(T* or G*) CPG support and the [1'-^{13}C]-5'-*O*-dimethoxytrityl 3'-*O*-(β-cyanoethyl *N*,*N*-diisopropylphosphoramidite) building blocks.[8,13]

Assignments of the ^{13}C resonances were made by a heteronuclear experiment derived from the HMQC sequence.[14-18] The HMQC spectrum of the duplex is shown in Figure 1. Clearly, the spreading of both the H1' and C1' resonances brings about an excellent dispersion of the 20 ^{1}H1'-^{13}C1' correlations. It is well-known that, in a right-handed DNA, the H1' proton sugar (*i*) is close to the H8 or H6 nucleobase protons of the 3'-neighboring nucleotide (*i* - 1) and far from all the sugar protons of its 5'-neighboring nucleotide (*i* + 1).[19] Using this property, the sequential assignments of the ^{13}C and ^{1}H resonances were made by the C1'(*i*)-H1'(*i*) and C1'(*i*)-H1'(*i*-1) correlations on the relayed HMQC-NOESY spectrum (Figure 2). As soon as the H1' and H8-H6 resonances were assigned, the examination of the through-bond *J* coupling correlations in the HMQC-TOCSY experiment gave the H2', H2'', H3', and H4' resonance assignments. Assuming that the only sugar protons close to H1' are those belonging to their own residue (as generally observed in canonical conformations of DNA), their assignment can also be directly made on the HMQC-NOESY spectrum. For the first time to our knowledge, the resonances of C1' and all nonexchangeable protons (except for H2 and H5',5'') of an oligonucleotide were obtained using 2D relayed ^{13}C-^{1}H HMQC-NOESY and HMQC-TOCSY spectra. It should be noted that this kind of experiment, having about the same sensitivity as conventional ^{1}H-^{1}H NOESY, can be run with a small amount of ^{13}C-labeled duplex. In our example, a 0.6 mM concentration was used.

The good dispersion of the ^{1}H1'-^{13}C1' correlations is favorable for studying much longer oligonucleotides where the overlap of the H1' resonances bars the complete assignment of the proton resonances. This strategy is expected to greatly facilitate the NMR conformational studies of a nucleic acid when interacting with a ligand. Moreover, significant information on the extent and time scale of the internal dynamics for sugar units can be obtained by measuring the ^{13}C relaxation parameters. This is because the ^{13}C-selective enrichment at 100% offers the advantage of sensitivity without complicating both the spectrum by ^{13}C-^{13}C coupling constants and the analysis of T_1 or NOE data by additional ^{13}C-^{13}C relaxation pathways.

Acknowledgment. We are grateful to the Ligue Nationale Française contre le Cancer for a predoctoral fellowship (L.C.).

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Molecular Monolayer Rods and Tubules Made of α-(L-Lysine),ω-(Amino) Bolaamphiphiles

Jürgen-Hinrich Fuhrhop,*[†] Dragan Spiroski,[†] and Christoph Boettcher[†,‡]

Institut für Organische Chemie der Freien Universität Berlin
Takustrasse 3, 1000 Berlin 33, Germany
Fritz-Haber-Institut der Max-Planck-Gesellschaft
Faradayweg 4-6, 1000 Berlin 33, Germany

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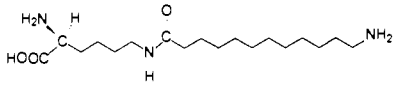
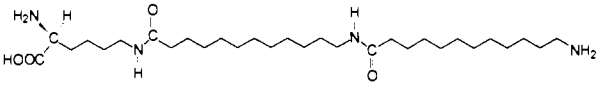
Spherical micelles and vesicles are formed from amphiphiles[1] and bolaamphiphiles[2] by the hydrophobic effect.[1] The head groups are hydrated, and their interaction is of a repulsive nature.[3] Micelles and vesicles thus have fluid character and lose their shape upon drying. Introduction of secondary amide bonds into the head groups, however, leads to strong hydrogen bond chains. The fluid micelles and vesicles are converted to solid micellar rods[4,5] and vesicular tubules.[6] Such molecular assemblies should be isolable in the dry state under favorable conditions. We have synthesized unsymmetric bolaamphiphiles **1** and **2** with one amino acid head group (D- and L-lysine or -ornithine) and one ammonium chloride head group. Electron micrographs of aqueous gels show micellar rods and, more interesting, vesicular tubules with a membrane of monomolecular thickness.



1



2

The N^{6}-acylated L-lysine **1**[7] dissolves up to 1% (10^{-2} mol L^{-1}) in water at room temperature below pH 5.5. It becomes insoluble above pH ≈ 8.5. At pH 10.5-11.0, opaque dispersions are obtained. In electron micrographs of the dried and negatively stained probes, one observes single as well as clustered micellar fibers with a diameter of 25 ± 5 Å (Figure 1). This corresponds exactly to a micellar monolayer. We assume a connecting amide hydrogen bond chain, which forms a thread along the rod axis and arranges both head groups on two different cylinders (Figure 1b). This is in loose analogy to amide bond chains found in a crystal structure of an α,ω-bis-gluconamide bolaamphiphile[8] (model A). The major binding fource should *not* originate from the hydrophobic effect, but from these hydrogen bond chains. Similar, but

[†] Institut für Organische Chemie der Freien Universität Berlin.
[‡] Fritz-Haber-Institut der Max-Planck-Gesellschaft.

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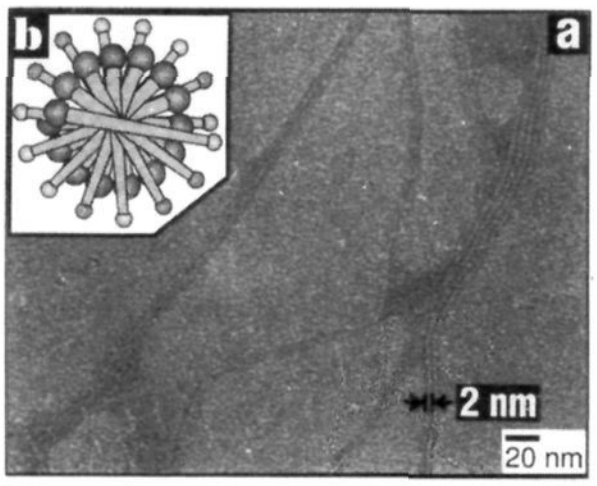

Figure 1. (a) Electron micrograph of molecular monolayer rods made of **1** (pH 10.5). Negatively stained with 2% phosphotungstate. (b) *Model of a cross section of the fiber. The large spheres correspond to* the amino acid and the small spheres to the amino head groups; the crossing indicates the position of the amide hydrogen bond chain.

much shorter rods have been reported by Newkome[9] for an arborol with extremely bulky head groups and by Kunitake for a diammonium bolaamphiphile in 10^{-2} M suspensions.[10]

Elongation of the hydrophobic chain by 11 methylene groups and introduction of an extra primary amide link in **2** reduce solubility in comparison to **1**. **2** only dissolves in water below pH 5.5 up to 0.01% at 85 °C (2×10^{-4} mol L^{-1}) and precipitates at pH 10.5. Bilayers in the form of tubular vesicles rather than rodlike micelles were now formed. The amide hydrogen bond chains again enforce fiber growth, and long tubular vesicles are *observed (Figure 2). The inner diameter of the tubules is about* 500–700 Å, depending on preparation conditions, cooling rate, and base used. Similar long-lived and uniform tubules have been obtained with ornithine as a head group. The measured membrane thickness of 40 ± 5 Å according to one molecular length shows that the tubules have not collapsed, in contrast to observations with monolayered vesicles.[11] It is not known whether the arrangement of end groups is statistical (model in Figure 2) or asymmetric with the small amino groups on the inner surface, such as observed in some vesicles.[11]

Negative staining of the tubules with phosphotungstate (pH 7; 2%) or uranylacetate (1%) solution and removal of excess staining solution by suction and evacuation on the electron microscope grid leads to stained centers of the tubes. It is thus possible to partly fill the tubules with water–soluble compounds by imbibement. This can be seen in the electron micrographs of Figure 2: almost all of the tubules are white (=empty) at the ends and black (=filled) in the middle parts. Capillary forces will fixate these compounds within the tubules, although the ends of the tubules are open to the bulk water volume. One may therefore regard the tubules as extremely elongated vesicles, which separate entrapped material from the environment by the length of one molecular monolayer. It can also be imaged that U-shaped bolaamphiphile molecules with at least two gauche bends in the CH_2 chain could form bilayered membranes of the same thickness. This, however, is ruled out by the infrared spectrum of the lyophilized tubules, which showed sharp C–H stretching bands at 2850 and 2920 cm^{-1} without any shoulder at higher wave numbers as well as CH_2 wagging band progressions at 1217, 1239, and 1269 cm^{-1}. This is typical for an all-trans oligomethylene chain.[12,13] The water-suspended tubules could be filtered off with a filter crucible (D4, 10–16-μm pores). The residue was lyophilized and

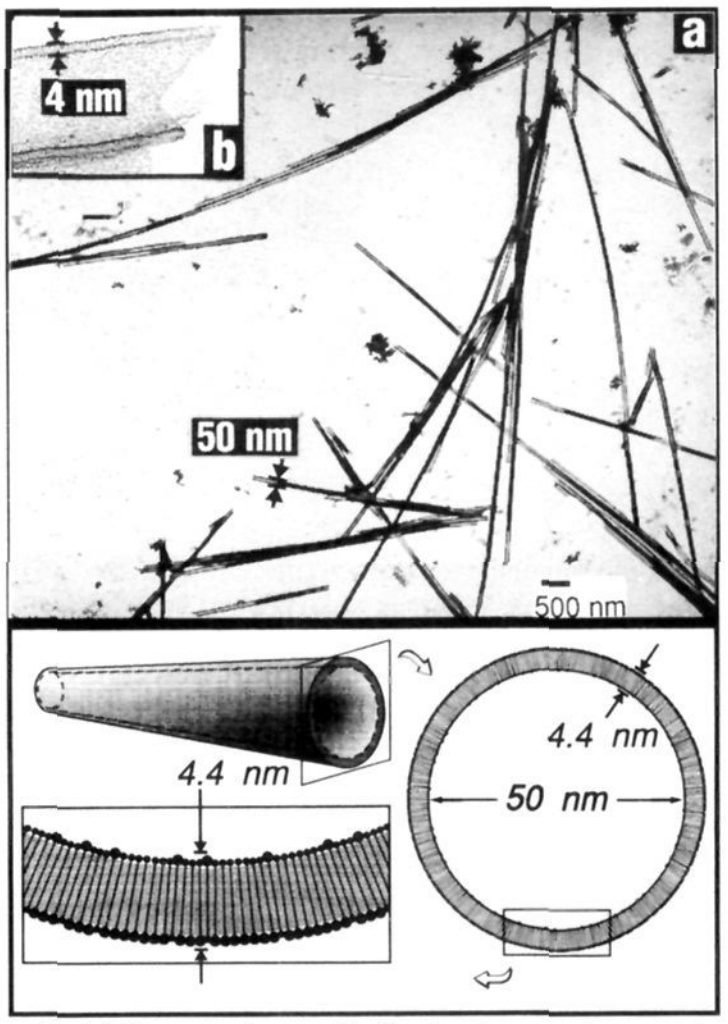

Figure 2. (a) Electron micrograph of molecular monolayer tubules made of **2** (pH 10.5). Negatively stained with 2% phosphotungstate. (b) Magnification of part a showing the 4-nm monolayer membrane. The model of the tubule assumes a statistical arrangement of head groups with some preference for the smaller amino head group on the smaller inner surface.

dried over phosphorus pentoxide at 40 °C. The dried residue had about the same weight as the applied material. This indicates that the tubule yield should be close to quantitative. Lyophilizate samples which had not been further dried were resuspended in water and examined in the usual way under the electron microscope. The same intact tubules as in the original probes were observed. It is also possible to store the lyophilized tubules for at least several weeks. They constitute stable, ultrathin vessels for water–soluble compounds at pH 10–11. Comparable molecular bilayer tubules usually consist of much thicker multilayers, are less uniform, and cannot be isolated.[14–16]

The enantiomers of **1** and **2** have also been prepared from D-lysine. They produce the same fibers and tubules. The racemate of **1**, however, precipitates in the form of planar platelets and/or disorganized structures. This constitutes a further indication for the chiral bilayer effect.[17] Electroneutral fibers with high curvature are long-lived only if their surface is chiral. This effect is, however, not apparent with tubules. Pure enantiomers and the racemate of **2** produce identical supramolecular assemblies. The effect of chirality in molecular monolayers thus depends on curvature in the same manner as in bilayers.[4,17]

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