compared to the barriers for the respective ammine proton transfer reactions results from the increased distortion of the core structures in the transition states and the lower acidity of the amide protons. Zero point vibration and entropic contributions lower the Gibbs free energy barrier difference between the two pathways to 54 – 63 kJ mol^{-1} by destabilizing the highly ordered ammine proton transfer transition states **12**, **18**, and **24**. This difference could well be overcome by steric congestion induced by bulky substituents of amines and unsaturated hydrocarbon substrates. For comparison, the steric destabilization for complexes with three 2,6-dimethylanilide ligands at a titanium center such as in **4a** and **5a** has been computed to be 67 – 78 kJ mol^{-1}.

In allene and ethyne hydroamination with the simplified [CpTi=NH(NH_2)] system, where proton transfer takes place after initial amine coordination, the transition state for the cycloaddition is the highest point in the catalytic pathway and thus is rate-determining. However, it remains unclear whether the zero-order dependence on the 2,6-dimethylaniline concentration derived from the kinetic data for allene hydroamination[4] results from a rate-determining [2+2] cycloaddition or a rate-determining proton transfer from an amide ligand. A first-order dependence on the amine concentration can occur if the Gibbs free activation energy for the amine coordination plus proton transfer pathway is higher than the barrier for the initial [2+2] cycloaddition, but lower than the barrier for a competing amide proton transfer. A rate-determining amide ligand exchange with free amine could also result in such a rate law (see Supporting Information for computed ligand exchange pathways).

For alkene hydroamination, our model calculations predict that both the ammine and the amide proton transfer to the Ti–C bond have Gibbs free activation energies that are more than 50 kJ mol^{-1} higher than the cycloaddition step (Figure 4 and 5c). This explains the relative ease of allene and alkyne hydroamination compared to alkene hydroamination. Increasing the rate of this proton transfer step as well as stabilizing the metallaazacyclobutane intermediate compared to the catalyst resting state could be the key to making the alkene process successful. We are using these new insights into the hydroamination mechanism to isolate additional intermediates involved in the catalytic cycle, and to tailor more general hydroamination catalysts.

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Self-Assembly of Cyclic Peptides into Nanotubes and Then into Highly Anisotropic Crystalline Materials**

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Syntheses of supermolecules rely on the stabilization provided by noncovalent interactions between recognition sites in each unit.[1–3] The construction of new supramolecular architectures with well-defined shape and size by using tube building blocks is an important subject in organic materials chemistry because novel electronic and photonic properties can result from their three-dimensional (3D) organization (Figure 1a).[2] These tubular structures have also attracted considerable interest because of their utility as models for biological channels.[4–9] It is also thought that in tubes built from stacked cyclic peptides, uniform alignment of amide groups could give rise to a macrodipole moment such as that of an α-helix.[10] Voltage gating and current rectification are important expected new properties for such channel structures.[11]

To date, all attempts to grow crystals of a useful size were frustrated by the inherent insolubility of these materials.[12–15]

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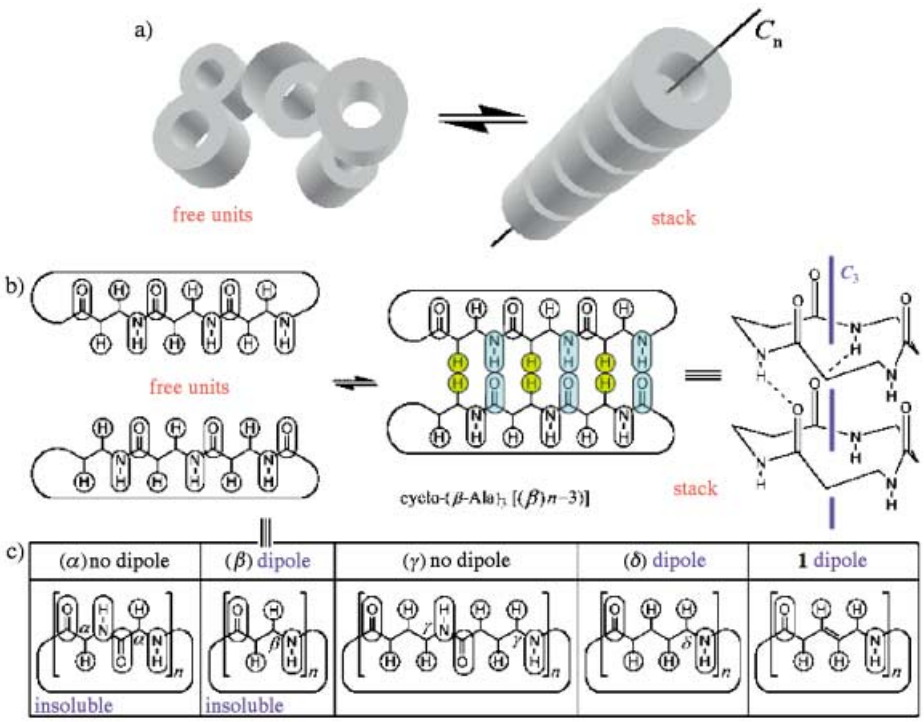

Figure 1. Structure of cyclic peptide nanotubes. a) A modular tube is formed by stacking of free units. b) In the case of cyclo-(β-Ala)$_3$, each free unit associates with the growing stack by means of three H bonds (blue) from amides and three van der Waals contacts (yellow) from pseudo-axial aliphatic hydrogen atoms. c) Types of macrolactams: lactams α and β are notoriously insoluble materials.

Consequently, their tubular structure could not be unequivocally characterized and this undesired insolubility prevented these nanotubes from being practically useful. Here we show how we successfully addressed the critical solubility problem by designing and synthesizing special organic C_n lactam units built from novel amino acids. We could then demonstrate the tubular shape of our supermolecules by X-ray crystallography. Apart from this primary aim, we also managed to extend the dipolar anisotropy of the macromolecular column components to a whole monocrystal to give useful macroscopic properties.

Flat ring-shaped cyclopeptides have the potential to aggregate as "endless" stacks through backbone–backbone H-bond interactions and van der Waals contacts (Figure 1b).[12] In this way, some tubes made from cyclo-(α-amino acid)$_n$ (Figure 1c, α, $n=3$, 4) have been prepared; but they proved difficult to handle because of their strong propensity to aggregate (their structures could only be defined by electron diffraction, calculations, and infrared (IR) spectroscopy of microcrystals).[16–18] The problem was only partially alleviated by using appropriate side chains.[6, 16] The same extreme insolubility was also the main characteristic of tubes made of cyclo-(β-amino acid)$_n$ (β, $n=3$, 4, their structures were obtained by X-ray diffraction analyses of powders, or inferred more indirectly by calculations or IR spectroscopy).[14, 15, 19, 20]

Nothing is known about tubes made of more lipophilic cyclo-(γ-amino acid)$_n$ and cyclo-(δ-amino acid)$_n$ (γ and δ). γ-Amino acids would yield dipole-less tubes and cyclo-(δ-aminopropanoyl)$_3$ would certainly not be rigid enough to retain the necessary tubular shape. However, in the latter case rigidity can be introduced by means of a double bond while lipophilicity would remain unchanged. A structure such as **1** (Figure 1c, $n=3$) is isosteric to cyclohexaglycine (α, $n=3$).[21] Cyclohexaglycine does not crystallize as hollow tubes, rather, two intramolecular H bonds allow the molecule to form two β-turns leaving only two amide groups for stacking along its S_2 axis. On the other hand, **1** can only form one such β-turn, and might still prefer to retain a C_3 symmetrical shape (such as in the hexadepsipeptides enniatins)[18, 22] appropriate for the formation of supramolecular tubes (Figure 2).

The macrocycle **1** was prepared from the thioester **3** with a silver(I) salt in 55% yield.[23] The thioester **3** was

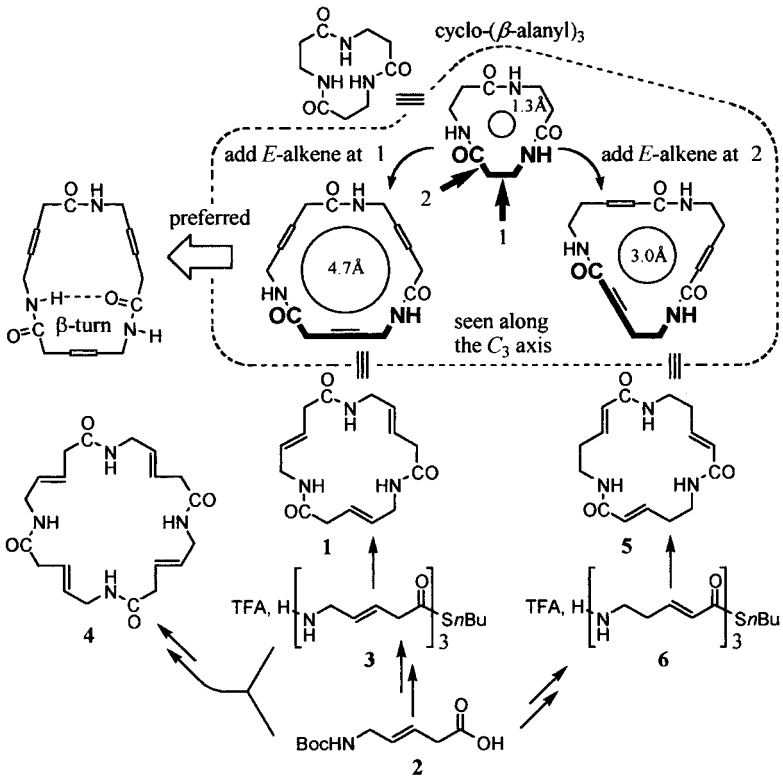

Figure 2. Design and synthesis of lactams **1**, **4**, and **5**. Cyclo-(β-alanyl)$_3$ self-assembles as insoluble "endless" rods (inner diameter of 1.3 Å). *E*-Alkenes inserted at positions 1 and 2 yield more lipophilic lactams **1** and **5** that could stack as tubes with inner diameters of 4.7 Å and 3.0 Å, respectively. However, lactam **1** does not lead to such tubes as it prefers to form a β-turn. The cyclic tetramer **4** was also prepared from **2**; Boc = *tert*-butoxycarbonyl.

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obtained from the Boc-protected amino acid **2** in six straightforward steps (overall yield of 83%).[24] The material was easily crystallized by diffusion (ethanol and diethyl ether) and X-ray crystallography showed that **1** and cyclohexaglycine pack in a very similar way. The rectangular shape of **1** is governed by one β-turn and by that two out of three amides are involved in the stacking (Figure 3a).[25–27] We decided to take advantage of the tendency of **1** to form β-turns to create a higher analogue of S_4 symmetry with four β-turns, reminiscent of the backbone of octavalinomycine (Figure 3b).[28] The tetramer **4** was prepared in three steps from **2** and **3** (overall yield of 32%, 67% for the cyclization; Figure 2) and was also crystallized by the same diffusion technique (isopropanol and diethyl ether). However, the crystal structure showed a disclike dipole-less S_2 structure with no intramolecular H bonds (Figure 3c).[26, 27, 29] Despite the overall resemblance to alternating L,D-cyclooctapeptides, no nanotubes are formed since all the units prefer to assemble in a more compact lattice. In that spatial arrangement all eight H-bonding sites are fulfilled, each unit being H bonded to four neighbors (rather than only two in a tubular structure).

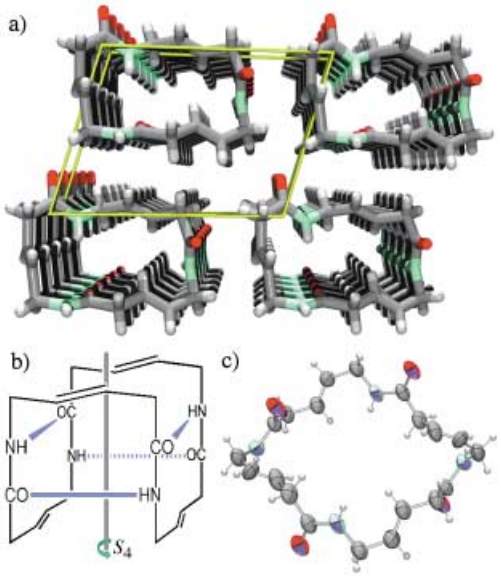

Figure 3. Crystal structures of lactams **1** and **4**. a) The lactam **1** displays one β-turn in the crystal state and self-assembles as flat tubes. b) The cyclic tetramer **4** could also fold by means of β-turns to adopt an S_4-symmetric structure. c) The tetramer **4** is in fact S_2 symmetric, all its amide groups being involved in intermolecular H bonds.

These preliminary results indicated that our systems were still too flexible. To lock the conformation into a more rigid bracelet or crown of C_3 symmetry, it was necessary to prevent β-turns from forming. Our first unit **1** can be seen as cyclo-(β-alanyl)$_3$ in which an *E*-alkene had been inserted at the central bond, position 1 (Figure 2). The resulting 18-membered ring (**1**) is isosteric to cyclohexaglycine and behaves accordingly. However, the *E*-alkene could have been inserted next to the carbonyl of cyclo-(β-alanyl)$_3$ at bond position 2 to afford a new 18-membered lactam **5**. In this new environment, β-turns become impossible and the ring, which now cannot collapse as in structure **1**, has no choice but to adopt a rigid crown structure (Figure 4a). The lactam **5** was then prepared from the thioester **6** in 50% yield.[23] The thioester **6** was obtained from the Boc-protected amino acid **2** in seven steps (overall yield of 34%). The lactam **5** crystallized very easily by diffusion (ethanol and diethyl ether), X-ray data confirmed the expected tubular structure (Figure 4b).[26, 27, 30] However, beyond all expectations, the packing found in the crystal shows all the highly polarized tubes orient in the same direction so that the anisotropy of the units first amplified in the tubes is then further transferred to the whole crystal (Figures 4c and d). The gross dipole of a monocrystal of **5** arising from identical orientation of all amides (Figure 5) should be extremely strong and the resulting material highly anisotropic.

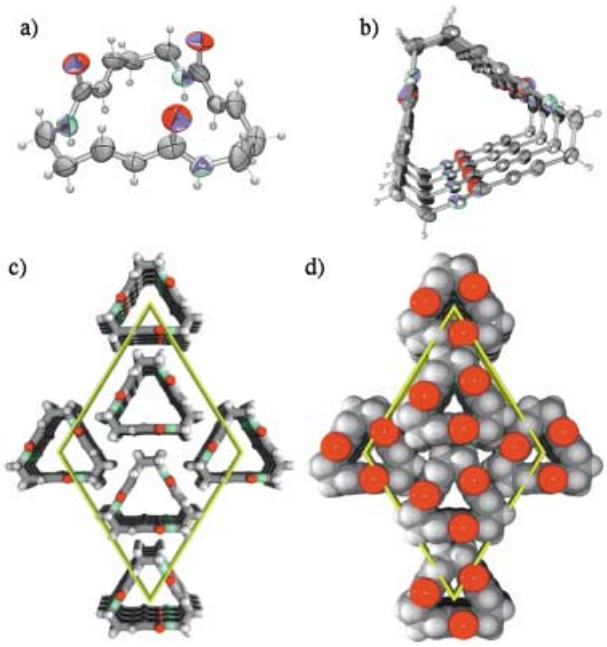

Figure 4. a) The macrocycle **5** adopts a rigid crown structure with all amide groups parallel to the C_3 axis. b) The units stack on top of each other to yield a tube endowed with a very strong dipole. c) The anisotropy is further transferred to the whole crystal since all dipoles remain aligned in the same direction when the tubes aggregate. d) The space-filling diagram shows the very compact packing of the tubes and the parallel channels.

In summary, we have designed special lactam units that were shown to assemble as supramolecular tubes that further

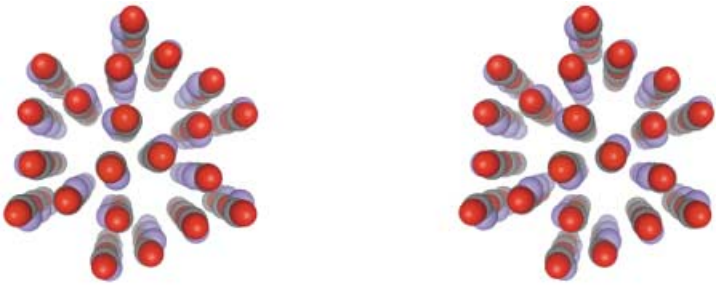

Figure 5. Stereo view of amide groups in the crystal of **5**. The amides in the crystal are perfectly aligned (as in parallel β-sheets). Each resulting "H-bond tape" is separated from its closest intra-tube and inter-tube neighbors by 5.1 Å and 5.0 Å, respectively.

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aggregate as bundles. Since all the strong columnar dipoles are oriented in the same direction, intense anisotropy exists that can in principle expand to macroscopic levels. Growing monocrystals of such materials is now possible. We will soon be in a position to find out if highly polarized nanotubes can be used in devices to rectify current or display unexpected properties.[11] Our approach allows us to control precisely the internal diameter of the tube simply by modifying the positions and number of alkenes inside the monomers. We have prepared the higher C_3 symmetric lactam homologue, which incorporates conjugated dienes rather than simple conjugated alkenes; its crystal structure should yield further information about the capacity of conjugation to provide adequate rigidity to the tube units.

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[26] The data were collected on a Nonius CAD4 diffractometer; $Cu_{K\alpha}$; $\lambda = 1.54184$ Å; $\omega 2\theta$ scan; 293(2) K; the structure was solved by the application of direct methods and refined using SHELX97 (G. M. Sheldrick, *Acta Crystallogr. Sect. A* **1990**, *46*, 467 – 473); the refinements were against $|F^2|$, the data were reduced using XCAD4 (K. Harms, S. Wocadlo, University of Marburg), all programs included in the WinGX package (L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837 – 838); the H atoms were geometrically placed.
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[30] Crystal data for **5** (colorless): dimensions $0.08 \times 0.17 \times 0.45$ mm, trigonal, $R3$, $a = 17.299(5)$, $b = 17.299(5)$, $c = 4.819(5)$ Å, $V = 1248.9$ Å^3, $Z = 3$; $\rho_{calcd} = 1.162$ g cm^{-3}; $2\theta_{max} = 130^\circ$; 988 reflections (878 independent, 518 with $F > 2.0\sigma F$, 878 used in refinement); 65 parameters were refined; the max. and min. electron density map were 0.237 and -0.202 e Å^{-3}; the final residues were $R(F) = 0.0937$, and $R_w(F^2) = 0.2556$, GoF = 0.991.

Single-Step, Highly Active, and Highly Selective Nanoparticle Catalysts for the Hydrogenation of Key Organic Compounds**

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More than three quarters of the organic molecular products that are manufactured industrially entail the processes of either hydrogenation or oxidation; and with the impending arrival of the so-called hydrogen economy and the parallel drive towards clean technology this fraction will inevitably rise in the near future, the most desirable agents of conversion

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