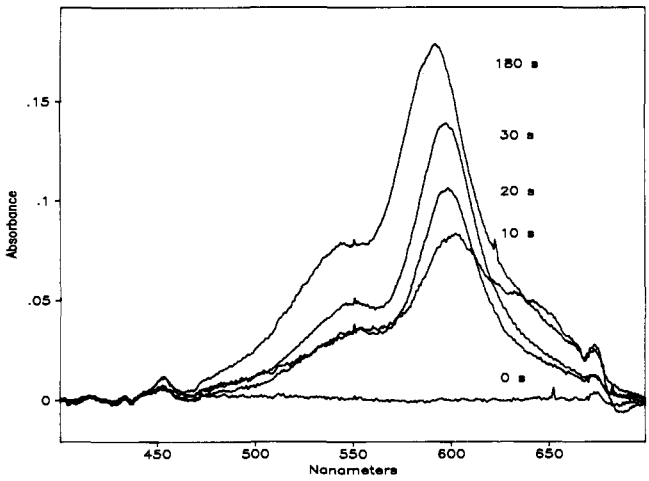

Figure 2. Visible absorption spectra of a suspension of tubules of **2**. The spectra were recorded after exposure (25 °C) to 254-nm light from a low-pressure Hg lamp for the indicate times.

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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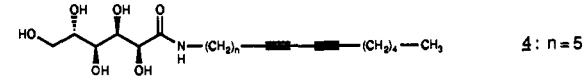
The hydrophobic effect, amide hydrogen bond chains, and the chirality of the head act together to form ultrathin and extended micellar fibers from *N*-alkylgluconamides in aqueous media.[1,2] These fibers totally disintegrate if dried. By the introduction of diyne units into the hydrophobic chain, we 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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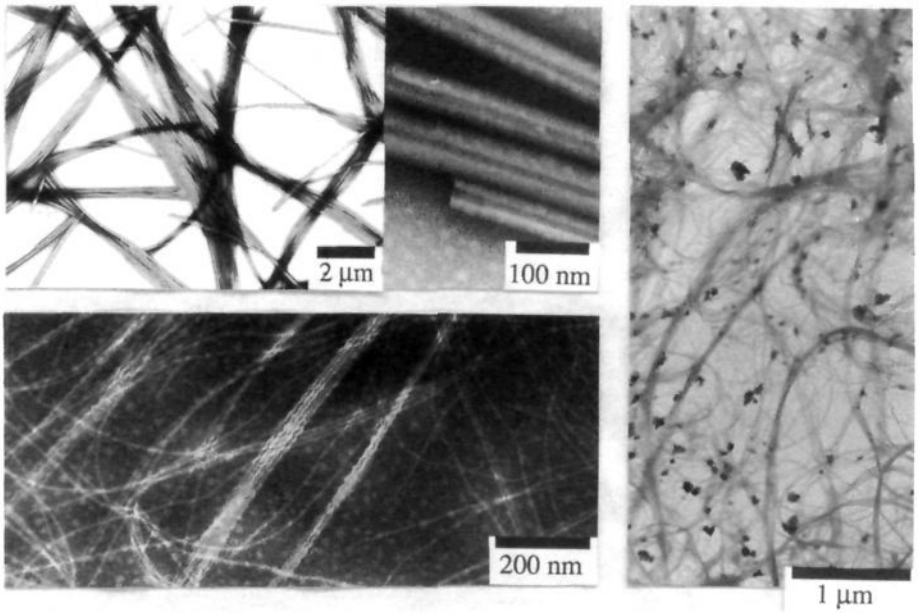

Figure 1. Electron micrographs of fibrous aggregates made of diacetylenic gluconamides **2** and **3** in the presence of 2% phosphotungstate (pH 7). Fibers made of **1** looked similar to those made of **3**. Polymerized **1** was not stained. Concentration: 2% (w/w).

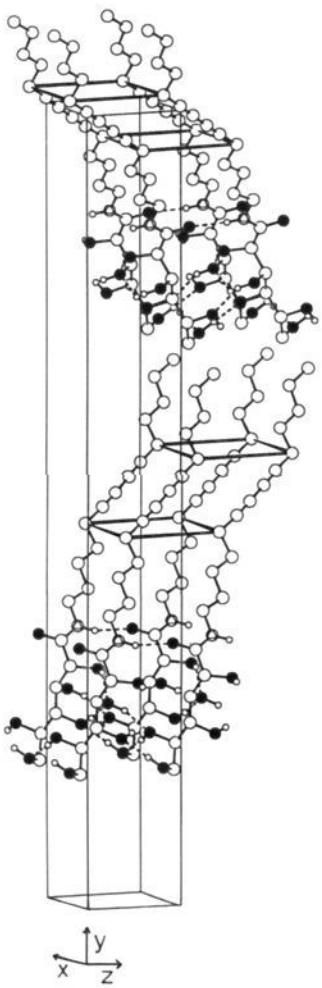

Figure 2. Crystal structure of **3**. The void in the hydrocarbon chain and the homodromic hydrogen bond cycle are indicated.

of **3**. Compound **2** aggregates to uniform micellar rods with a diameter of 4 nm, which corresponds to a molecular bilayer. These ultrathin rods have an extreme tendency to arrange in bundles, but the parallel rods do not merge. Micrographs at high magnification show that the tubes are composed of irregular M helices in analogy to "micellar cloths" obtained from tartaric acid monoamides.[8] We assume that the micellar rods of 4-nm width aggregate to bundles, which then form the tubes. The exact arrangement of the micellar rods remains unknown, since the resolution of the electron micrographs is not high enough to reveal any structural details of the open ends of the tubes (Figure 1).

UV irradiation of the fibrous gels made of **2** and **3** had no influence on the appearance of the gels. Compound **1**, containing only one methylene group between a diacetylenic and an amide group, polymerized readily. However, the tubular aggregates disappeared upon polymerization. Electron micrographs of the resulting polymer showed rods with an approximate diameter of 5 nm together with a few ribbons. No terminals of the strands could be detected, and so a totally interconnected system of micellar fibers was thus formed. Evaporation and resuspension gave identical electron micrographs. A polymeric material with a micellar structure and a chiral surface has thus been prepared. The polymer was insoluble in boiling water or organic solvents. Its aqueous dispersions showed no defined peaks in scanning calorimetry.[6]

From compound **3** were obtained crystals suitable for X-ray diffraction analysis. The first crystal structure of an amphiphilic diyne portrays the head-to-tail arrangement of the sheets, which has also been observed in the corresponding saturated *N*-alkylgluconamide. A homodromic cycle of hydrogen bonds is also found.[9] The diacetylenic unit produces the "jog" predicted by Schoen et al.,[4] together with a void of approximately 4.8 × 5.2 × 6.8 Å^3. The distance between the acetylenic units (3.37 Å) is too large to permit topochemical solid-state polymerization.[10] The voids in the *z* direction form channels (Figure 2).

Electron micrographs of the tubular aggregates and the polymeric fibers clearly indicate that all compounds **1**–**4** aggregate to form very similar micellar rods. Only rods made of **1**, **3**, and **4** assemble to tubular bundles, whereas **2** and polymerized **1** form isolated rods. The micellar polymers in aqueous or organic suspensions provide unique opportunities to construct organized

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reaction systems with an optimal internal surface area and integrated redox-active dyes.

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Supplementary Material Available: Tables of bond lengths, valence angles, and atomic parameters for **3**, experimental details for the syntheses of **1-4**, and ^{1}H NMR spectra of **1-3** (11 pages); listing of observed and calculated structure factors for **3** (19 pages). Ordering information is given on any current masthead page.

Stereospecific Method to *E* and *Z* Terminal Fluoro Olefins and Its Application to the Synthesis of 2′-Deoxy-2′-fluoromethylene Nucleosides as Potential Inhibitors of Ribonucleoside Diphosphate Reductase

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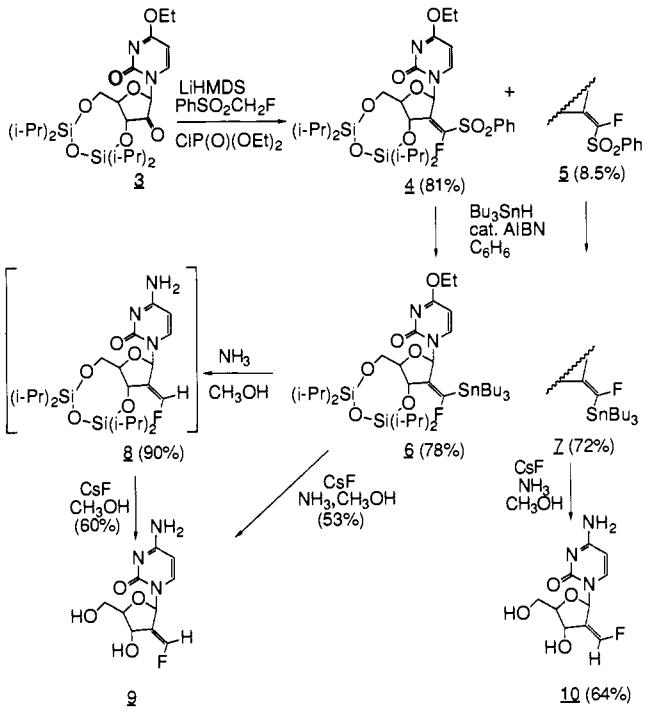
The terminal fluoro olefin group is a useful functionality in the design of mechanism-based enzyme inhibitors.[1] Because the potency of these inhibitors often depends on the geometry of the olefin, there is considerable interest in developing stereospecific methods for fluoro olefins. Most methods reported thus far[1a,2a-e] yield mixtures of *E* and *Z* isomers, which are often difficult to separate. The only general stereospecific synthesis[2f] relies on acetylenes as starting materials and provides the terminal fluoro olefins contaminated with 5-15% nonfluorinated olefins.

We report a stereospecific method to *E* and *Z* terminal fluoro olefins from (fluorovinyl)stannanes **1** and **2**,[3] which are readily accessible from ketones. The utility of this method is demonstrated with the synthesis of (*E*)- and (*Z*)-2′-deoxy-2′-(fluoromethylene)cytidine, **9** and **10**, respectively (Scheme I). The fluoro olefins **9** and **10** were designed as bioprecursors of mechanism-based inhibitors of ribonucleoside diphosphate reductase (RDR) (EC 1.17.4.1). It was envisioned that **9** and **10** would be transformed by the action of kinases to the corresponding diphosphate derivatives,[4] which could be substrates of RDR, and inactivate the enzyme via a fluoroallyl radical. This enzyme contains an essential tyrosyl radical and catalyzes the rate-determining step in the de novo synthesis of deoxyribonucleic acid (DNA).[5]

Scheme I



Using the Horner-Wittig reaction,[2a] 2′-ketonucleoside **3**[6] was converted to a mixture of readily separable fluorovinyl sulfones **4** and **5**.[7] Our lack of success in reducing the fluorovinyl sulfones to the fluoro olefin with amalgamated aluminum[2a,8] led to the discovery of a new and stereospecific method to fluoro olefins.

Fluorovinyl sulfones **4** and **5** were transformed to (fluorovinyl)stannanes **6** and **7** with 2 equiv of tributyltin hydride.[9] Analysis of the crude reaction mixtures by ^{19}F NMR showed the absence of **7** in **6** and vice versa. Watanabe and co-workers[10] proposed an electron-transfer mechanism for the conversion of vinyl sulfones to mixtures of (*E*)- and (*Z*)-vinylstannanes. On the basis of our observations that fluorovinyl sulfones obtained from ketones are transformed to (fluorovinyl)stannanes with retention of configuration,[9] a radical addition-elimination mechanism is proposed. To our knowledge, this is the first report of a stereospecific radical reaction of this kind involving tributyltin hydride.[11,12]

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