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# Interfacial behavior and film-forming properties of an amphiphilic hexasubstituted [60]fullerene

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**Abstract**—A new amphiphilic hexasubstituted [60]fullerene bearing 10 cholesterol units and a polar head made of two carboxylic acid functions has been prepared and its aptitude to film forming (Langmuir and Langmuir–Blodgett) evaluated. The results show that this amphiphile has the prerequisite qualities for its incorporation into the cellular membranes of living organisms.

The growing number of bio-related studies in which [60]fullerene is used impulses the current quest for new fullerene-based amphiphiles.[1] Molecules incorporating $C_{60}$ in their structure have successfully been used in various therapeutic approaches such as photodynamics, radical scavenging, anti-tumor and anti-HIV procedures, drug transport, and gene transfection, to name but a few.[2] In these studies, the $C_{60}$ can either be the active element of the molecule, and therefore its natural hydrophobicity obviously has to be counter-balanced, or simply serve as a versatile corner stone for supramolecular synthesis. Steroids (e.g., cholesterol), on account of their wide occurrence, particularly in mammalian tissue, broad biological activity profile, ability to penetrate the cell membrane, and bind to specific hormonal receptors have also found favor as building platforms for a variety of bio-active molecules. Therefore, coupling a fullerene with a steroid can potentially produce a compound having a good bio-compatibility and an enhanced therapeutic activity.[3]

$C_{60}$-hexasubstitution seems to be a method of choice for the preparation of new compounds displaying interesting properties with the carbon sphere playing the role of a spherical template for new 3D organizations. As compared to fullerene-bearing dendrimers, hexasubstituted [60]fullerenes can be multifunctional, a property quite important for new biological applications. Thanks to the methodology based on dimethylanthracene (DMA)-templating developed by Hirsch et al.[4] and recently improved,[5] new $C_{60}$ hexaadducts with applications in the field of materials sciences have been reported.[6]

We report in this letter the preparation, spreading behavior at the air–water interface and Langmuir–Blodgett (LB) film formation of amphiphilic hexasubstituted [60]fullerene **1** bearing 10 hydrophobic cholesterol units and a polar head group made of two carboxylic acid functions. It is expected that the substitution with cholesterol units will enhance and favor the interactions of **1** with the membranes of cells and the present work, as a preliminary, explores the interfacial behavior of the molecule. This study is part of the research pursued in our group and aimed at developing new hexasubstituted-$C_{60}$-based organic materials for materials science or biological applications.

The synthesis of amphiphile **1** is depicted in Scheme 1. We recently described the synthesis of hexaadduct **2**.[7] Treatment of **2** with trifluoroacetic acid in a mixture of water/dichloromethane kept under argon at room temperature led to compound **1** in 99% yield after 8 h under vigorous stirring. Amphiphilic derivative **1**[8] was obtained as a bright orange glassy solid and was fully characterized by $^{1}H$ and $^{13}C$ NMR, UV–vis, IR spectroscopies, and Mass spectrometry. All of those studies were consistent with the proposed molecular structure (see Supplementary data).

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*Keyword*: Amphiphile-$C_{60}$-hexasubstitution.

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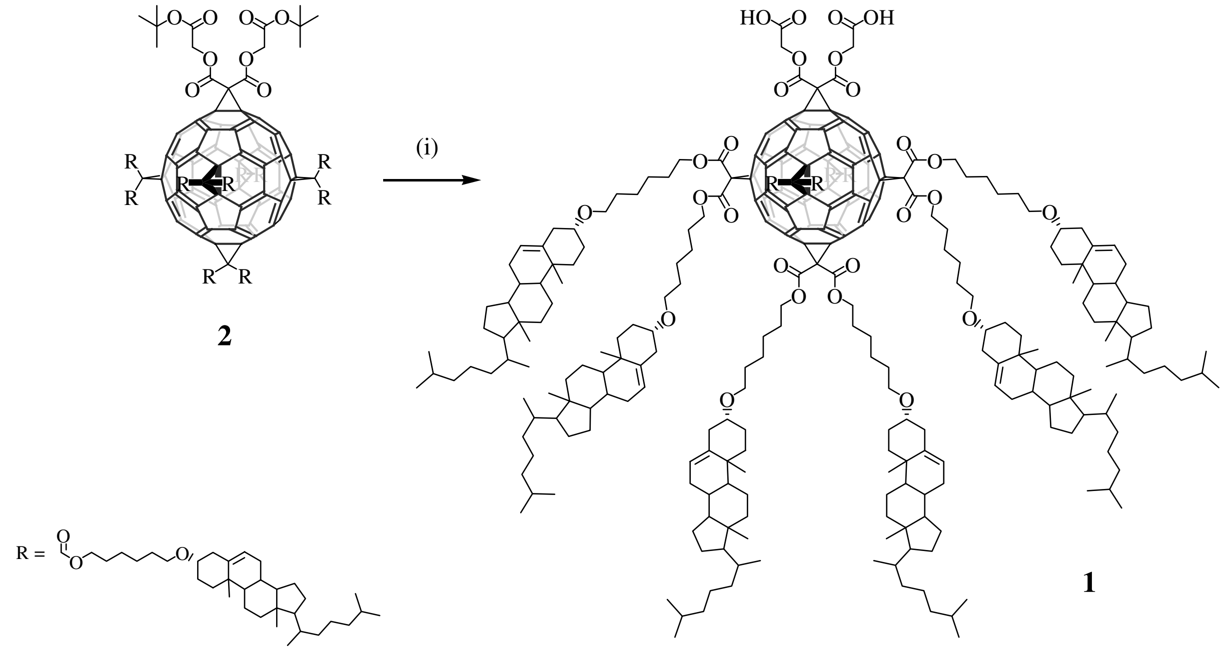

**Scheme 1.** Synthesis of **1**. Reagents and conditions: (i) TFA, water, $CH_2Cl_2$, Ar, rt, 12 h (99%).

The pressure–area isotherm for **1** is depicted in Figure 1a. The surface pressure starts to increase slowly at a molecular area of 600 Å$^2$, before rising in a steeper way at ca. 350 Å$^2$. This liquid-expanded phase between 600 and 350 Å$^2$, previously observed for a disubstituted [60]fullerene bearing 4 cholesterol moieties,[9] is indicative of long-range intermolecular interactions in the film. The final molecular area to extrapolated zero surface pressure is $370 \pm 10$ Å$^2$. This observation, corroborated by layer thickness measurements (Fig. 2) and molecular modeling (Fig. 3), clearly proves that a monomolecular film is obtained.

BAM pictures (Fig. 1a) taken at the end of the compression show a high quality homogeneous film, without defects or aggregates. It must be noted that although compound **1** displays a liquid-crystalline behavior from 40 to 165 °C (a smectic A phase was identified),[7] no birefringent domains were observed during the film formation. More evidence of the film cohesion is confirmed by the hysteresis curve (Fig. 1b) showing a good reversibility of the isotherm as long as the pressure is kept below the collapse pressure $\Pi_c \approx 50$ mN m$^{-1}$. The shift between the three successive compression–expansion cycles is due to the deposition of the product on the barriers of the Langmuir trough usually observed during hysteresis measurements.

It has been possible to transfer the Langmuir film of **1** onto hydrophilic quartz slides and prepare multilayer Langmuir–Blodgett films. As already observed for fatty acids, the films quality improved much when cadmium acetate was dissolved in the subphase (2.0 mmol). The average deposition ratio was $0.8 \pm 0.1$, decreasing

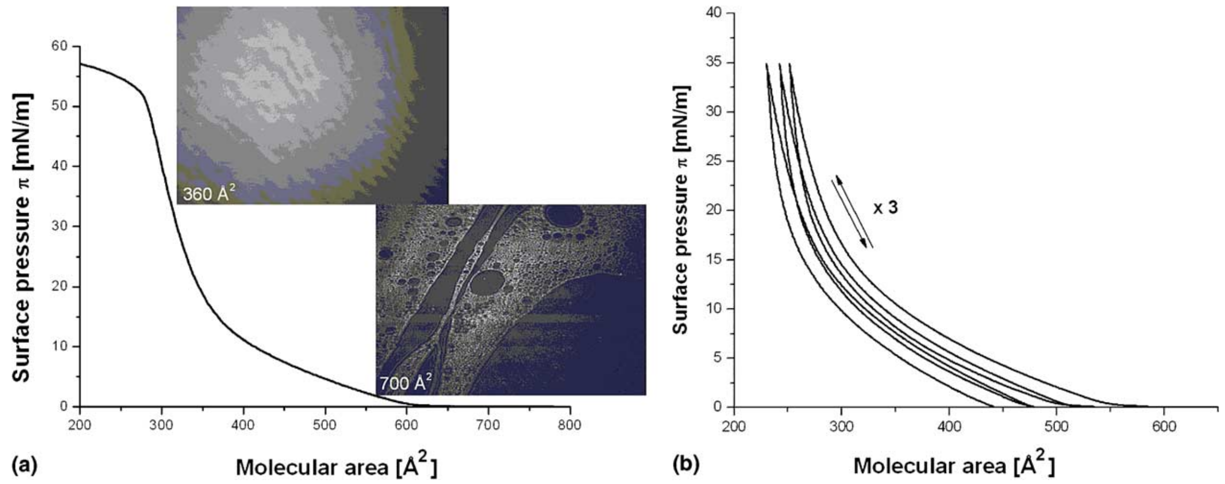

**Figure 1.** (a) Pressure–area isotherm for **1** and Brewster angle microscopy images at A = 700 and 360 Å$^2$; (b) three successive compression/expansion cycles with a monolayer of **1** showing the reversibility of the process (the small shift is due to the loss of product on the edges of the trough).

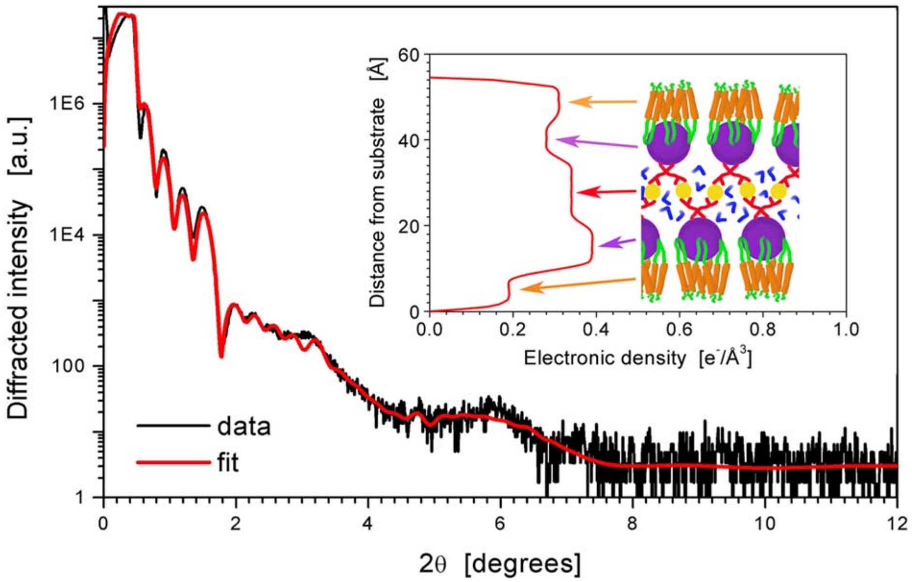

**Figure 2.** X-ray scattering pattern of an 11-layers LB film and its best fit. Inset gives the electronic density of the repeat unit and a crude sketch of the molecular packing. The purple circles are the $C_{60}$, the orange sticks are the cholesterol units, the green lines are the alkyl chains. In the middle layer, the red lines, yellow circles, and blue boomerangs, respectively, stand for the carboxylic groups, $Cd^{2+}$ ions, and water molecules.

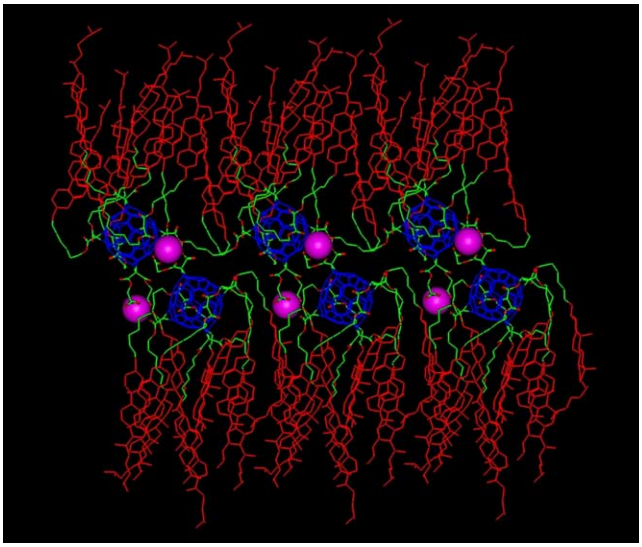

**Figure 3.** Bilayer of **1** obtained by molecular modeling.[10]

slowly from one (first layer) to ca. 0.5 for the 60th layer. A transfer ratio smaller than 1 implies either a re-organization of the molecules during transfer or the presence of defects. Since the X-ray analysis of the LB films revealed that the layers had a density lower than expected, the transfer ratio smaller than one therefore indicates that defects (voids) are present in the LB films. The roughness of the layers also was rather high. Still, given the size and structure of the molecule, the LB films had a reasonably good quality.

The grazing incidence X-ray scattering pattern of an 11-layers LB film is given in Figure 2, together with the best fit. Inset in Figure 2 also gives the electron density profile of the repeat unit of the LB film.

In order to better visualize things, a crude sketch of the bilayer is also given. It can be seen that the electron density profile is not symmetric, meaning that the molecular packing is not the same in the upstroke and downstroke layers. Suggesting an explanation would only be speculation; we can only say that this fact is consistent with the observation of a transfer ratio smaller than 1.

A bi-layer thickness of 56 Å has been obtained from X-ray scattering measurements and confirmed by molecular modeling studies (Fig. 3), which gave a thickness of ca. 59 Å for a bilayer of **1**.

In conclusion, we have shown that hexasubstituted [60]fullerene **1** is an amphiphile able to form good quality Langmuir and Langmuir–Blodgett films. A stable and reversible film was easily obtained and successfully transferred onto hydrophilic substrates in mono- or multi-layers. Hexasubstitution on the $C_{60}$ sphere is therefore a method of choice for preventing aggregation phenomenon and preparing well ordered $C_{60}$-based supramolecular assemblies. Studies aiming at understanding the interactions of **1** with the membrane of living cells are currently underway.

## Acknowledgments

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.07.079.

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8. Selected spectroscopic data for **1**: $^1$H NMR ($CDCl_3$, 300 MHz): 0.67 (s, 30H), 0.85–2.32 (m, 480H), 3.12 (m, 10H), 3.44 (br s (t), 20H), 4.24 (br s (t), 20H), 4.25 (s, 4H), 5.34 (br s (d), 10H). $^{13}$C NMR ($CDCl_3$, 75 MHz): 11.87, 18.73, 19.40, 20.08, 22.56, 22.69, 22.81, 23.90, 24.31, 25.75, 25.90, 26.08, 28.02, 28.25, 28.48, 29.32, 29.36, 29.39, 29.63, 29.66, 29.70, 30.15, 31.91, 31.96, 35.64, 35.82, 36.90, 37.30, 39.22, 39.52, 39.81, 42.33, 50.21, 53.41, 56.22, 56.79, 66.90, 67.93, 69.17, 79.03, 121.44, 141.05, 145.75, 163.86. UV–vis ($CHCl_3$): $\lambda_{max}$ (nm) 267 (6745), 279 (6655), 303 (5135), 334 (sh, 3025). IR ($CHCl_3$): 1737 $cm^{-1}$ (C=O). MALDI-MS calcd for $C_{412}H_{576}O_{38}$ $[M+Na]^+$: 6160.07, found 6161.17.
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10. The molecular mechanics studies have been performed on SGI Origin 2800 and Octane$^2$ calculators using Insight II and Discover 3 softwares from Accelrys (www.accelrys.com) with the cvff forcefield. The previously minimized structure of **1** was packed in an hexagonal cell with a 370 Å$^2$ section and was allowed to equilibrate for 220 ps at a 298 K isotherm by the molecular dynamics simulation (in the NVT-PBC ensemble and with a 1 fs timestep).