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Communications to the Editor

Fullerene Lipid Chemistry: Self-Organized Multibilayer Films of a C_{60}-Bearing Lipid with Main and Subphase Transitions

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Increasing attention is being given to the chemistry and physics of fullerenes.[1] The formation of thin fullerene films is also of interest from both a fundamental and a practical application point of view.[2] Synthetic lipid bilayer membranes[3] possess fundamental physicochemical properties similar to those of biomembranes and can be immobilized as molecular lipid films.[4] The combination of fullerene chemistry and the chemistry of synthetic lipid bilayer membranes affords an exciting area in science; however, no report has been published thus far describing the synthesis of fullerenes which form self-assembled bilayer membranes. Here, we present the first report on the design, synthesis, and characterization of a C_{60}-bearing triple-chain lipid **1** (see Chart 1). Differential scanning calorimetry (DSC), UV−vis and FT-IR spectroscopies, and X-ray studies have revealed the cast films of **1** form a highly oriented multibilayer structure and possess phase transitions which influence fullerene electronic properties.

The synthesis of **1** is as follows. The reaction of *N*-(chloroacetyl) tris(((hexadecanoyl)oxy)methyl) iminomethane[3a] with 2 equiv of NaN_3 in DMSO at 60 °C gave the azide compound (43.3%; mp 61.0−62.0 °C), which was reacted with C_{60} in chlorobenzene for 24 h[2g] to produce fullerene lipid **1**. Purification of **1** was carried out by column chromatography (silica gel, eluent: AcOEt/hexane = 1:5). The product was obtained as a brown solid (26.3%; mp 50.0−51.0 °C).

The FAB-MS spectrum of **1** showed the molecular ion peak ($[M + H]^+$) at *m/z* 1611 together with a peak at *m/z* 720 due to the fragment of C_{60}. The ^{13}C NMR spectrum of **1** exhibited 12 fullerene peaks (with four unresolved signals) in the region of δ 140−150 ppm, indicating C_{2v} symmetry in the fullerene moiety.[5] There was one peak at 83 ppm corresponding to the two sp^3-hybridized carbons. The UV−vis spectrum of **1** in hexane showed λ_{max} at 209.0 ($\epsilon = 1.2 \times 10^5$ $dm^3\ mol^{-1}\ cm^{-1}$), 255.0 (1.1×10^5), and 322.5 nm (3.7×10^4) together with a weak absorption at 420.5 nm. The absorption at 420.5 nm has been reported to be specific for closed 6/6-ring bridged fullerene derivatives.[6] These data explain that **1** exists as a closed aziridine structure at a 6/6-ring junction of C_{60}.

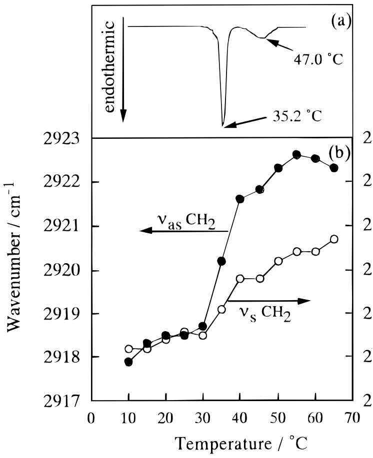
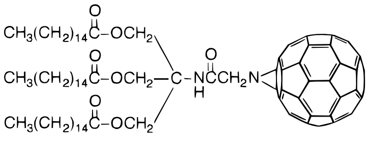


Figure 1. (a) DSC thermogram of a cast film of **1** in air. (b) Plots of wavenumbers of the asymmetric and symmetric CH_2 stretching bands in the FT-IR spectra of a cast film of **1** as a function of temperature.

Chart 1



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Amphiphile **1** is not soluble in water because of the lack of a high hydrophilic moiety in the chemical structure but is soluble in organic solvents such as DMF, DMSO, chloroform, benzene, and hexane. Casting from chloroform solutions containing **1** gave films which were characterized using DSC, FT-IR and UV−vis spectroscopies, and X-ray diffraction.

The phase transition between the crystalline phase and liquid-crystalline phase is one of the most fundamental characteristics of lipid bilayer membranes. The existence of the phase transition in the films of **1** was examined by DSC. The films of **1** in air were found to exhibit two endothermic peaks at 35.2 °C (transition enthalpy, $\Delta H = 5.1$ kcal mol^{-1}) and 47.0 °C ($\Delta H = 0.9$ kcal mol^{-1}) (Figure 1a), which shifted to 39.9 °C ($\Delta H = 7.6$ kcal mol^{-1}) and 48.6 °C ($\Delta H = 0.6$ kcal mol^{-1}) in water, respectively. The shift to higher temperatures in water is not

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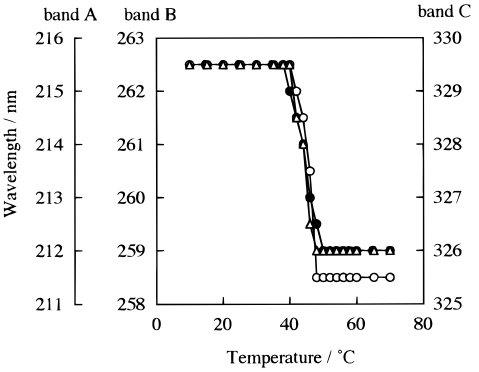

Figure 2. Plots of wavelength for bands A (●), B (△), and C (○) in the UV−vis spectra of a cast film of **1** as a function of temperature.

unusual.[7] In order to assign these two endothermic peaks, we examined the temperature dependence of the FT-IR and UV−vis spectra of the **1** films. The wavenumber of the asymmetric and symmetric methylene stretching vibrations in the FT-IR spectra of the film changed drastically near 35 °C (Figure 1b). The shifts of $\nu_{as}(CH_2)$ and $\nu_s(CH_2)$ from 2917.9 to 2922 cm^{-1} and from 2849.2 to 2851 cm^{-1}, respectively, are ascribable to the *trans*−*gauche* conformational change of the long alkyl chain which leads to the phase transition of the thin films.[8] It is evident that the main peak in the DSC thermogram is attributable to the bilayer phase transition typically observed for liposomal[9] and synthetic lipid bilayer membranes.[7,8] At 25 °C, the UV−vis spectrum of the film in air shows three bands, A, B, and C, with absorption peaks at 215.5, 262.5, and 329.5 nm, respectively; the peak maxima at bands A, B, and C are being shifted to longer wavelength by 6.5, 7.5, and 7.0 nm, respectively, compared to those in hexane. This shift implies the existence of an electronic interaction between the C_{60} moieties in the film.[2i,10] Figure 2 shows temperature dependence of the absorption maxima of the lipid film. It is noteworthy that the peak maxima change drastically in the temperature range of 40−45 °C, which is close to the range for the subtransition in the DSC thermogram. The observed temperature dependence was reversible. The red shift of the spectra at temperatures below the subtransition suggests head-to-tail orientations of the fullerene electronic transition moments, which are loosened at the fluid bilayer phase.

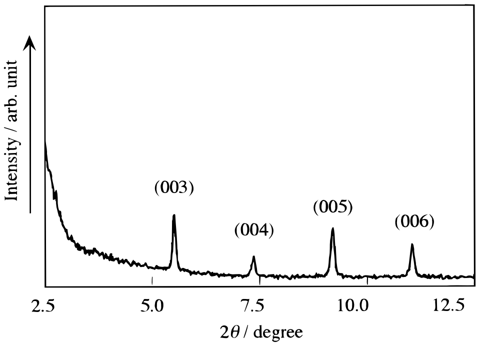

Figure 3. X-ray diffraction diagram of a cast film of **1**.

Figure 3 shows the X-ray diffraction diagram (instrument; Rigaku RINT 2000) for a cast film of **1**. The observed high-ordered reflection peaks indicate the existence of a well-organized multilayer structure. The *d*-spacing is calculated to be 48.1 Å from the Bragg equation, which is longer than the molecular length of **1**, 35.4 Å, estimated from the CPK space-filling model. This result suggests that the film forms a multibilayer structure with the molecular layers tilting by 42.8° from the basal plane.

In conclusion, we have demonstrated that lipid **1** forms multibilayer membrane films which possess main and subphase transitions, and the subtransition regulates electronic properties of the fullerene. The present study opens possibilities for development of methods for the regulation of physical and physicochemical properties of fullerenes based on the nature of self-organized lipid bilayer membranes. Intense efforts are currently under way in our laboratory to explore their potentials.

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