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Organic Supramolecular Self-Assembled Materials Stabilized by Multiple Hydrogen Bonds

Toshimi Shimizu

National Institute of Materials and Chemical Research, 1-1 Higashi, Tsukuba, Ibaraki 305-8565, Japan Fax: +81-298-54-4422, e-mail: tshmz@ccmail.nimc.go.jp

Self-assembling properties and morphologies of synthetic bola-form amphiphiles (bolaamphiphiles) are described in connection with the formation of multiple hydrogen bonds. The D-glucose-, oligoglycine-, and nucleobase-based bolaamphiphiles self-assembled in aqueous media to form well-defined helical fibers, vesicle-encapsulated microtubes, and double-helical ropes, respectively. The formation strongly depends on the length and even or odd carbon numbers of the spacer alkylene chains. Possible self-assembling models for the molecular arrangements within the assemblies are proposed on the basis of infrared spectroscopy and X-ray structural analyses. In addition, polymerization of bola-form butadiyne 1-glucosamide in self-assembled nanoscale-fiber morphology is also discussed.

Key words: Bolaamphiphile · Self-Assembly · Hydrogen Bond · Supramolecular Fiber · Organic Microtube

1. INTRODUCTION

So far mankind has ingeniously utilized natural polymers such as wool, fur, cotton and silk in his life. In contrast to this tremendously long history, approximately 70-years history of synthetic polymers is quite short. The synthetic polymers constitute fibers, synthetic rubbers, and plastics that are nowadays indispensable for our life. Usual polymers are socalled linear macromolecules in which tens of thousands to millions of low-molecular weight compounds (monomer unit) are connected to each other through covalent bonds. In recent years, a new family of polymers has attracted much attention[1]. It includes new polymer architectures such as topologically complex polymers[2] and supramolecular self-assemblies[3].

In contrast, biomaterials are highly organized organic and inorganic composites. In their hierarchical structures, we can find diverse fibrous structures such as collagen fibers, actin fibers, and bacterium flagella. These biological structures are stabilized by extended hydrogen-bond networks[4]. A large number of reports have been described on the construction of molecular complexes and assemblies via hydrogen bonds. However, they are concerned with the complex formation in aprotic organic solvents or the control of hydrogen-bond motif in gels[5], liquid crystals[6] and solids[7]. Little has been known about the formation of well-defined supramolecular architectures with 10^2-10^6 -nm size in bulk water[8]. We have so far investigated self-assembling properties and morphologies of newly designed amphiphiles. In this paper, we mainly report our current topics concerning the formation of supramolecular organic fibers and microtubes.

2. MOLECULAR DESIGN

In order to furnish both ends of rod-like molecules with multiple hydrogen bonds, we designed bola-form amphiphiles (bolaamphiphiles) with sugar-, peptide-, or nucleobase-headgroup as a hydrophilic moiety separated by a long-chain hydrophobic spacer. The hydrophilic and hydrophobic moieties are connected via amide linkage that can form linear hydrogen-bond chain (Fig. 1). Thus, more than ten hydrogen-bondforming functionalities were incorporated in the The stability of the hydrogen-bond molecules. networks increases with increasing the energy and the number of hydrogen bonds[9]. Bola-form lipids exist in archaebacterial plasma membranes. Monolayer lipid membranes formed from them can give a thin and unsymmetrical vesicle membrane, and resist membrane fusion[10]. Consequently, the bolaamphiphiles contribute to increase the membrane stability itself.



Figure 1. Schematic illustration of a bolaamphiphile and self-assembled materials with well-defined morphology, stabilized by multiple hydrogen bonds.

3. EXPERIMENTAL

The bolaamphiphiles were synthesized by the coupling of the corresponding hydrophilic moieties with long-chain 1, *n*-alkane difunctional derivatives of varying chain length. When allowed to cool and stand at room temperature, the aqueous solutions of the bolaamphiphiles produced self-assembling molecular objects. They were directly subjected to light microscopy (LM) and transmission electron microscopy (TEM).

4. RESULTS AND DISCUSSION

4.1 Formation of Helical Fibers from Sugar-Based Bolaamphiphiles

The hot saturated aqueous solutions of the sugarbased bolaamphiphiles 1(n) produced amorphous or fibrous assemblies, when allowed to gradually cool. The LM observation revealed the formation of helical supramolecular fibers of several hundred micrometers in length for 1(n) (n = 6, 10, 12, and 14), amorphous solids for 1(n) (n = 9 and 13), and a plate crystal for 1(11)[11](Fig. 2). The self-assembling morphology strongly depends on the spacer length and their carbon numbers. We thus found for the first time the stereochemical effect of the even-odd connecting spacers on the self-assembled morphologies[12]. Unlike common bilayer fibers so far known[8], they



1(n): n = 6,9,10,11,12,13,14, and 18



Figure 2. Light micrographs of (a) thin fibers, (b) a platelet, and (c) helical twisted fibers formed from 1(10), 1(11), and 1(12), respectively.

can be isolated into air, and are stable for years. The TEM displayed that the chiral fibers are composed of right-handed helical ribbons of 3 nm in thickness and 35 nm in width.

4.2 Molecular Packing and Orientation within Fibers

Infrared spectroscopy (IR) and powder X-ray diffraction (XRD) of the dried fibers indicated that the difference between the even- and odd-numbered amphiphiles can also be seen for the orientation of amide linkage and packing mode of the alkylene chains. The difference in hydrogen-bond networks is considered to be responsible for these even-odd phenomena[12]. Single crystal structure analysis of 1(11) revealed that the molecules form a pleated sheet structure through the formation of multiple hydrogen bonds[14]. One-dimensional and orthogonal, twodimensional networks of hydrogen bonds are



Figure 3. Molecular packing and hydrogen-bond network of 1(11) in a crystal lattice.

constructed between amide linkages and sugar hydroxyl groups, respectively (Fig. 3). On the basis of the XRD analysis of the fibers, we proposed a possible self-assembling model for 1(12), as shown in Fig. 4. The molecules are tilting their alkylene chains within the monolayer of 2.45 nm in thickness[15].



Figure 4. A possible molecular arrangement of 1(12) within the helical fibers.

4.3 Formation of Microtubes from Oligopeptide-Based Bolaamphiphiles

Sodium salts of 2(n,m) were dissolved into water and the obtained aqueous solutions were allowed to stand for 2–3 weeks. Fibrous assemblies formed from 2(10,2) were examined using dark-field and phasecontrast LM. As a result, we found that these assemblies are unprecedented microtubes with closed ends, which encapsulate a large number of vesicular



2(n,m): n = 6,8,9,10,11,12, and 14. m = 2 and 3

assemblies in the aqueous compartment (Fig. 5a)[16]. Furthermore, we observed needle-shaped microcrystals (length = 2–10 μ m, width = 10–100 nm), which are projecting outward from the tube surfaces. Surprisingly, no significant changes in tubular structures were observed upon heating up to 100°C or sonication of the solutions. In addition, this unique morphology was maintained after dehydration of the tube and the subsequent drying in vacuum (Fig. 5b). Interestingly, the dried tubes reproduced the vesicleencapsulated microtubes by the addition of excess water.



Figure 5. Light micrographs of (a) organic microtubes in water at 25° C and (b) dried tubes, formed from 2(10,2).

Bolaamphiphiles with a glycylglycylglycine moiety at each end 2(10,3) also gave similar microtubes. The bolaamphiphiles 2(6,2) and 2(8,2) with relatively shorter alkylene spacers produced microtubes, whereas the amphiphiles with longer or odd-numbered spacer 2(n = 9, 11, 12, and 14) gave no microtubes. The related homologues with amino acid residues except for glycine also produced no tubes. We can thus conclude that the glycylglycine moiety is indispensable for the tube formation[17].

4.4 Molecular Packing and Orientation within Microtubes

We carried out X-ray single crystal analysis of a successfully obtained the needle-shaped crystal of 2(2,10). As a result, we found that the molecules form a layer structure[18]. The terminal carboxylic acid functionalities formed interlayer acid-acid dimers through hydrogen bonds. On the other hand, the IR analysis of the isolated tubes showed that protonation to the terminal carboxylic anions gradually proceeds during aging. The resultant intralayer acid-anion hydrogen bonds contribute to the stabilization of the tube membranes[17]. From the IR, we also found defects in the hydrogen-bond networks between glycine headgroups.

Atomic force microscopy (AFM) gives a useful methodology for observing molecular packing and orientation in the self-assembled systems adsorbed on substrates. We applied it to the observation of supramolecular arrangement on the surface and edge of the microtube membranes. On the basis of AFM, the



Figure 6. AFM image of the tube membrane surfaces prepared from 2(2,10).

thickness of the tube membrane is evaluated to be 100 nm that corresponds to 30-40 layers of a fully extended molecule[17]. The peptide headgroup forms a distorted hexagonal packing on the top of the surfaces (Fig. 6). Layered molecular arrangement was visualized along the molecular long axis in the edge of the membrane. We confirmed that bent molecules, layer structures, and columnar domains[19] hierarchically construct the microtube membranes. In addition, we found that intralayer interactions are dominant in the tube membranes. This contrasts to

usual 3-D crystals of carboxylic amphiphiles where interlayer interactions determine the structure.



Figure 7. Hierarchical structure of the microtube membrane formed from 2(2,10).

4.5 Formation of Nylon 2-Type Superstructure

Using vapor diffusion method of diluted acetic acid into the aqueous solutions of 2(2,10), we obtained a single crystal, as previously mentioned. Crystal structure showed that the molecules construct a linear polymolecular chain stabilized by one-dimensional hydrogen bonds between the two terminal carboxylic acids. The resultant layered structure has a 2.72-nm long-range spacing[18]. Each polymeric chain adopts pseudo-hexagonal lattice and is intermolecularly linked to its six closest neighbors (Fig. 8). This finding provides the first example of noncovalent formation of nylon 2-type (polyglycine II) structure by glycylglycine



Figure 8. Nylon 2-type superstructure formed on the microtube surfaces of 2(2,10).

bolaamphiphiles[20]. Nylon 2 can be classified as a polyamide that should give a robust fiber. However, it has been useless because of the infusible and insoluble character in all solvents. Therefore, the above results mean that thin fibers with a nylon 2 structure can be

4.6 Formation of Double-Helical Ropes from Nucleobase-Based Bolaamphiphiles

noncovalently prepared from a glycylglycine derivative.

When the 10%-ethanolic aqueous solution of thymine-based bolaamphiphiles 3(10) was allowed to stand for 1–2 days, gel-like assemblies were obtainable. Dark-field LM revealed the presence of double-helical ropes where two independent ropes of $0.2-1.0 \ \mu m$ in



diameter intertwine in the same helical sense[21]. Furthermore, the TEM displayed that the ropes are composed of nanoscale fibers with a minimum width of 14 nm (Fig. 9a). It has been well documented that double-helical strands appear as a precursor of higher ordered bilayer assemblies[22]. The present helical ropes are very stable for months and very huge compared to those so far reported. To the best of our knowledge, this is the first example of mesoscale double-helical ropes. Meanwhile, the adenine-based bolaamphiphiles 4(10) produced microcrystalline solids with a diameter of 10 µm, which exhibit birefringence in polarized LM image. However, a 1:1 mixture of the adenine- and thymine-based bolaamphiphiles gave no helical ropes, but well-defined nanoscale fibers of 9.5 nm in width (Fig. 9b). We thus observed the suppression of helical rope formation by the addition of the complementary nucleobase-based homologue. The base pairing between the thymine and adenine residues would be hinder for the ropes or fibers to form double helix. In a solid state or assembled systems, thymine residue can reversibly photodimerize and photodissociate by the irradiation of UV light ($\lambda > 270$ nm or $\lambda < 270$ nm, respectively)[23]. Among the resultant four kinds of photodimers, two isomers are optically active. From the high-resolution NMR analysis, we were able to detect a trace amount of



Figure 9. TEM images of (a) double-helical ropes and (b) nanoscale fibers, formed from 3(10) and a 1:1 mixture of 3(10) and 4(10).

photodimeric compounds in the self-assembled ropes. Therefore, it can be assumed that the obtained enantiomeric chiral dimers trigger the formation of mirror-imaged helical ropes.

4.7 Formation of Polydiacetylenic Molecular Wires from Bola-form Butadiyne 1-Glucosamide

Molecular self-assembly is a key methodology for constructing nano- and mesoscale materials with welldefined morphology and dimensions of 10^2-10^6 nm. In order to stabilize the self-assemblies, one can envisage the introduction of a variety of polymerizable groups into self-assembling molecules. However,



little is known about the construction of polymerized nanoscale fibers[24]. We have recently synthesized a series of bola-form butadiyne 1-aldosamide, in which tetra-acetylated 1-D-glucosylamine or 1-D-galactosylamine is linked via β -N-glycosidic bond to 5,7-dodecadiynedioic acid at each end[25]. The bola-form compound **5** formed an organogel with ethyl acetate/*n*-hexane. The TEM observation showed that the gel is composed of nanoscale fibers with minimum



Figure 10. TEM image of polymerized molecular wire formed from 5.

width of 3 nm. This fiber width is in good agreement with an extended molecular length of 5. The fibers changed the color from colorless to violet or red on exposure to 254-nm light or r-ray. Gel permeation chromatography of the UV-irradiated fibers revealed polymerized entity with Mw = $3.3 \times 10^4 - 1.6 \times 10^3$. No remarkable changes in the morphology of the fibers were found on exposure to 254-nm light under observation with TEM. On the other hand, the octaacetylated derivatives 6 formed no gel, but amorphous solids in ethyl acetate/*n*-hexane. These findings suggest that the self-assembled fibers formed from 5 have high molecular ordering for the diacetylenic group to polymerize within the fibers. Furthermore, we first demonstrated the direct observation of single oligodiacetylene chain by TEM.

5. SUMMARY

Supramolecular self-assembled materials, such as helical fibers, microtubes, double-helical ropes, and molecular wires, have been prepared from sugar, peptide-, and nucleobase-based bolaamphiphiles in aqueous media. A variety of hydrogen-bond networks provide diverse nano- and mesoscale materials with well-defined morphology and a high-axial ratio. These unique materials are applicable to reversible polymers, drug-delivery systems, oil gelator, and nanomachine parts, etc.

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