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DESIGN AND CONSTRUCTION OF SUPRAMOLECULAR AND MACROMOLECULAR ARCHITECTURES BY TANDEM INTERACTIONS

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Abstract The self-assembling behaviour of several molecular building blocks are used to construct a variety of chiral and non-chiral supra-molecular and macromolecular architectures. These structures can be finely tuned by slight changes in e.g. the shape of the building blocks, the pH and by the addition of guest molecules.

INTRODUCTION

The design and synthesis of ultralarge molecules and assemblies of molecules with nanometer-sized dimensions and molecular weights (MW) of 10^4 to 10^{12} is currently a rapidly growing area of interest.[1] These 'nanostructures' are expected to have numerous applications in the fields of catalysis, microelectronics and materials science.[2-5] The study of these assemblies and structures (Nanochemistry) and their application, (Nanotechnology) are emerging subdisciplines of Chemistry and Technology.

An important goal in Nanochemistry is the ability to attain control over both the size and properties of the nanomolecules constructed. Fine examples of such control can be found in numerous natural systems,[5] which are built up using a variety of self-assembling processes, based

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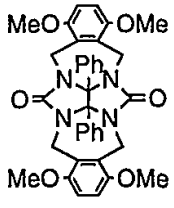
primarily upon relatively weak non-covalent interactions such as hydrogen-bonding, electrostatic and Van der Waals interactions, and metal-ligand interactions. Biological self-assembly in general, uses several interactions in tandem, which leads to a level of specificity and architectural control currently without parallel in chemical synthesis. The greater the number of interactions between the building blocks, the greater the specificity of interaction and in turn the greater the order within the superstructure. This specificity generates well-defined assemblies which posses long-range 3-dimensional order.

Developing strategies for the design and construction of synthetic nanomolecules with well-defined properties and architectures is one of the challenges facing the nanochemist. In the following report, recent efforts in our group to design nanostructures from different building blocks by the process of self-assembly and self-organization will be discussed.

MOLECULAR 'CLIP' BUILDING BLOCKS



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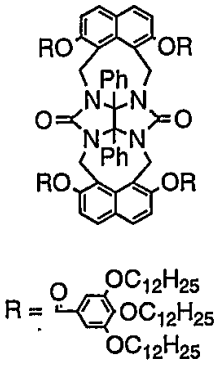

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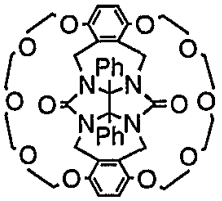

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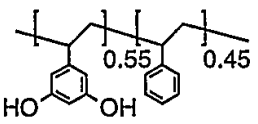

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Cavity containing molecular 'clips' **1-3** have been synthesized and studied in our group.[6] They consist of a concave diphenylglycoluril frame to which a variety of aromatic walls can be attached via methylene

spacers. These molecules are ideal receptors for aromatic dihydroxybenzene derivatives, which complex within their cavities by a combination of π–π interactions with the aromatic walls and hydrogen-bonding to the urea carbonyl functions. Using the ability of these clip molecules to selectively complex in a specific orientation with 3,5-dihydroxybenzene derivatives a variety of supramolecular and macromolecular assemblies have been constructed (Fig. 1).

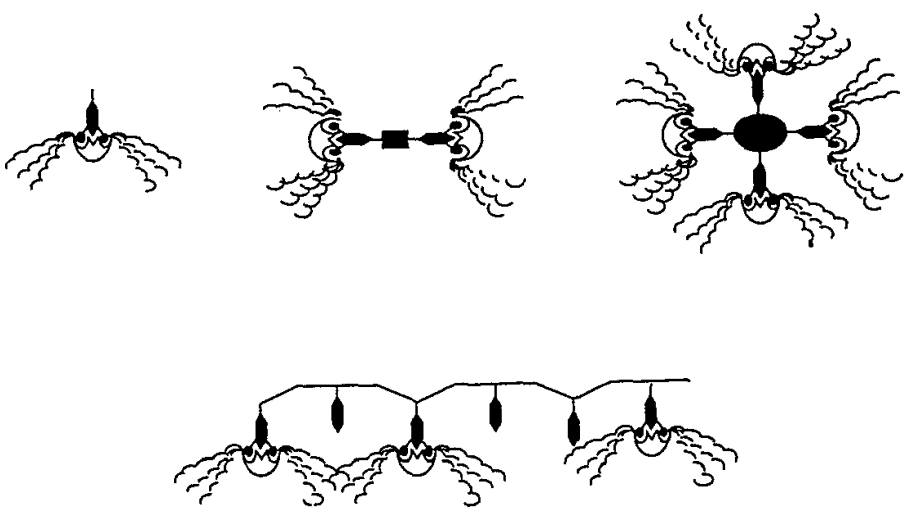


Fig. 1. A schematic representation of the supramolecular and macro-molecular structures formed by the complexation of molecular clip **2** with various 3,5-dihydroxybenzene functionalised molecules.

A naphthalene side-walled clip molecule with long aliphatic tails was found to alter its conformation upon the addition of a dihydroxy-benzene guest. Although non-liquid crystalline, clip **2** in the presence of a low molecular weight guest (resorcinol), formed ordered liquid crystalline smectic phases.[7] This liquid crystalline behaviour could also be induced in larger macromolecular systems. A copolymer of styrene and 3,5-dihydroxystyrene **4** (MW 35000) upon the addition of one clip molecule of **2** to every second 3,5-dihydroxybenzene formed two liquid crystalline discotic phases. One between 86 and 131°C and a second

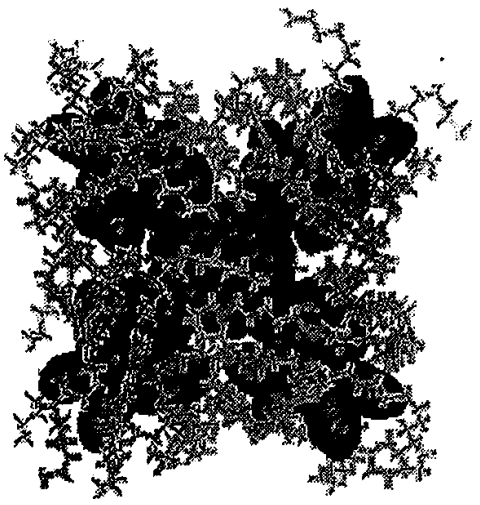
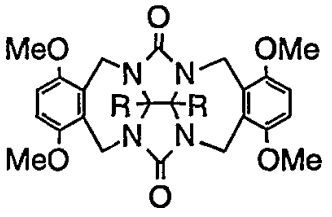


Fig. 2. Computer generated structure of a 4:1 complex of molecular clip **2** with a tetra(3,5-dihydroxyphenyl)porphyrin.

higher ordered phase between 21 and 86 °C.[8] These results clearly indicate that a higher degree of organization can be induced in a polymer by molecular recognition, using a combination of $\pi-\pi$ and hydrogen-bonding interactions.

Upon the addition of four equivalents of clip **2** to a tetra(3,5-dihydroxyphenyl)porphyrin derivative a well-defined nanometer sized superstructure was formed (Fig. 2). This nanomolecule was also observed to form liquid crystalline phases. In addition to being liquid crystalline this supramolecular structure exhibited electrochemical properties indicative of a porphyrin enclosed within a hydrophobic environment mimicking those found for metallo-enzymes like cytochrome P-450. This nanocomplex is a step toward highly ordered enzyme mimics and is of interest for future catalytic applications.

Modification of the convex face of the clip molecules by replacing the phenyl groups for charged pyridinium groups generates water soluble molecules, which are still capable of binding guest molecules but also can self-assemble.



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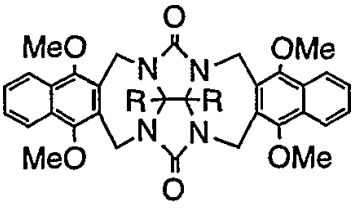

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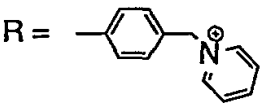


Compound **5** was found to form head-to-head type dimers when dissolved in water at a concentration >2mM. The cleft of one molecule is filled by the side-wall of another and vice-versa. This dimerization process is caused by hydrophobic effects in tandem with favourable $\pi-\pi$

Fig. 3. Electron microscopic pictures of 'razor-blade' aggregates formed by **6** in water; (A) and (B) platinum shadowing technique, (C) freeze fracturing technique.

stacking interactions. At higher concentrations larger aggregates were not observed. In contrast, molecular clip **6** which possesses a larger hydrophobic cavity gave well-defined nanometer-sized 'razor blade-like' structures upon standing (Fig. 3A and B).[9] According to freeze-fracture electron microscopy these 'razor blade-like' structures were built up from a very limited number of layers (ca. 50) (Fig. 3C). Electron diffraction studies proved that these aggregates were not crystals. A detailed (^{1}H NMR, X-ray) study was undertaken which indicated that the aggregates are constructed from a head-to-head dimeric seed to which subsequent growth occurred in a head-to-tail fashion. In this way the outer layer of the array is always hydrophilic (Fig. 4).

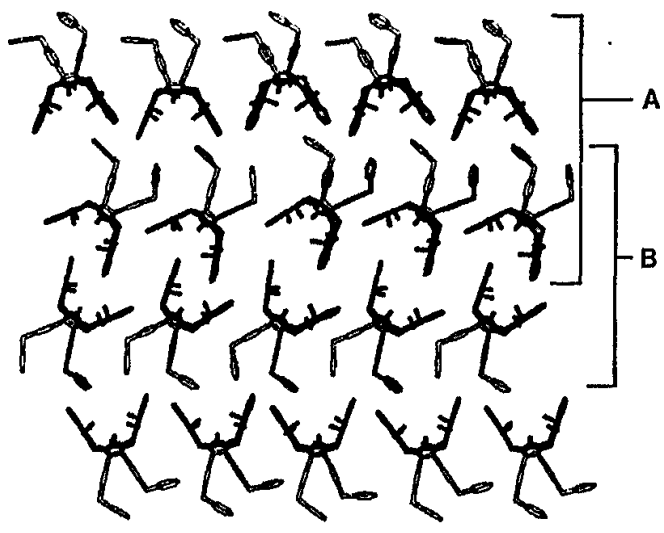
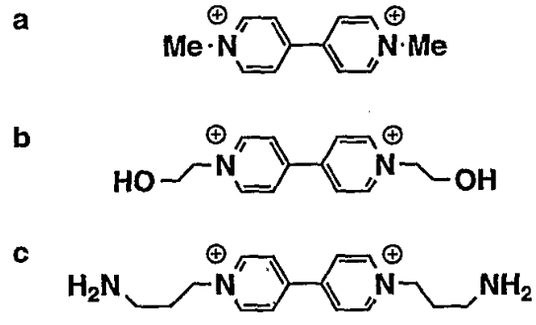


Fig. 4. Computer generated structure of the 'razor blade-like' aggregates of **6**; (A) head-to-tail dimer (17 Å), (B) head-to-head dimer (32 Å).

Relatively few self-assembled synthetic systems are known which have a

finite shape and size.[10] In our system the assembly occurs due to several favourable non-covalent interactions. The finite size is the result of a balance between the natural curvature enforced by the dimerization geometry and hydrophobic forces. Not only can finite nanostructures be generated, they can also be tuned by the addition of guest molecules. In the presence of caffeine or riboflavine guests, the 'razor blades' are transformed into sphere-like structures.

In addition to binding dihydroxybenzene guests, modified clip molecules, molecular baskets **3**, were found to be exceptionally good receptors for viologens (**7**) and polymeric viologens.[11] The latter macromolecules are interesting polymers in that they form redox active films which may be used as optical data storage materials. Complexation of molecular basket **3** to viologen polymers, modified both the viscosity and electrochemical properties of the macromolecules. Unfortunately, upon electrochemical formation of the dark blue, 1 electron reduced viologen species, decomplexation was found to occur. In order to overcome this decomplexation a porphyrin-capped molecular clip (**8**) has been recently



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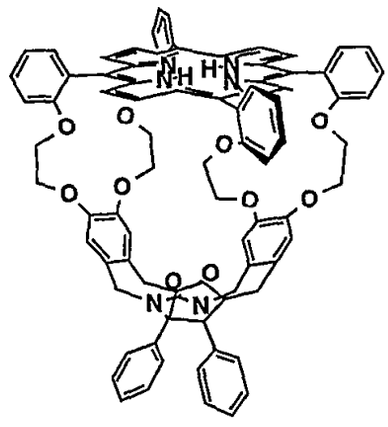

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developed. This new clip was found to have very high binding affinities for viologens. In acetonitrile methyl viologen (**7a**) was found to complex

ten times stronger to porphyrin clip **8** than to basket **3** (association constant K_a=500 000 and 57 000 M^{-1}, respectively). Ethanol viologen derivative **7b** upon binding formed a pseudo-rotaxane complex with an association constant of 7.5 x 10^6 M^{-1}. This is one of strongest organic supramolecular complexes known. The strength of this complex is a result of several favourable interactions, working in tandem, between the viologen guest and the host. A propyl-amine viologen derivative **7c** also formed a pseudo-rotaxane complex with **8** in which the propylamine arms point out of the cavity. Condensation of the complex of **7c** and **8**, with 3,3,3-triphenylpropionyl chloride gave rigid porphyrin-viologen rotaxanes. Condensation with a difunctional acid chloride (sebacoyl chloride) led to the formation of an ordered porphyrin-viologen polyrotaxane macromolecule (Fig. 5).

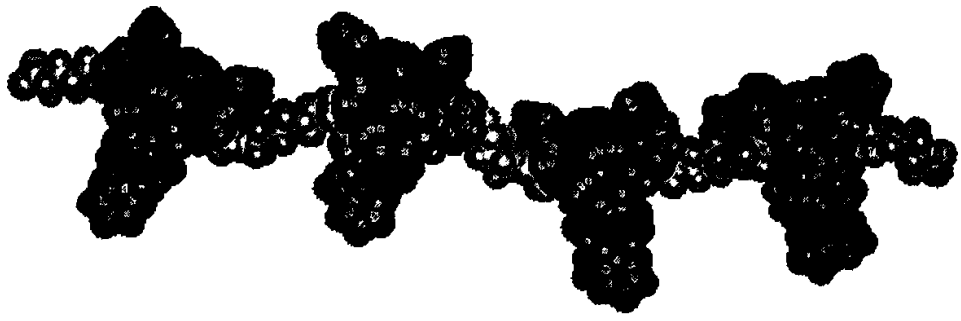


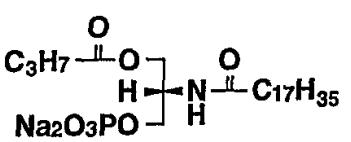
Fig. 5. Computer generated model of the polymeric rotaxane formed from **7c**, **8** and sebacoyl chloride.

The use of supramolecular complexation to generate order in tandem with macromolecular polymerization is an interesting development toward the future construction of nanometer-sized molecular assemblies.

CHIRAL BUILDING BLOCKS

The construction of chiral supramolecular structures by the self-assembly of chiral surfactants has received considerable attention in the last decade. Synthetic surfactants derived from sugars,[12] amino acids,[13] nucleic acids[14] and phospholipids[15] have all been shown to form a variety of chiral superstructures such as helical fibers and twisted ribbons. In general, most of these compounds contain hydrogen bonding moieties which provide the intermolecular interactions needed to form these aggregates. In addition the shape of the molecules and the solvation of their head groups play an important role in the aggregate formation. Although many studies on surfactant aggregation have been carried out, relatively little is known about how the shape and chirality of the superstructure is related to the chirality and shape of the basic building block. In order to try and understand this relationship the aggregation behaviour of phospholipids has been investigated.

PHOSPHOLIPIDS



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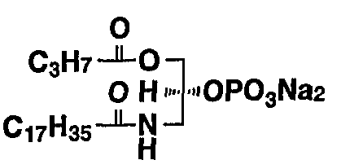

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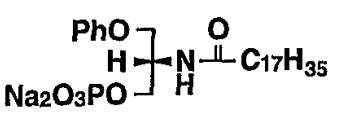

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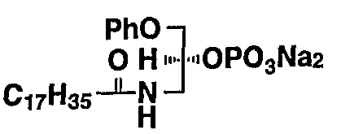

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The two related pairs of phospholipid analogues (**9** and **10**) were studied in order to assess the expression of the chirality of the building

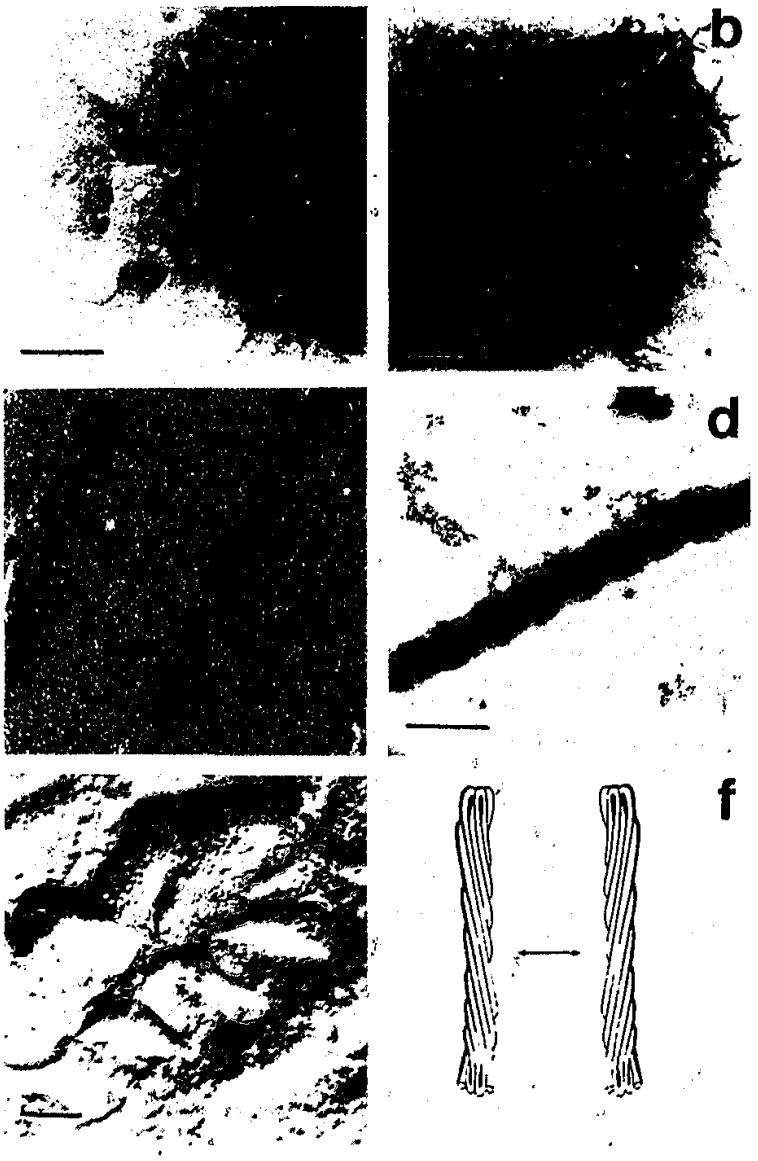

Fig. 6. Electron micrographs of dispersions of **9** and **10**; Planar bilayers structures formed by **9** (a), platinum shadowing technique; left-handed helices formed by **10** (b) and (c), platinum shadowing technique; right-handed super helix formed by **10** (d) unstained, (e) freeze fracture technique; super coils formed by DNA molecules (f)(see ref. 16).

block in the supramolecular structure. Compounds **9** and **10**, although they have a strong structural resemblance and only differ in the position

of the phosphate and amide functions, gave dramatically different expressions of molecular chirality at the supramolecular level. Transmission electron micrographs of a 2% ww solution of **9** in water revealed planar structures (Fig. 6a) whereas for a similar solution of **10** left handed helical strands (diameter 22 nm, pitch 92 nm) were observed (Fig. 6b and c). These strands in turn aggregated to form left-handed rope-like structures. In addition to the strands and ropes, large right-handed super helices were also observed (diameter 350 nm, pitch 250 nm)(Fig. 6d and e). It is thought that these right-handed super helices are formed by the inter-twining of left-handed helices in an analogous manner to the formation of supercoiled DNA (Fig. 6f).[16] The latter self-assembly behaviour is thought to be controlled by small changes in salt concentrations. Monolayer studies of phospholipids **9** and **10** at various pH's were carried out to study this phenomenon.

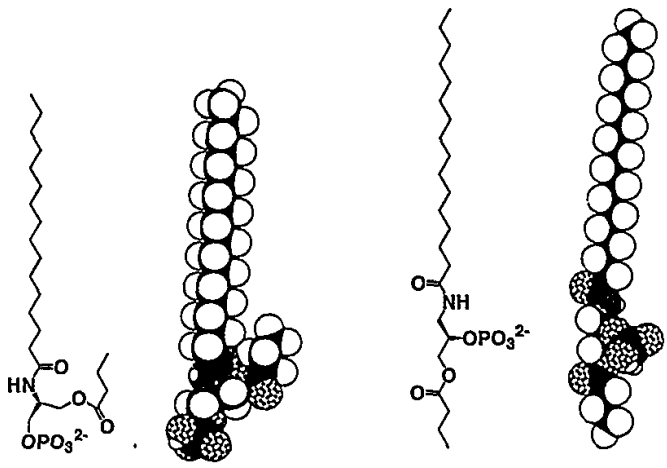

Fig. 7. Molecular conformations of compounds **9** (left) and **10** (right).

For molecule **9** a very large lift-off area (ca. 320 $Å^2$/molecule) was determined, whereas the isomer **10** could be compressed to a much

smaller area (ca 80 $Å^2$/molecule). From additional data it was concluded that the structures of the two molecules are considerably different, the former being bent and the latter being linear (Fig. 7). Examination of the monolayers by Brewster angle microscopy at different pH's revealed no distinct morphologies for **9**. In contrast upon compression of **10**, chiral branches domains, with a counter-clockwise pattern were observed at pH 6.5. At lower pH 2.5, the chiral domains of **10** displayed a clock-wise pattern in agreement with the observed inversion of chirality upon formation of the superhelices by electron microscopy.

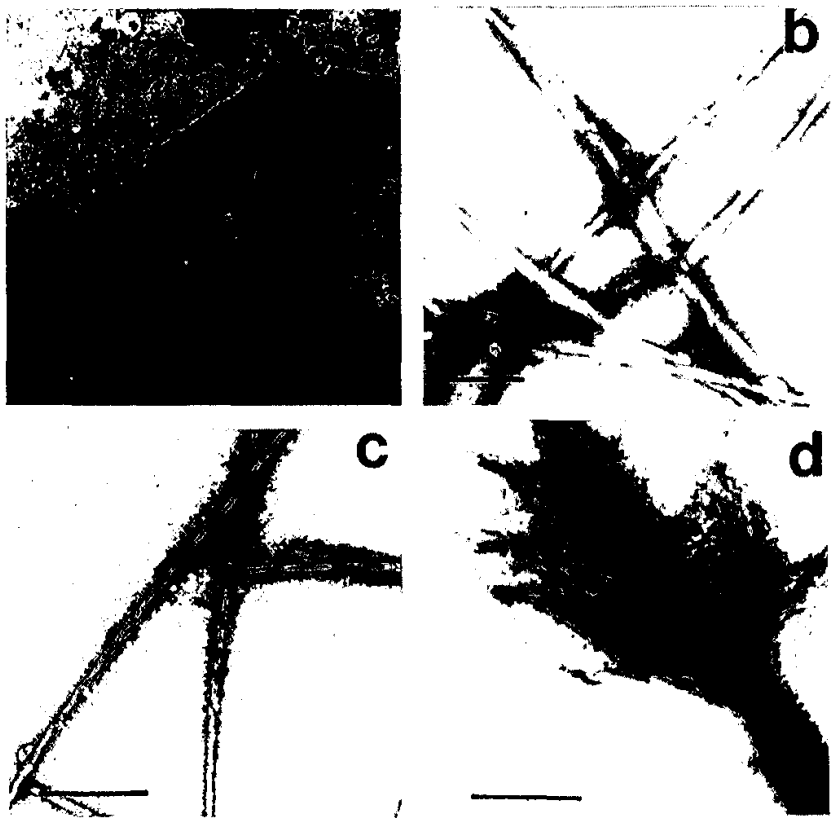

Fig. 8. Electron micrographs of the structures formed by **11**; after 5 minutes (a), after 1 hour (b), after 1 day (c), and by **12** (d), platinum shadowing technique.

The other isomeric pair **11** and **12** also showed markedly different aggregation behaviour. At pH 6.5 compound **11** when dispersed in

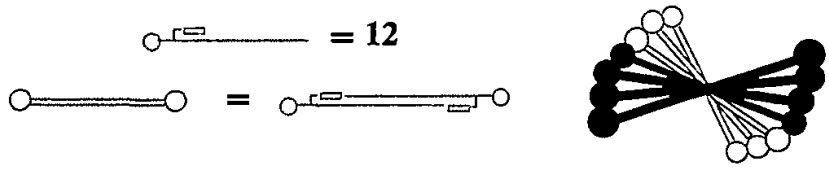

Fig. 9. Schematic representation of the arrangement of molecules of **12** in a micellar fiber.

solution, formed large vesicles with diameters of 500-1000 nm. Over time these vesicles rearranged to yield ribbons (Fig. 8a). At lower pH (pH=2.5) the ribbon-like structures rearranged to form left-handed helices (Fig. 8b), which twisted further to give tubular structures (Fig. 8c). Molecule **12**, however, formed micellar type fibers (Fig. 8d). These fibers were shown by X-ray studies to be constructed from two intercalating molecules of **12**, which yields a staircase-like arrangement of building blocks (Fig. 9).

CONCLUSIONS

It has been shown that a wide variety of building blocks can be used to form ordered nanometer-sized superstructures. By using several molecular interactions in tandem it is possible to create arrays with a high fidelity and 3-dimensional order. It has also been shown that the architectures of these nanomolecules can be significantly altered by slightly varying the geometry of the building blocks, by adding guest molecules and by changing the pH.

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