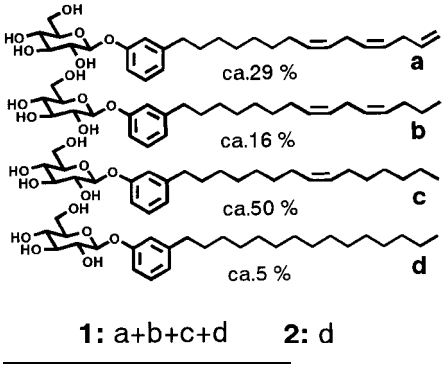
Nanotube Formation from Renewable Resources via Coiled Nanofibers**

By *George John*,* *Mitsutoshi Masuda*, *Yuji Okada*, *Kiyoshi Yase*, and *Toshimi Shimizu*

The self-assembly of low molecular weight building blocks into meso- and nanoscale structures has recently attracted considerable interest for its application in the *bottom-up* construction of engineered materials.[1] The building blocks currently used in supramolecular chemistry are synthesized mainly from petroleum-based starting materials. However, bio-based organic synthesis presents distinct advantages for the generation of new building blocks since a) they are obtainable from renewable resources, b) they are likely to be biodegradable, and c) natural compounds have a wealth of structural diversity that has yet to be explored. This study is an effort to combine the philosophies of green chemistry[2] and supramolecular chemistry,[3] making use of renewable plant-derived resources as the starting materials (an alternative feedstock) for the non-covalent synthesis of organic nanotubes. The industrial use of cardanol[4] (obtained from *Anacardium occidentale* L, a renewable resource and a by-product of the cashew industry) and its derivatives for various applications is well known.[5] However, its use in the synthesis of aryl glycolipids and their self-assembled nanostructures is reported here for the first time.

Hollow tubular structures of nanoscale dimensions may offer a variety of applications in chemistry, biochemistry, and materials science. Synthetic nanotubes have been obtained from novel forms of carbon[6] and tubular derivatives (imogolite) of aluminosilicate.[7] Nanoscale tubes based on organic materials have also been reported previously.[8] The number of tube-forming molecules identified so far is still relatively small and principally includes certain diacetylenic phospholipids,[9] glutamates,[10] long-chain diamides,[11] anionic glucophospholipids,[12] block copolymers,[13] lipid–biotin conjugates,[14] and porphyrin derivatives.[15] Here we report the facile synthesis of renewable resource–based molecular building blocks **1** (which is derived from cardanol and is a mixture of a) 1-O-3′-*n*-(8′(*Z*),11′(*Z*),14′-pentadecatrienyl)-phenyl-β-D-glucopyranoside, b) 1-O-3′-*n*-(8′(*Z*),11′(*Z*)-pentadecadienyl)phenyl-*β*-D-glucopyranoside, c) 1-O-3′-*n*-(8′(*Z*)-pentadecenyl)phenyl-*β*-D-glucopyranoside, and d) 1-O-3′-*n*-(pentadecyl)phenyl-*β*-D-glucopyranoside) and **2** (saturated analogue d), and their self-assembly in water leading to nanotube formation. We anticipate that they may have possible applications in nanofabrication, inclusion chemistry, catalysis, medicine, molecular electronics, hydrogen storage, and molecular separation technology.



1: a+b+c+d **2:** d

The glycolipids **1** and **2** were dissolved in boiling water to give a clear solution and were gradually cooled to room temperature. Fine fibrous structures were obtained within 12–24 h under ambient conditions. The fibrous structures were confirmed by various methods, including light microscopy and transmission electron microscopy (TEM). Polarized and phase-contrast light microscopies demonstrate that the flexible fibers formed with glycolipid **1** retain a characteristic helical, coiled-ribbon structure (Fig. 1a,b), and **2** retains a twisted nanostructure (Fig. 1c,d). To explore the fine fiber structures, we carried out energy-filtering TEM (EF-TEM)[16] on the unstained nanofibers. EF-TEM clearly shows that the thinnest width of the fibers derived from **1** is about 30–35 nm (Fig. 1b). We found a variety of ribbons with non-uniform widths. The growth of a unit fiber into higher order assemblies appears to be uncontrolled. Helical morphologies are visible for fibers with a width of more than 50 nm. For compound **2**, all individual fibers showed twisted morphology (Fig. 1d), in contrast to the helical structure of the fibers from **1**.

Nanofiber association and network formation induce efficient gelation of organic solvents.[17] Compounds **1** and **2** were studied with regard to their gelation behavior in different solvents/mixtures (Table 1). Compound **2** was able to form gel structures when mixed with a 1:1 mixture of alcohol/water, acetone/water mixtures, and other solvent systems. The gels form spontaneously at room temperature and are thermoreversible in nature, i.e., they became clear, low-viscosity solutions upon heating and gelation re-occurred upon cooling. However, compound **1** formed no stable gels under the same conditions and the high viscosity of the gels suggests that network structures are formed. This was confirmed by various microscopy techniques.

X-ray powder diffraction (XRD) experiments were carried out using nanofibers collected from the aqueous suspensions. The diffraction patterns of the nanofibers show a Bragg peak typical of lamellar organization. It should be noted that the molecular orientation and packing within the fibers are different in the two compounds, depending on whether the long hydrocarbon chain is saturated or unsaturated. The cardanol-derived glycolipid **1** shows a *d* spacing of 3.9 nm, in comparison to the shorter (d = 3.1 nm) spacing of the saturated glycolipid **2**, suggesting an interdigitated morphology, since the extended molecular lengths of **1** and **2** can be evaluated to be ca. 3 nm. Also the saturated glycolipid shows higher ordering in the aliphatic region, possibly due to hydrocarbon crystallization, further supported by Fourier transform infrared (FT-

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[**] This work has been supported by CREST of JST (Japan Science and Technology).

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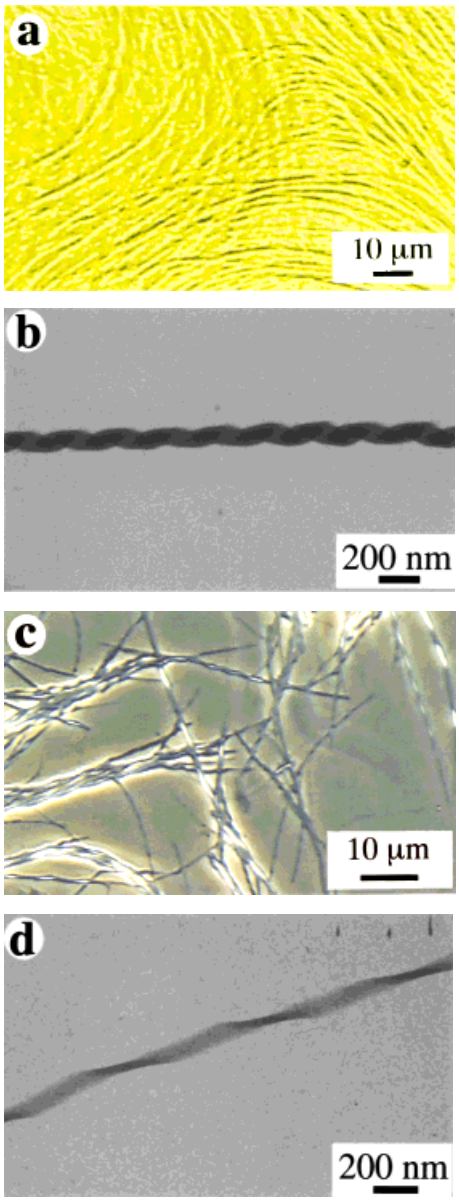

Fig. 1. a) A polarized light microscopy image of self-assembled fibers from compound **1**. b) EF-TEM image of an individual coiled nanofiber of **1**. c) A phase-contrast light microscopy image of self-assembled fibers of **2**. d) EF-TEM image of an individual coiled twisted nanofiber of **2**.

Table 1. Gelation behavior of glycolipids **1** and **2** at 25 °C.

Solvent	Glycolipid **1**	Glycolipid **2**
Ethanol	solution	solution
Ethanol/water (80:20, v/v)	solution	solution
Ethanol/water (50:50, v/v)	solution	gel
Ethanol/water (20:80, v/v)	solution	fiber
Water (25°C)	suspension	suspension
Water (100°C) [a]	fiber	fiber
Acetone	solution	solution
Acetone/water (80:20, v/v)	solution	solution
Acetone/water (50:50, v/v)	solution	gel
Acetone/water (20:80, v/v)	solution	fiber
Diethylene glycol	solution	gel
Glycerol	solution	gel

[a] Dissolved in boiling water and cooled to 25 °C.

IR) spectroscopy studies of the C–H stretching values at 2854 cm^{-1} for **1** and 2850 cm^{-1} for **2**. Also the OH stretching patterns of the two compounds are different: compound **1** showed sharp peaks at 3487 and 3293 cm^{-1}, whereas **2** gives a broad peak at 3380 cm^{-1}, suggesting higher ordering of the headgroup. In compound **1**, headgroup crystallinity seems to be higher compared to that of the aliphatic side chain. It is reasonable to argue that the cis–cis double bonds could not stack or crystallize as in the saturated analogue and the side chain has a fluid-like nature. It has been reported that fatty acids contain cis-configured double bonds, which cause a distortion of the chain's linearity around the double bond and methine carbon atoms in unsaturated fatty acids, which in turn causes a rise in the flexibility of the neighboring methylene groups.[18]

The driving forces and mechanism for the formation of ribbons and their self-organization into tubes have been extensively debated, but are still not well understood.[19] Various *n*-alkyl aldonamides are also known to form helical fibrous structures in water; the hydrogen bonds formed between the hydroxyl groups of the sugar moiety and the amide groups stabilize the aggregates and determine the morphology.[20] Compounds **1** and **2** have only four hydroxyl groups, and it is likely that π–π interactions between the phenyl groups play a dominant role in directing aggregation, since alkyl β-D-glucopyranosides (β-GPs) do not display self-assembled fiber formation at all. Whilst hydrogen-bond directed self-assembly is a well-studied mechanism for fiber formation with amphiphiles,[21] π–π stacking directed self-assembled nanofibers of glycolipids are much less common.[22] Here, the aromatic units induce rigidity in the structure and also help with stacking the glycolipids in a cylindrical fashion by providing interactions between the rings (Fig. 2). The lipids self-organize to linearly stack with the headgroups perpendicular to the aliphatic tail. Each component is stabilized by a combination of hydrogen bonding, π–π interactions, and hydrophobic forces. Stacking of each molecule is also favored by the interdigitated hydrophobic association and inter-headgroup hydrogen bonding. The interdigitated glycolipids are very similar in structure to a conventional bola-amphiphile, with an oligomethylene spacer and two amide linkages at either end and sugar moieties as head group. The mechanism of fiber formation from bola-amphiphiles is well documented as hydrogen bonding between sugar hydroxyls, further stabilized by amide hydrogen bonding.[23] In the present system, we propose that amide hydrogen bonding is replaced by π–π stacking of the phenyl groups in the glycolipids, **1** and **2**. We have previously demonstrated the remarkable effect of the headgroup conformation and chirality on the helical morphologies of nanofibers formed with peptide lipids.[24] To our knowledge, the present finding provides the first example of morphological regulation by a hydrophobic moiety. Thus, we could easily control the helical morphology of fibers from twisted to coiled ribbons by altering the aliphatic side chain to saturated or unsaturated, using simple hydrogenation.

The coiled nanofibers self-assembled from the glycolipid **1** gradually turn into tubular structures that are hundreds of

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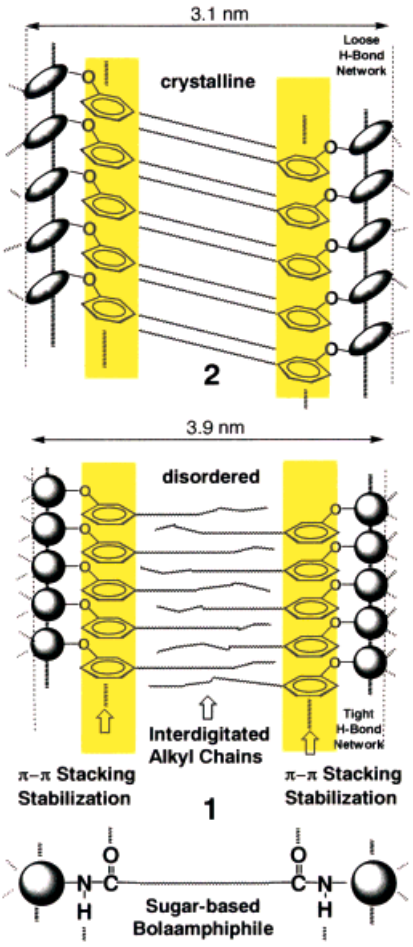

Fig. 2. π–π stacking assisted self-assembly of glycolipids **1** and **2** in comparison to sugar-based bola-amphiphiles.

micrometers long and have internal diameters of 10–15 nm. The tube morphology was confirmed using light microscopy and EF-TEM. The tubes are open-ended, with uniform shape and internal diameter. EF-TEM micrographs of unstained samples in water show nanotubes with uniform external diameters between 50 and 60 nm, lengths between 10 and 100 μm, and wall thicknesses of 8–15 nm (Fig. 3). The present non-covalent assembly of nanotubes can provide nanostructures with almost the same dimensions as multilayer carbon nanotubes. Examination of nanotubes at high magnification revealed that the tubes are composed of a hollow inner core and a wall consisting of two to four lipid interdigitated bilayers (Fig. 4). Although we can only speculate on the mechanism of nanotube formation at this time, it is notable that the nanotubes are devoid of the helical markings that are characteristic of similar systems from water or aqueous alcoholic solutions. The helical lines observed on the surface of microtubes are believed to result from the fusion of curved lipid ribbons that meet edgewise to form tubes;[25] their absence in the nanotubes reported here may indicate a different mechanism of tube formation.

The nanotubes were examined using differential scanning calorimetry (DSC), revealing a phase transition at 46 °C for the cardanol derivatives **1**. Confirmation of the values using a

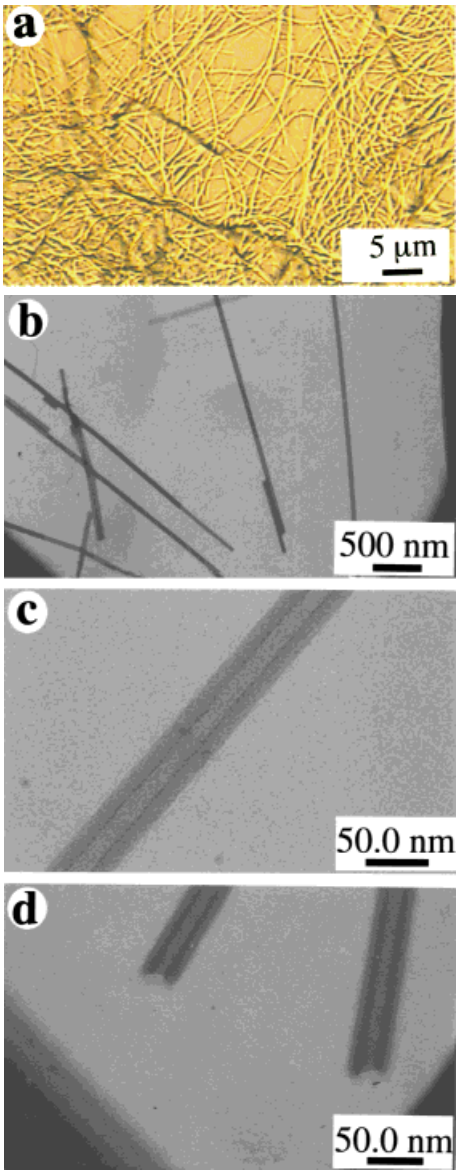

Fig. 3. a) A polarized light microscopy image of nanotubes of **1**. b–d) EF-TEM images of nanotubes.

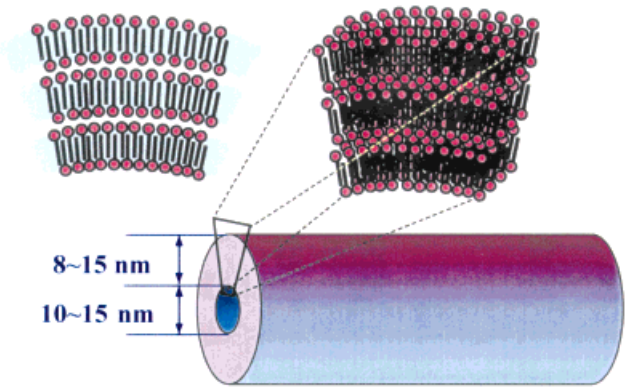

Fig. 4. Schematic representation of interdigitated lamellar layers in the nanotubes.

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light microscope equipped with a hot stage revealed that tubes from cardanol glycolipids form vesicles above the phase transition temperature. It is interesting to note that the modified cardanol derivative (saturated analogue **2**) does not form any nanotubes under the same conditions as that of cardanol. This also illustrates the influence structural diversity of natural systems has on the fine-tuning of materials properties. More detailed studies on these molecules and the fine structure of the nanotubes are in progress.

Experimental

*3-Alkylphenyl-β-*D*-glucopyranosides (**1** and **2**)*: Cardanol was obtainable by double vacuum distillation of cashew nut shell liquid (CNSL) at 3–4 mm Hg and the fraction boiling between 220–235 °C was collected. Cardanol (a mixture of long chain phenol differing in the degree of unsaturation in the side chain) (1.52 g, 5 mmol) in anhydrous CH_2Cl_2 (10 mL) and 2 g of 4 Å molecular sieves were added to penta-O-acetyl-β-D-glucopyranose (3.9 g, 5 mmol) and $BF_3{\cdot}OEt_2$ (0.62 mL, 5 mmol). The reaction mixture was stirred at room temperature for 24 h and then poured into 40 mL of 5 % aqueous $NaHCO_3$. The organic layer was separated, washed with aqueous $NaHCO_3$ and subsequently with water, and dried over anhydrous Na_2SO_4. Organic solvents were removed under vacuum. The crude product was crystallized from ethanol and was further purified by column chromatography to give a white solid **1** (m.p. 135.2 °C). The saturated homologue **2** was prepared in the same way (m.p. 143.5 °C). 1 mg of the glycolipid of saturated component **2** was transferred to a weighed sample bottle. 0.25 mL of the solvent/solvent mixture was added to the sample bottle, which was then heated in a water bath at about 70–80 °C. The glycolipids dissolved and formed a very clear solution, which upon cooling gave opaque gels. The self-assembled fibrous structure was prepared by dissolving 1–5 mg of **1** or **2** in 50–100 mL of boiling water. The clear solution obtained was cooled to room temperature under ambient conditions. The helical fibers obtained from compound **1** were aged for several days under ambient conditions and yielded tubular structures. The tubes were separated and washed by dropping into distilled water and were analyzed using various microscopy techniques. For EF-TEM, the fiber was put on a carbon-coated grid (Copper, 400 mesh) and the solvent was left to evaporate at room temperature. All X-ray powder diffraction patterns were taken on a Rigaku diffractometer (Type 4037) using graded *d*-space elliptical side-by-side multiplayer optics monochromated Cu Kα radiation (40 kV, 30 mA) and imaging plate (R-Axis IV). Centrifugation at 35 000 rpm separated the self-assembled fibrous sample. The fiber sample was transferred to a quartz capillary tube and excess water was removed using a syringe. The capillary was sealed and the XRD was measured. The melting and clearing points were measured on the first heating cycle using polarized light microscopy (Olympus BX50), and optical images were recorded with three charge coupled device video cameras (Olympus CS520MD).

Received: November 2, 2000
Final version: January 22, 2001

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Free-Standing Thin Films Containing Hexagonally Organized Silver Nanocrystals in a Polymer Matrix**

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The recent development of nanocomposites consisting of metal nanoparticles embedded in a polymer matrix has spurred broad scientific interest due to several potential appli-

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[**] The authors thank Prof. Francis J. DiSalvo for many helpful discussions and comments. This work was supported by DARPA under contract N66001-97-1-8922.

  0935-9648/01/1005-0718 $ 17.50+.50/0