Supramolecular Assemblies of Diacetylenic Aldonamides

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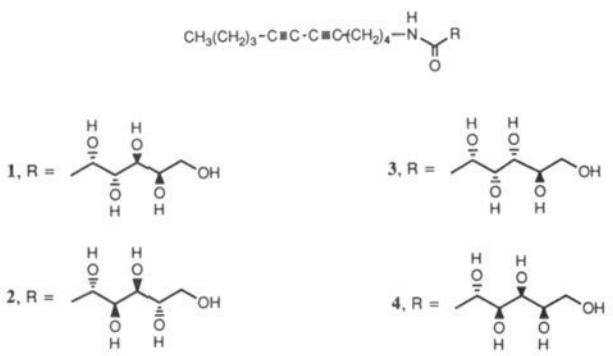
The widely studied phosphatidylcholines (PC) generally form lamellar supramolecular assemblies upon hydration. The introduction of a diacetylenic group into the fatty acid chains allows the polymerization of these assemblies to yield polydiacetylenes in two dimensions.[1-3] This relatively simple change in the structure of the PC molecule also favors the formation of hollow tubular microstructures (tubules) under certain conditions.[4-6] A variety of applications have been proposed for these interesting materials.[7] Other amphiphiles, e.g., selected glutamate lipids[8,9] and aldonamides,[10-13] are also known to form tubelike assemblies. The helical or tubule structures of the aldonamides may have technical utility if they can be stabilized. Diacetylenes were selected in order to test the molecular order in the assembly[14] and subsequently stabilize the assembly to organic solvents. In addition, the electron-dense diacetylenes or polydiacetylenes allow the direct electron microscopic imaging of the assembly morphology without the aid of staining reagents. As part of our research into the relationship between molecular structure and supramolecular morphology we have prepared diacetylenic aldonamides and summarize their behavior in this communication.

Diacetylenic aldonamides (**1**–**4**) were successfully prepared from the aldonic acid δ-lactones of D-galactose, L-mannose, D-glucose, and D-gulose, respectively.[15] Supramolecular assemblies of these aldonamides were prepared by heating the compounds (0.25–1.0 mg/mL) in water to 100 °C and allowing the solution to cool toward room temperature.



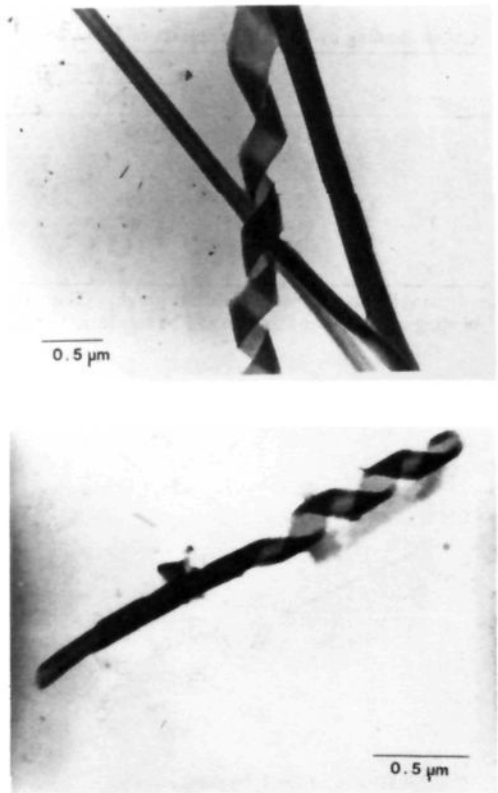


Figure 1. Transmission electron micrograph (unstained) of dried samples from hydrated assemblies of **1**: (top) unpolymerized **1** and (bottom) polymerized **1**.

Transmission electron micrographs (TEM) of assemblies of *N*-dodeca-5,7-diyne-D-galactonamide (**1**) in water (0.25 mg/mL) are shown in Figure 1.[16] After formation of the assemblies the sample was divided, and half was exposed to 254 nm light to polymerize the assembly. The sample rapidly became purple with UV exposure (λ_{max} = 610 nm). Both the unexposed and the exposed samples were deposited on EM grids and allowed to air-dry before examination. An unpolymerized aggregate of **1** is shown in Figure 1 (top), and a polymerized aggregate of **1** is shown on the bottom. The images of both the unpolymerized and polymerized aggregates show a similar morphology with a right-handed helical structure associated with a more tightly wrapped tubular segment. Closed tubule structures predominate on the TEM grids, but a low percent of the structures show helices. These and other micrographs show no apparent difference in morphology between the polymerized and the unpolymerized assemblies in aqueous buffers. If the samples were treated with a strong hydrogen bonding solvent, e.g., formamide at room temperature, the unpolymerized tubules were dissolved, whereas the polymerized diacetylenic structures were not disrupted. In some TEMs the end of tubules were observed at sufficient resolution to distinguish the individual layers as they wrap around the interior space. These layers observed were 3.5-nm thick, which is reasonable for a bilayer sheet of **1**. The tubules of **1** have an

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(15) Dodeca-5,7-diyne-1-nitrile was prepared by the oxidative heterocoupling of 1-iodohexyne and 5-cyano-1-pentyne, and then it was reduced with lithium aluminum hydride in diethyl ether to yield the corresponding amine. This *N*-dodeca-5,7-diyne-1-amine was refluxed with the appropriate aldonic acid δ-lactone in methanol to give the desired diacetylenic aldonamide in good yield.

(16) Carbon-coated formvar copper grids were dipped into water suspensions of the assemblies and observed without further preparation on a Hitachi H-500 transmission electron microscope at 75 or 100 kV.

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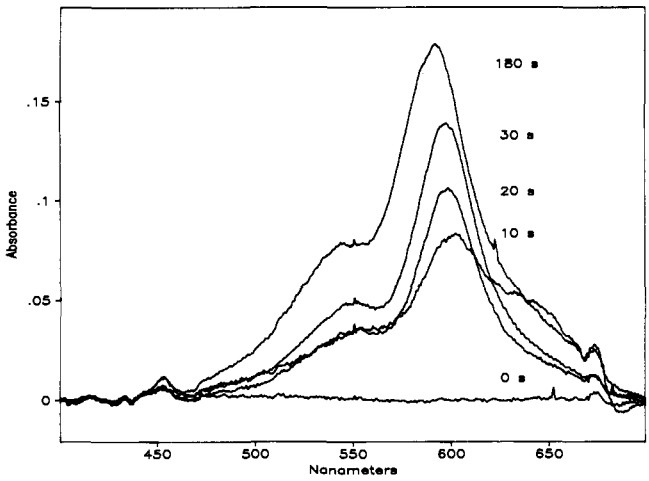

Figure 2. Visible absorption spectra of a suspension of tubules of **2**. The spectra were recorded after exposure (25 °C) to 254-nm light from a low-pressure Hg lamp for the indicate times.

average diameter of 0.3 μm with a length of several microns.

The L-mannonamide (**2**) formed tightly wound hollow tubule structures, which were very photosensitive and gave a polydiacetylene (PDA) absorption maxima at 600 nm (Figure 2). The tubule morphology was retained after the polymerization. The tubules of **2** have a slightly larger average diameter (nearly 0.4 μm) than those of **1**. The formation of long wavelength PDAs in assemblies of **1** and **2** indicate that the diacetylene chains are well ordered in these tubules. In contrast UV exposure of the assemblies of **3** and **4** yielded reddish-orange PDAs that adsorbed at 500 and 523 nm, respectively, which is indicative of short polymer chains. These data suggest that the diacetylene chains in the assemblies of the D-gluconamide (**3**) and D-gulonamide (**4**) are less well-ordered than those of **1** and **2**. Both **3** and **4** assemble into hollow tubes, which in the case of the gulonamide **4** appear to be composed of smaller aligned fibers.

In summary these preliminary findings demonstrate that well-ordered diacetylenic and polydiacetylenic microstructures may be formed from easily synthesized single chain amphiphiles. The observation that the diameter of the tubules is sensitive to the head group composition may prove to be important in the design and utilization of these assemblies.[17] The electron micrographs of assemblies of **1** provide direct evidence for an equilibrium between a open helical structure and a tightly wound tubular structure. These data may help to clarify the mechanism of microtubule formation[18] and provide experimental support for the theory that a bilayer sheet of chiral molecules can form a helix due to the tensions resulting from the interactions of molecules with the edges of bilayers.[19]

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Registry No. 1, 135615-24-6; **2**, 135615-25-7; **3**, 135615-26-8; **4**, 135615-27-9; D-galactonic acid δ-lactone, 15892-28-1; L-mannonic acid δ-lactone, 124915-65-7; D-gluconic acid δ-lactone, 90-80-2; D-gulonic acid δ-lactone, 120523-34-4; dodeca-5,7-diyne-1-nitrile, 135615-28-0; 1-iodohexyne, 1119-67-1; 5-cyano-1-pentyne, 14918-21-9; *n*-dodeca-5,7-diyne-1-amine, 135615-29-1.

Supplementary Material Available: Synthesis of the aldonamides and intermediates (3 pages). Ordering information is given on any current masthead page.

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Supramolecular Assemblies, a Crystal Structure, and a Polymer of N-Diacetylenic Gluconamides

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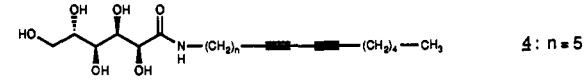
The hydrophobic effect, amide hydrogen bond chains, and the chirality of the head act together to form ultrathin and extended micellar fibers from *N*-alkylgluconamides in aqueous media.[1,2] These fibers totally disintegrate if dried. By the introduction of diyne units into the hydrophobic chain, we tried converting the rods to tubes[3,4] and stable micellar polymers. We are aiming for new polymeric fibers with a flexible, dye-dissolving core and a chiral surface. Since gluconamide rods have an extremely high curvature compared to the more or less planar lecithin bilayers, the success of both tube formation[3,4] and polymerization[5] was uncertain.

1,3-Nonadiynyl units were combined with *N*-methyl, *N*-propyl, and *N*-pentylgluconamides to attain the amphiphiles **1-3**. The L-gluconamide **4** was also prepared. **2** and **3** are stable, colorless compounds whereas compound **1** soon turned red due to partial polymerization (λ_{max}: 529, 575 nm). Gluconamides **1-4** were insoluble in water at room temperature, but readily dissolved upon refluxing. Rapid cooling to room temperature produced a whitish gel with compound **1** in the concentration range of 0.5-10% v/w, whereas **2**, **3**, and **4** gave white, viscous dispersions. Scanning calorimetry of the gel or dispersions gave fully reversible melting curves.[6] Gluconamides **1-4** all have liquid crystalline phases which occur in increasing temperature ranges with growing chain lengths (**1**, 142-148 °C; **2**, 134-164 °C; **3** and **4**, 122-166 °C). In the case of **1**, polymerization occurs before melting, while **2**, **3**, and **4** show behavior very similar to that of the saturated *N*-alkylgluconamides.[7]

1: n = 1
2: n = 3
3: n = 5



4: n = 5

Transmission electron microscopy of the fresh gels showed the expected tubular structure in the case of gluconamides **1** and **3**. The tubes are much thinner and longer than those obtained from double chain phospholipids.[3,4] The thickness of the tubes ranges from 50 to 70 nm, the hollow centers have a diameter of about 8-10 nm, and length-to-diameter ratios are up to 10^4 in the case

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