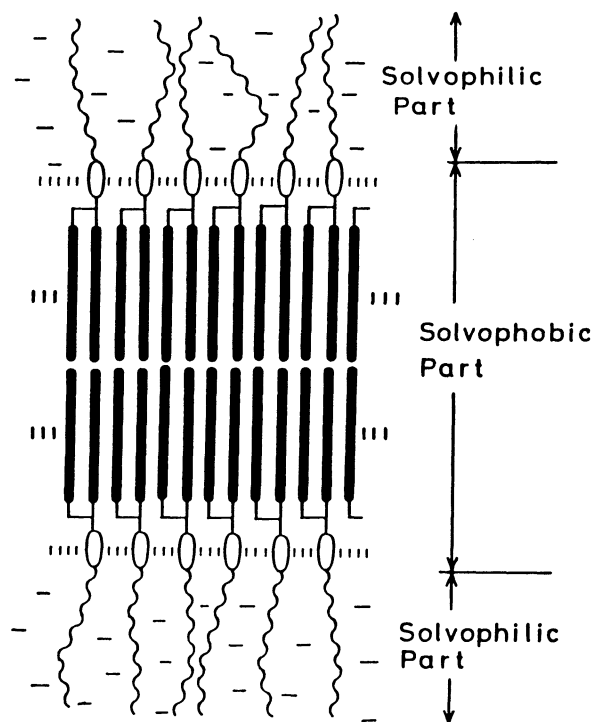
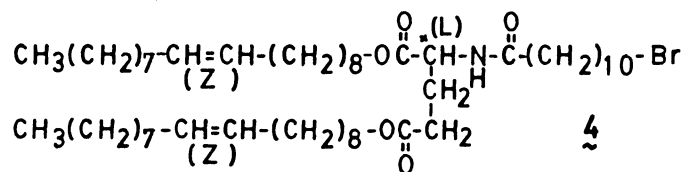


Fig. 4. Schematic representation of a bilayer membrane in organic solvents.

Conventional amphiphilic molecules such as hydrated lecithin (DPPC) form reversed micelles and gels in organic solvents.<sup>17,18)</sup> We often encountered gel formation in organic solvents during the course of syntheses of bilayer-forming compounds. N-octyl-aldonamides form helical aggregates in xylene.<sup>19)</sup> These aggregates are, however, not shown to be stable at the molecular scale. Compound 3 which is closely related to 2 similarly shows bilayer behavior in organic media. Taken together, these data establish that stable molecular bilayers can be formed in organic media. A schematic illustration of these bilayers is given in Fig. 4. The fluorocarbon chains form an ordered solvophobic core. The oleyl unit is solvophilic in organic media, thus making the bilayer surface stable. The glutamate unit helps maintain the molecular organization by the intermolecular hydrogen bonding.

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