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Micellar fibres with crystalline surfaces and their co-crystallization

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Amphiphiles with an amide bond between the head group and the hydrophobic chain show strong binding interactions between the members of micellar fibres. The surface of such fibres has high curvature and becomes crystalline. This is shown, for example, by very regular helicities, sharp melting points at which dissolution of the fibres occur, the amide I infrared band at 1650 cm^{-1}, and solid state NMR spectra. Furthermore, diastereomeric glyconamides (glucon, gulon, talon) form crystals with very different sheet arrangements (head to tail or tail to tail) and hydrogen bond patterns (homodromic or other cycles). The same diastereomers also form molecular assemblies of extremely different curvatures (bimolecular rods, ribbons, scrolls, tubules and sheets). There are strong correlations between interactions in crystals and molecular assemblies. The micellar structures with crystalline surfaces should not be stable. They should quickly rearrange to three-dimensional crystals with much smaller surface energies. Effects which impede in such a rearrangement are discussed (e.g. chiral bilayer effect, dissolution of crystallization nuclei). Guest molecules can only be included into the micellar fibres by co-crystallization processes. The fibres thus obtain the character of covalent polyamides or proteins with selective uptake of functional molecules such as porphyrins. The crystalline micellar fibres are thus sharply differentiated from the usual micellar aggregates. Hydration and steric forces lead to head group repulsion and the viscous liquid character of the much less organized molecular assemblies.

INTRODUCTION

Water-insoluble surfactants may form long-lived suspensions of molecular bilayers in water. At low concentrations ($\leqslant 10^{-3}$ M) these bilayers may occur as spherical micelles,[1] rod-like micelles,[2,3] twisted ribbons,[4–6] tubules,[7,8] rolled-up sheets,[4] or practically planar sheets (myelin figures).[9] Highly curved surfaces of micellar structures as well as planar surfaces of lamellar structures are not thought to be crystalline in any model which has been proposed so far. The interactions between the head groups have been related to repulsive hydration and steric forces[10] and head groups should have a complete rotational freedom. Only the binding interactions in the hydrophobic, highly viscous, hydrocarbon core[1,11] should stabilize the amphiphilic molecular bilayers. The dynamic interplay between repulsive and attractive forces is then responsible for the longevity of micellar, vesicular and lamellar aggregates in water. It prevents both complete monomolecular dissolution and crystallization. Furthermore, if the size, shape and aggregation number of the molecular bilayers is known, peculiar 'packing shapes' for the molecules can be deduced, e.g. a cone for a fatty acid salt in a micelle.[12] This packing shape has nothing to do with the actual molecular geometry of the molecules, such as is found in crystals. Recently, however, it has been shown that glyconamides with hydrocarbon chains as short as heptyl aggregate in water to form fibres of 4–12 nm thickness and several micrometres in length at concentrations below 10^{-3} M.[3,13,14] These fibres show, in some cases, a very regular helicity and curvature, which depends on the chirality of the head group. Quite often the fibres disintegrate to spherical micelles at a very sharp melting point. This combination of properties is not consistent with repulsive interactions between the head groups. Binding forces, in particular amide and hydroxy hydrogen bonds, clearly dominate these molecular assemblies (Fig 1).

In this paper are described and compared structures of crystals and crystalline glyconamide assemblies, with some explanation of their unprecedented longevity, and discussion of possible co-crystallizations to produce functionalized bilayer assemblies in bulk water.

MOLECULAR AND CRYSTAL STRUCTURES

Seven *N*-alkylaldonamides **1**–**8**, an *N*-alkyl tartaric acid monoamide **9**, and two protoporphyrin diamides with 2-aminoglucose and gluconhydrazide head groups **10** and **11**, are compared. We selected these amphiphiles because detailed structural information on the crystals and/or their fibrous aggregates is available. For

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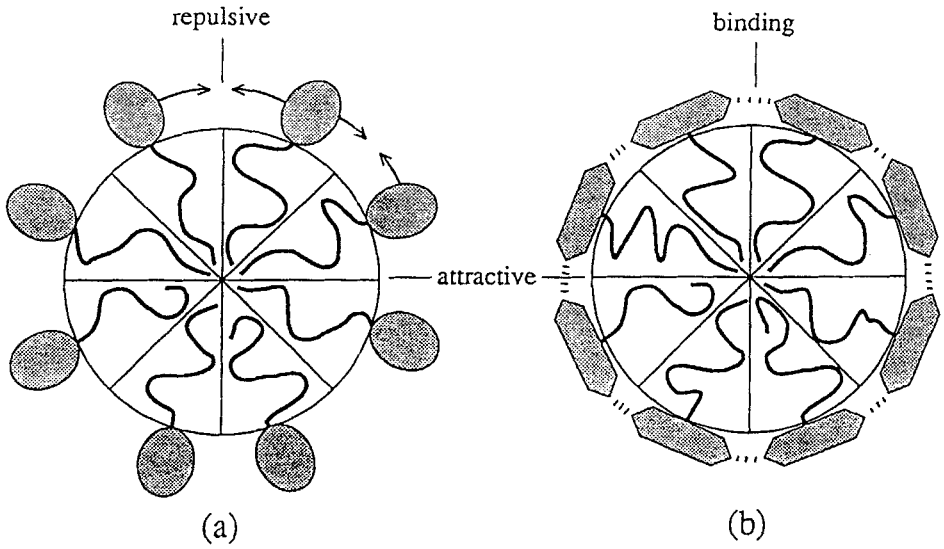
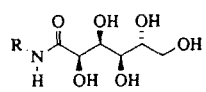
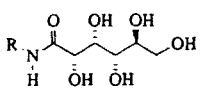


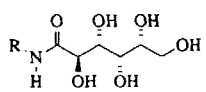
Figure 1 Micellar molecular assemblies. These usually have a fluid surface (*a*). The head groups are hydrated and reject each other. The amide amphiphiles discussed in this paper are, on the contrary, connected by binding forces (*b*). The micellar rods have a crystalline surface. The hydrophobic interior is, in both cases, a viscous fluid.



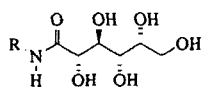
1a R= heptyl
1b R= octyl
1c R= dodecyl



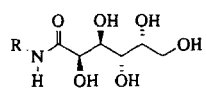
2a R= octyl
2b R= dodecyl



3 R= octyl



4 R= octyl



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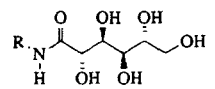
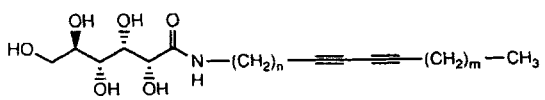
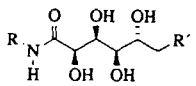


6 R= octyl



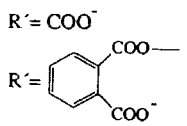
7a : n = 1 m = 4
7b : n = 2 m = 4
7c : n = 3 m = 4
7d : n = 4 m = 4
7e : n = 5 m = 4
7f : n = 9 m = 2

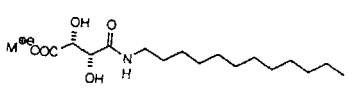


8a R= octyl
8b R= octyl

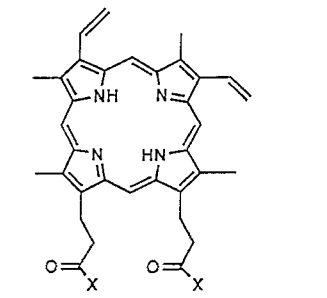
R′= COO^-

R′=

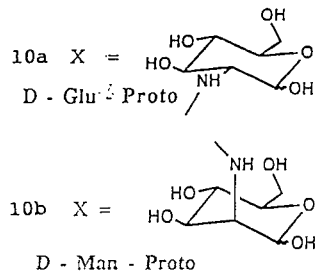




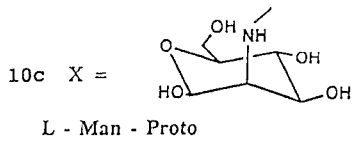
9a M = K
9b M = Na



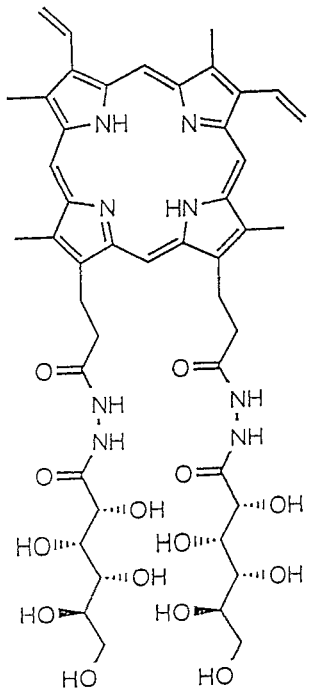
10a X = D - Glu - Proto



10b X = D - Man - Proto



10c X = L - Man - Proto



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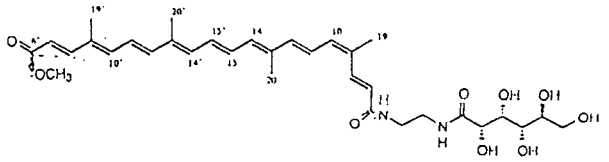

12

co-crystallization experiments we also used the carotenoid bixin amide **12**. Some other amphiphiles with chiral head groups, which aggregate to form micellar fibres are mentioned in the last paragraph.

The head groups in glyconamides **1**–**4** contain one *syn-axial* pair of 1,3-positioned hydroxy groups and one *gauche*-oriented pair. Steric interactions between the hydroxy groups should therefore be very similar and should be dominated by repulsions between the *syn-axial* hydroxy groups. The following are expected: (i) similar deviations to the linearity of the all-*trans* configured chain of the open-chain carbohydrates and (ii) similar arrangements of bilayer sheets. Both generalizations fail as is discussed later.

The crystallization of membrane-forming single-chain amphiphiles is in general difficult and unrewarding. The elongated molecules do not pack well along their long axis and only very thin crystals are obtained (Fig 2). In the case of the tartaric acid amide **9b**, the largest crystal that could be obtained had the dimensions 280 × 80 × 16 μm. Its crystal structure could only be determined with synchrotron radiation.[13b] The gulonamide **3** gave a 1200 × 300 × 70 μm crystal in which the octyl chain displayed an extraordinary mobility.[15a] The weighted *R* value which could be obtained in this case was 14.8%. Only the gluconamide derivatives **1** and **7** crystallized well. All other structure determinations needed a lot of patience, both for the crystallization and for the analysis of poor data.

The most stable crystals, namely those formed of *N*-alkylgluconamides **1**, also produce the most surprising arrangements.[14] First the carbohydrate head group is not bent, and the 2,4-hydroxy groups lie in practically ecliptical positions. The heptyl chain in **1a** adopts a torsion angle at the amide bond which is different from the even-numbered chains. Secondly the four terminal hydroxy groups on four neighbouring molecules are connected in a stable homodromic hydrogen bond cycle. As a result of this cyclic hydrogen bond pattern the methylene group forms a hydrophobic surface on the crystal sheets. Third and most importantly, the crystal sheet arrangement is not the

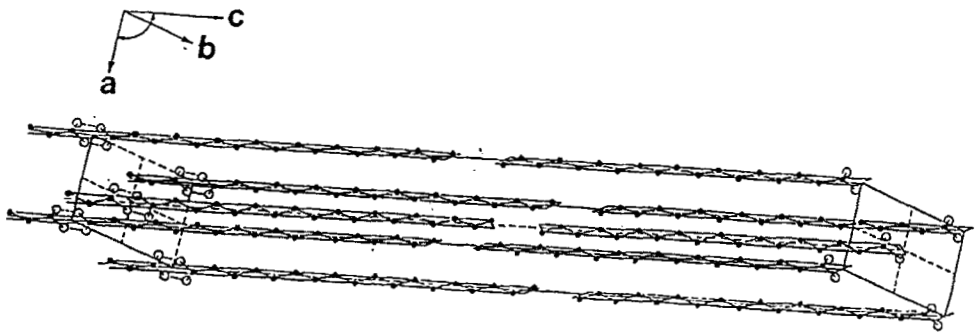

Figure 2 Typical amphiphiles. These form micelles and bilayer membranes which have one long axis (*c*) along which regular packing to form crystalline bilayers is difficult. Strong interlayer bondings (α,ω-diammonium salts; hydrogen bonds) must be present to stabilize crystal sheets.

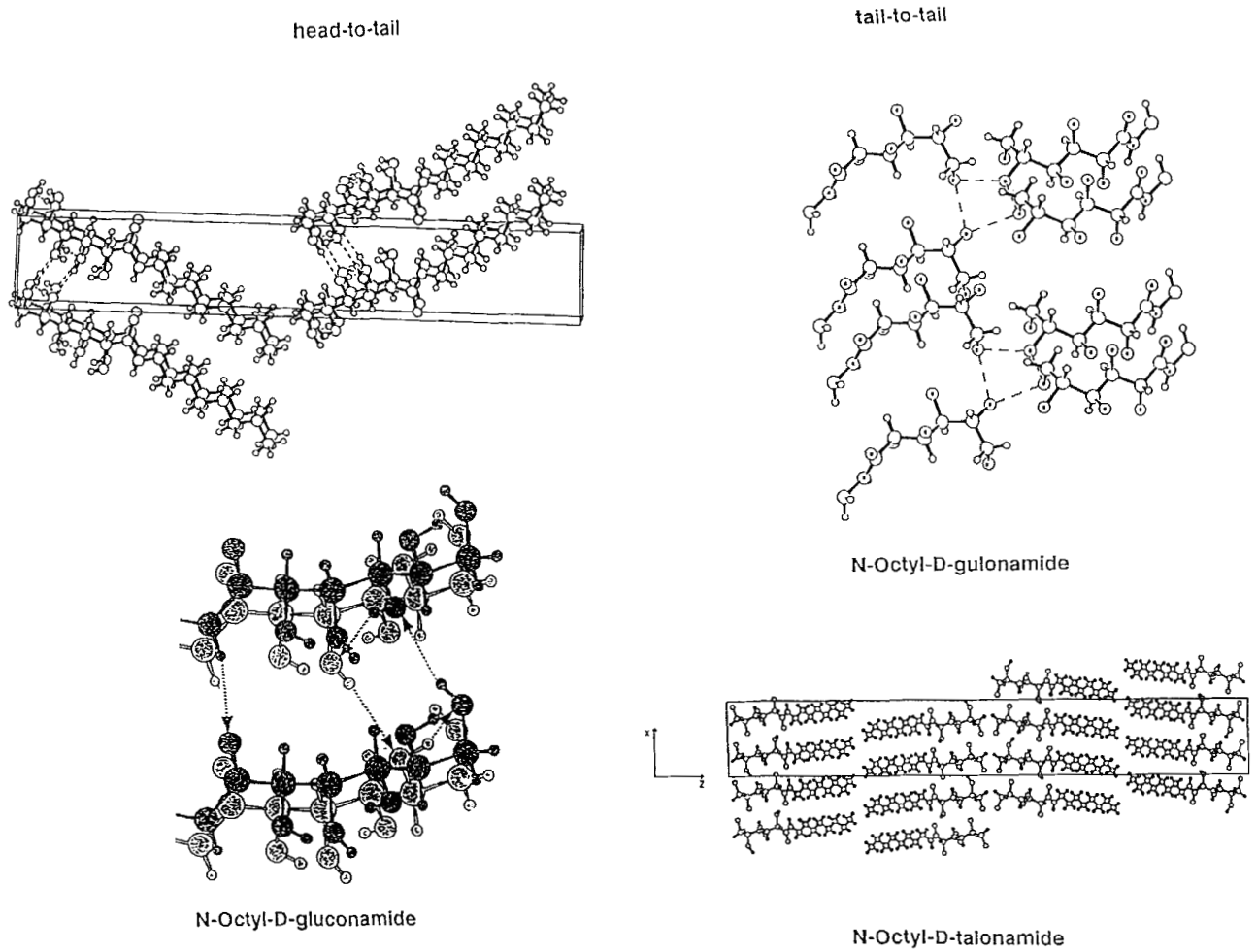

Figure 3 Crystal structures of (*a*) *N*-octyl-D-gluconamide **1b**,[14] (*b*) *N*-octyl-D-gulonamide[15a] **3**, and (*c*) *N*-octyl-talonamide[15b] **4**. Note the head-to-tail arrangement in (*a*) and the homodromic hydrogen bond cycles in (*a*) and (*b*).

expected tail to tail arrangement which is usually found for amphiphiles; hydrophobic alkyl chains pack onto the carbohydrate end groups (Fig 3*a*). In gulonamide **3**, the acyclic chain carbohydrate chain is bent to a *gauche* conformation at the outer hydroxymethine and hydroxymethylene groups.[15a] The homodromic cycle occurs this time between adjacent sheets. As a result the terminal hydroxy groups and not the methylene groups form the hydrophilic surface of the crystal sheets and they are connected by interlayer hydrogen bond cycles. The sheet orientations are therefore head to head and tail to tail (Fig 3*b*). Furthermore a second

bend occurs at the amide bond and leads to a relatively large S-shaped structure. This then leaves a large lateral space for the oligomethylene chain which therefore appears in different orientations (Fig 3*b*). The instability and softness of the gulonamide crystals thus becomes understandable. In talonamide **4** the sheet arrangement is again tail to tail and there is a *gauche* bend in the talon head group between carbon atoms 2 and 3 resulting in an unexpected CO interaction between C-1 and O-4 (Fig 3*c*).[15b]

Three very similar diastereomers thus appear in three very different molecular conformations and the orientation of the crystal sheet jumps unpredictably from tail to tail to head to tail. Clear cut rationalizations of these findings can hopefully be obtained from molecular modelling procedures but these have not been performed so far. Intuitively we presume that the formation and position of the homodromic hydrogen bond cycle plays the decisive rôle. If this cycle occurs within one layer, it favours the crystallization process.

N-Alkyl-galactonamides and -mannonamides[5] could not be crystallized. A safe guess would predict non-disturbed linear head groups and tail to tail arrangements of the sheets. Since no disturbing 1,3-hydroxy group interaction is possible, the terminal group should be a hydroxy group which is hydrogen bonded to the neighbouring sheet. The sheet-like structure of their aggregates[5,16] (see below) also makes the rearrangement of sheets upon crystallization unlikely.

A diacetylenic unit in the hydrocarbon chains of *N*-alkyl-gluconamides not only allows polymerization but also introduces a stiff region next to freely rotating methylene groups and opens up space within the chain assembly. The crystal structure of the tetradecanediynyl derivative **7e** shows a very similar chain conformation and head to tail arrangement as the saturated analogue **1**, and a void of 4.8 × 5.2 × 6.8 Å^3. The homodromic cycle of hydrogen bonds is also found (Fig 4).[8] The odd-numbered homologue with a tridecanediynyl chain next to the amide bond also shows the same bending of the hydrocarbon chains as the corresponding heptyl derivative **1a**, and in both cases the CH_2 group forms a hydrophic surface on the crystal sheets (C. André, P Luger, P. Blumtritt and J.-H. Fuhrhop, unpublished results).

Negatively charged gluconamides **8** with 6-carboxylate or 6-phthalic acid groups could not be crystallized, but crystal structures of amphiphiles with tartaric acid sodium and ammonium salts have been determined by X-ray crystallographic analyses. A racemic 3-monoacetate crystallized out as a racemic tail to tail compound. The methyl group of the acetyl side chain provides the connection between the hydrophilic head group of one molecule and the *interdigitated* hydrophobic chain of its mirror image. The ammonium counterion is only bound to two carboxylate oxygens by four hydrogen bonds and thus connects two opposing head groups of mirror image symmetry. Two *gauche* conformations occur in the head group. The pure enantiomer **9** with a sodium counterion crystallizes in a head to head fashion, and each sodium ion is surrounded by four hydroxy and four carboxylate oxygen atoms (P. Luger, C. Lehmann, C. Demoulin and J.-H. Fuhrhop, unpublished results). Again two *gauche* conformations occur in the head groups, whereas the tails are all-*anti* (Fig 5).

The crystal structures depicted in Figures 2–5 reveal many different conformations and/or sheet arrangements, although the compounds are quite similar. We select some particular aspects and summarize them as follows. (i) *N*-alkyl-D-gluconamides crystallize head to tail irrespective of the number of methylene groups (n = 6, 7, 9, 10) or the presence of diacetylenic groups in the side chain. There is, however, some circumstantial evidence that with more than 14 methylene groups, the *N*-alkyl-gluconamides crystallize tail to tail. Furthermore, it has been clearly shown that racemic *N*-alkyl-D,L-gluconamides crystallize tail to tail. (ii) All other *N*-alkyl-glyconamide and

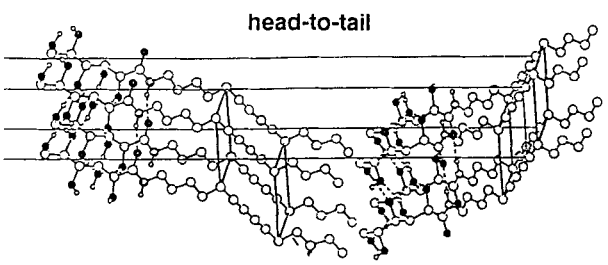

Figure 4 Crystal structure of the diacetylenic D-gluconamide **7d**.[8] Note the head-to-tail arrangements of sheets, the homodromic hydrogen bond cycle and the overall linearity of the carbohydrate and hydrocarbon chains.

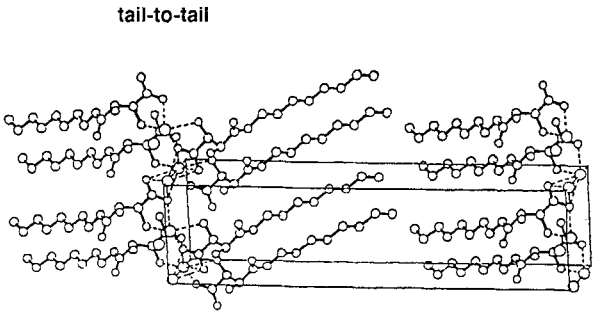

Figure 5 Monosodium monoamido tartrate **9**. This was the only sodium salt of a long-chain amphiphile that could be crystallized. Strong intralayer hydrogen bondings are probably responsible for the crystallization.

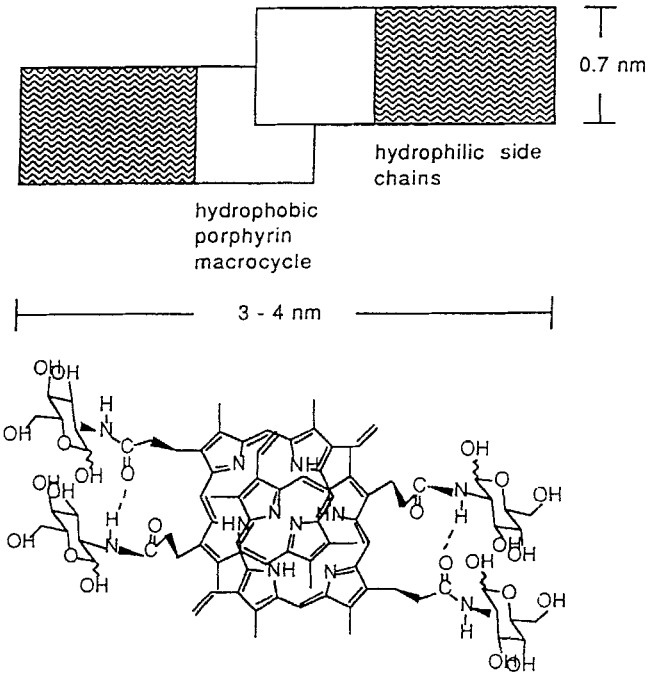

Figure 6 Likely dimer unit in hypothetical crystals of amphiphilic porphyrin **10a**.

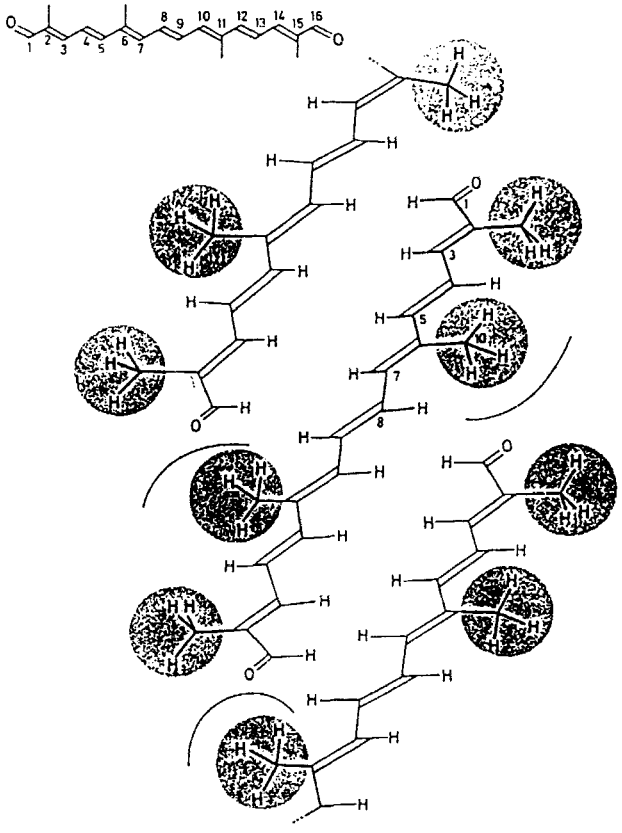

Figure 7 Crystal structure of crocetindialdehyde as a model for amphiphilic carotenoids. The methyl groups impede the neighborhood of end groups in crystals and domain formation in micellar rods.

N-alkyl-tartaric acid amides crystallize tail to tail. (iii) *Interdigitation* does not usually occur, although the head groups are broad and even charges may occur. This is surprising because anionic[17] or cationic[18] amphiphiles usually *interdigitate* in crystals. The only exception (Fig 5) is presumably caused by favourable hydrophobic interactions between a head group side chain and the oligomethylene chain. (iv) In gluconamides, odd side chains tend to introduce bends.

The crystal structures of the porphyrin glyconamides **11** and **12** are again not known. We assume, however, that these porphyrin amphiphiles always arrange in *interdigitated* bilayers where one porphyrin macrocycle places a pyrrole ring directly above the π-cavity at the centre of the other and where the hydrophilic side chains form the outer edges (Fig 6).

The crystal structure of carotenes, the other frequent dye type in biological membranes, is best exemplified by crocetine dialdehyde.[19] The typical arrangement of methyl groups, all to the left in one half of the molecule and all to the right in the other half, usually allows parallel alignments only for one half of the polyene chains (Fig 7). It may be predicted that amphiphilic carotenes do not pack very well if they are fixed with their polar ends in membrane structures. The bixin derivative **12** constitutes such an amphiphile and has not been crystallized so far.

ELECTRON MICROGRAPHS OF SOLID MICELLAR FIBRES

The best-defined molecular assembly in the series of glyconamide, tartaric acid amide and porphyrin amide amphiphiles is the quadruple helix made of *N*-octyl-D-gluconamide **1b** and its dodecyl homologue **1c**. In order to prepare this helix approximately 0.5–1 mg of **1** is dissolved in 1 ml of boiling water containing 2% phosphotungstate at pH 5–7. A clear micellar solution is thus obtained. The cmc of D-gluconamide **1b** is 28×10^{-3} M at 80°C; the cmc of the racemate **1b** + **2** is identical.[20] Upon cooling a slightly opaque gel is formed with a sharp solidification point at 339 K. Below this temperature, down to room temperature, the gel has a life-time of approximately 1 day, before 3D crystals precipitate. Below 10°C the gel degrades within a few minutes. Above 60°C and particularly in the presence of 2% SDS surfactant, the gel remains stable for at least 6 months. For stabilization of the gel and the quadruple helices it contains, the formation of crystallites must be prevented as this leads to rearrangement of tail to tail bilayers in fibres to head to tail monolayers in crystal sheets (Fig 3*a*).

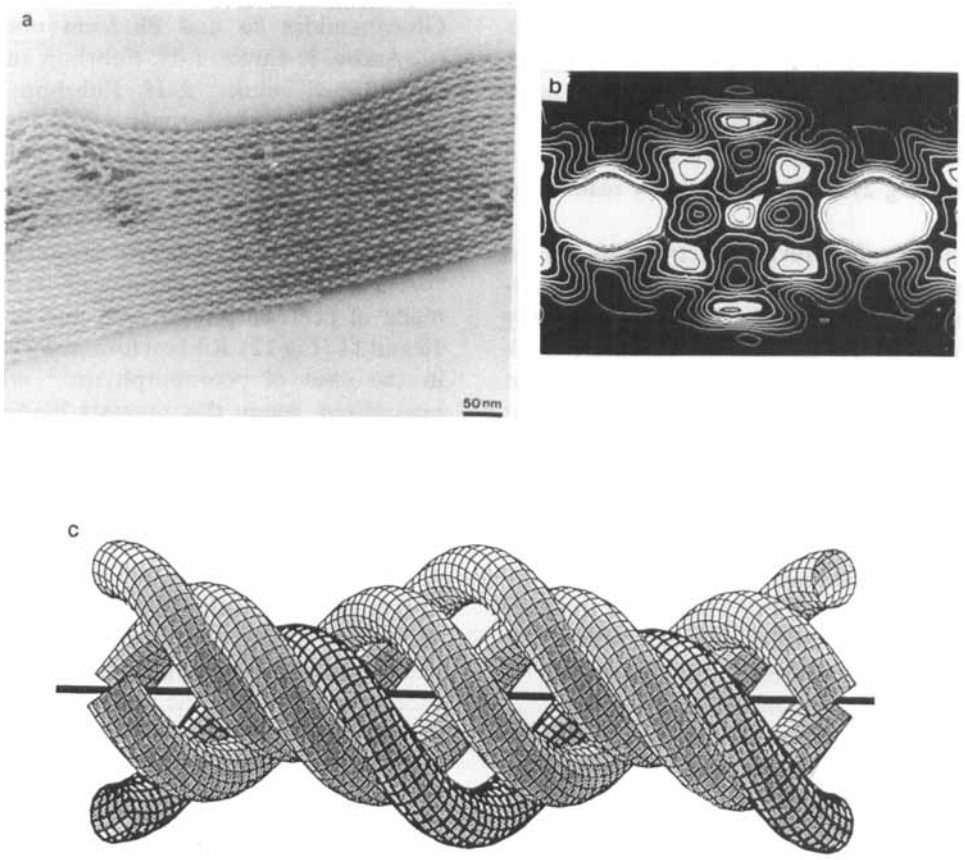

Figure 8 (*a*) Electron micrograph, (*b*) experimental contour line diagram and (*c*) geometrical model of a micellar fibre obtained by self-organization of gluconamide **1b**.[13a] Note the regularity of the supramolecular structure and the bimolecular thinness of the individual fibres. These findings are taken as strong evidence for specific binding interactions between the head groups in this long-lived aggregate of micellar dimensions.

The structure of the micellar fibres which are stabilized by a phosphotungstate coat has been determined by computer-aided image analysis and geometric modelling. The contour line diagrams obtained experimentally and from the final model were practically identical. The results (Fig 8) show that four micellar strands are assembled.[13a] This is presumably caused at first by rearrangement of the spherical vesicles to disc micelles at 339 K by the co-operative formation of amide hydrogen bond chains. The disc micelles immediately stack to form rods of bimolecular thickness 3.6 nm because their surfaces are hydrophobic. Furthermore, these rods assemble to form tetramers because the terminal CH_2 groups (see Fig 3*a*) also provide hydrophobic surfaces. Thirdly the chirality of the head groups, namely the 2,4-hydroxy group repulsion, which was overcome in the crystals but not in the curved micellar discs, induces helicity in the rods. The helices, however, do not stick together. Laterally they slide apart by the thickness of a lipid bilayer in the direction of the axis they separate by $\pi/2$. This may be caused by dipole–dipole repulsion of single head groups of neighbouring gluconamide molecules in different strands or of the whole helices. The latter effect would also explain the magic angle (54.7°) gradient of the helices with respect to the quadruple helix axis.

The regularity of this structure, composed of four 3.6 nm thick bilayers, is the strongest argument we can provide for the solid state character of its surface. There must be geometrically well-defined binding forces between the gluconamide head groups, which are responsible for the observed thinness (3.6 nm) of the fibres as well as the repetitive knots and bulges. It must be realized that each single molecule in this aggregate lies on the surface and is directly in contact with water. If it were bound only by the hydrophobic effect to eight methylene groups, it would not form such a stable bilayer. Furthermore the addition of other surfactants such as SDS should immediately destroy a regular arrangement in which head group repulsion plays an important rôle. It is, however, found that the helical fibres survive for extremely long periods of time in the presence of such surfactants.[20]

The quadruple helix can also be obtained without the addition of phosphotungstate, but must then be trapped quickly in vitreous ice. Otherwise it rearranges to a tubular helix made of a 4-fold molecular layer (Fig 9).[13a] It was assumed that the head to tail arrangement of the 3D crystals (see Fig 2) is already partially realized in these structures.

As was shown in the previous section, the crystal structures of gluconamides with and without diacetylenic groups in the hydrophobic chains are practically identical. The fibrous assemblies, however, look different. No helicity or quadruple packing is apparent in the fibres made of **7b**. It produces 4.0 nm straight rods. Other diacetylenic compounds on the other hand give well-defined multi-walled tubules with inner diameters of 8–15 nm. The solvent-filled centre of the tubules can thus be much smaller than in spherical vesicles. It has been shown that these tubules are probably made of twisted ribbons that fill in material upon growth. This mechanism was first verified by Kunitake[4] in light microscopic tubules made of double-chain glutamic acid amides.

Compounds **7a** and **7b** can also be polymerized by ultraviolet light. The polymers, however, showed no trace of tubule formation or retention. Only endless micellar fibres of similar appearance on electron micrographs as shown in Figure 10(*a*) were found.[8]

It is again evident, that neither in the micellar rods nor in the tubules made of the diacetylenic amphiphiles, are repulsive interactions between the head groups dominant. Otherwise neither the micellar rods of 4.5 nm thickness nor the central bilayers of highly curved tubules could survive in water. This becomes even more evident if a negative charge is introduced. Gluconamides **8a** and **8b** form non-helical fibres (C. André, P. Luger, J.-H. Fuhrhop and P. Blumtritt, unpublished results; J.-H. Fuhrhop and R. Bach, unpublished results) at pH 5 and tartaric amides **9** form fibrous cloths and tubules[21] (Fig 11). Only at the pH where strong hydrogen bonds between adjacent carboxylic acids and carboxylates should occur are stable micellar fibres observed in aqueous suspensions.

A final example is the not so well defined fibres made of protoporphyrin itself and its glyconamides **10** and **11** (Fig 12). Ribbon formation is only observed in the case of protoporphyrin[22] when it is half neutralized. Again this suggests binding interactions between the carboxy head groups and not repulsion. Furthermore the amide hydrogen bonds shift the amide II band to 1506 cm^{-1} in water as compared with 1559 cm^{-1} in DMSO solution. Only the amides of carbohydrate-derivatized porphyrins and not the analogous water-soluble esters give ribbons which show a split Soret band (360 and 460 nm) and a circular dichroism spectrum both produced by extended exciton interactions. The aqueous suspensions of these porphyrin fibres are stable for more than 8 months without any surfactant added.[23] The thinnest of the fibres again is such that each porphyrin amphiphile molecule is exposed to water.

Another experimental finding to be emphasized here is that none of the fibres which have been described so far could be formed by the swelling of crystals in water. All the crystals described in the previous section are stable in aqueous suspension at room temperature. Only upon heating above the amide hydrogen bond melting point, are the crystals disrupted completely in water and dissolve as spherical micelles with a cmc of

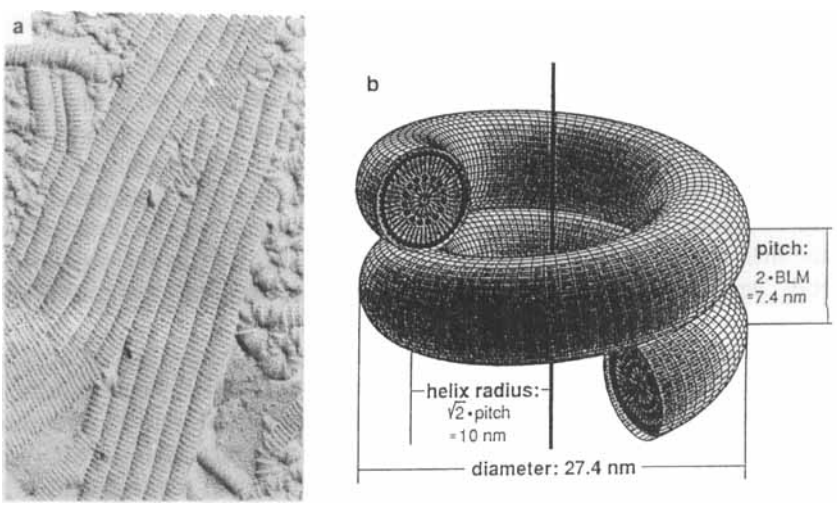

Figure 9 Rearrangement of the quadruple helix made of **1b** (Fig 8) to give tubular helices that are found from electron micrographs (*a*) and models of four-fold molecular layers or four parallel-running bilayers (*b*). This specific rearrangement in dilute ($\approx 10^{-3}$ M) aqueous suspension is again taken as strong evidence for strong binding interactions between the head groups. The fibrous structure here is nearer to the final crystal structure (see Fig 3*a*).

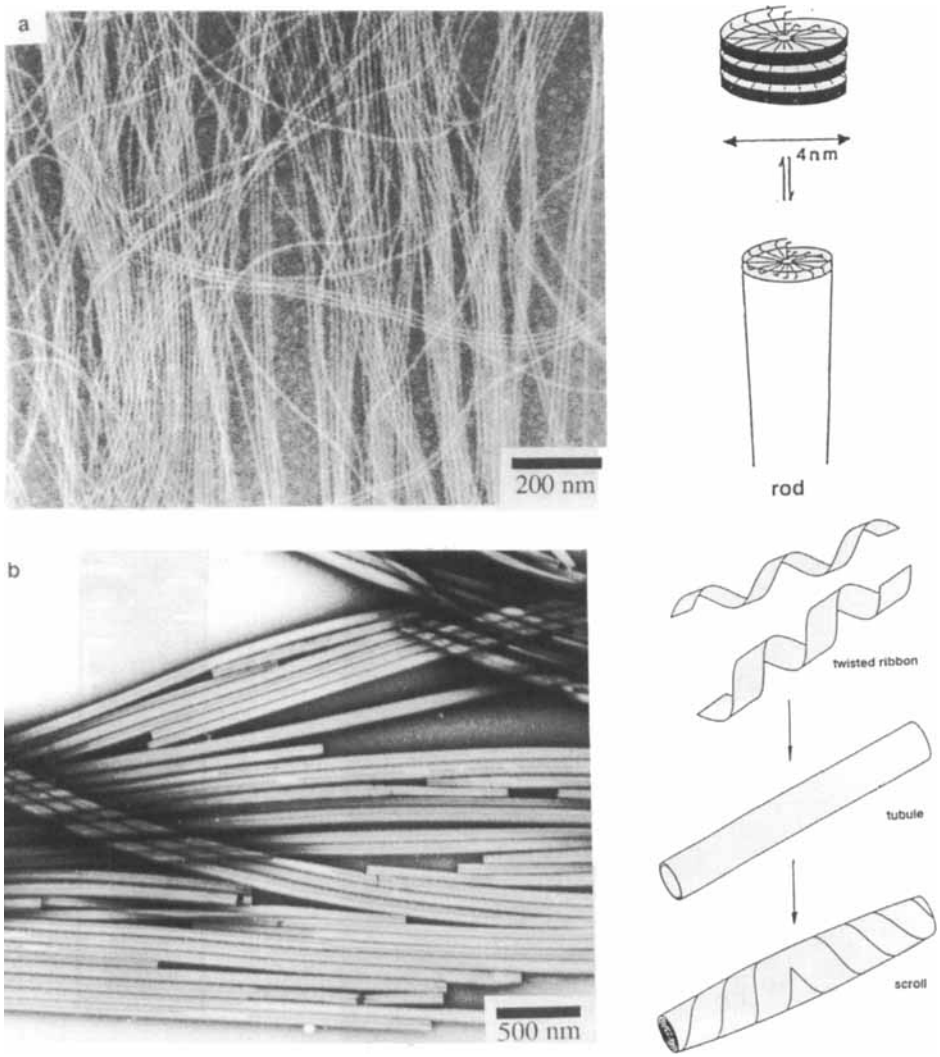

Figure 10 Diacetylenic *N*-alkyl-gluconamide **7** assembly to form, depending on chain length, either (*a*) micellar rods (here **7d**, a polymerizing assembly) or (*b*) tubules (here **7e**, a non-polymerizing assembly). The inner diameter can be as small as 10 nm. The tubules may later add more bilayers to become scrolls.

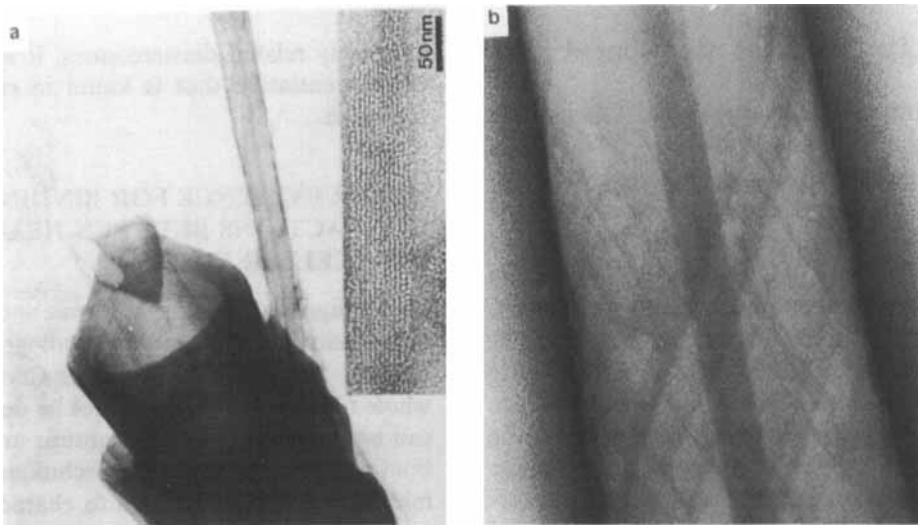

Figure 11 *Negatively charged* tartaric acid amide **9** producing (*a*) cloth-type aggregates with rough surfaces compared with (*b*) the smooth surface of mannonamide **6** scrolls. The 'cloths' may be made of micellar fibres (see inset in *a*), the mannonamide scroll of rolled-up lamellae. Both assemblies are thought to have crystalline surfaces.

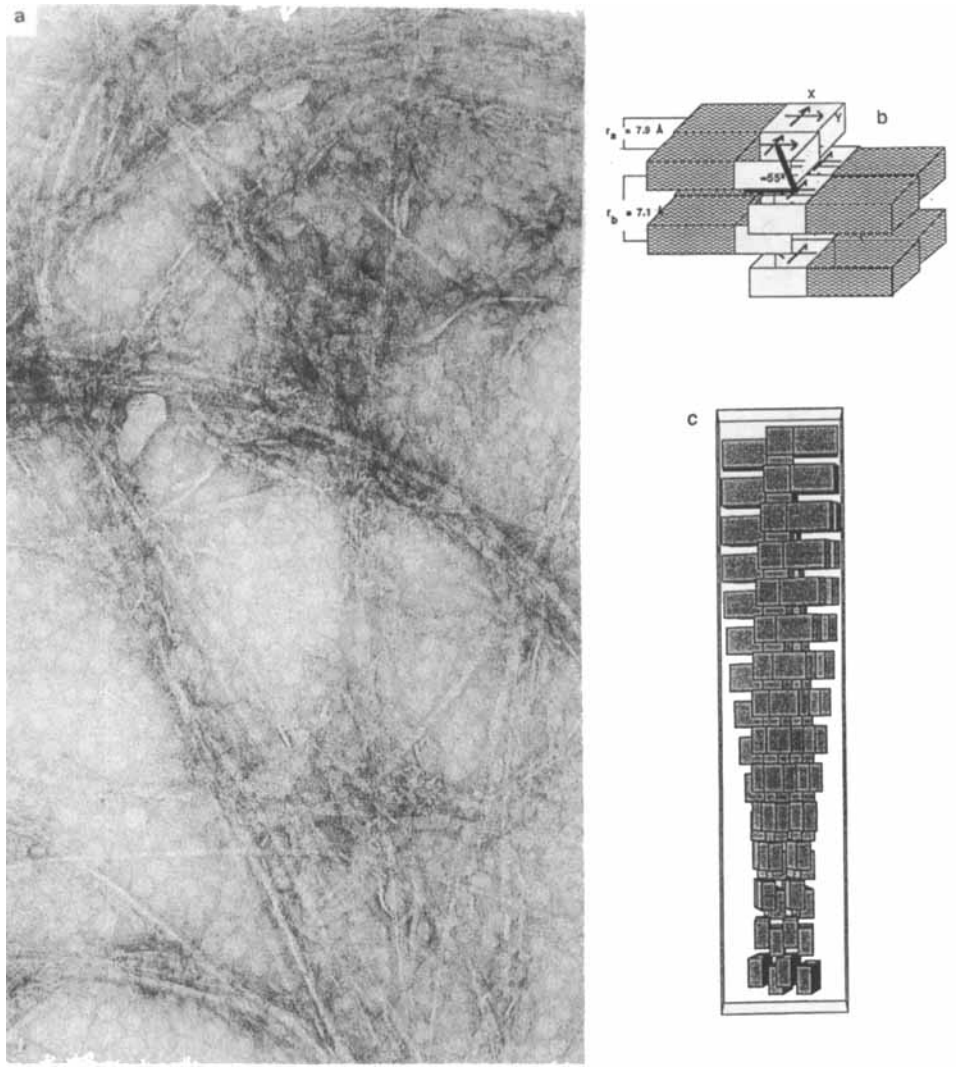

Figure 12 Protoporphyrin D,L-aminomannose amide **10b** + **c** ribbon. (*a*) Electron micrograph, and models of (*b*) the structural units and (*c*) the whole ribbon.

28×10^{-3} M. The fibres are then formed upon cooling.

The diastereomeric gulonamides and talonamides with the same arrangement of one 1,3-*syn-axial* hydroxy group pair as in the gluconamide **1** were also insoluble in water at room temperature, and dissolved at above 50°C to form micelles with a cmc of approximately 28×10^{-3} M. They also solidified at a sharp temperature. The resulting aggregates, however, were not micellar fibres. Bilayer platelets and ill-defined ring structures were observed instead[5] (Fig 13). This again shows that binding forces are responsible for the stereoselective aggregation of the head group, and not repulsive interactions. There are no hydration forces or steric forces between electro-neutral hydroxy groups, which are so short-range and directed that they could differentiate sharply between so closely related diastereomers. It is the same kind of differentiation that is found in crystal and fibre structure.

OTHER EVIDENCE FOR BINDING INTERACTIONS BETWEEN HEAD GROUPS IN MICELLAR FIBRES

Clean alignment of micellar fibres and fibre structure determination by X-ray crystallographic methods have, so far, not been achieved. Crystallinity of the whole fibres could therefore not be demonstrated, we can only say that the head groups are connected by binding forces. Several other techniques than electron microscopy have been used to characterize the solid fibres. Differential scanning calorimetry of solid hydrated crystals of *N*-octyl-D-gluconamide **1b** (Fig 3*a*),

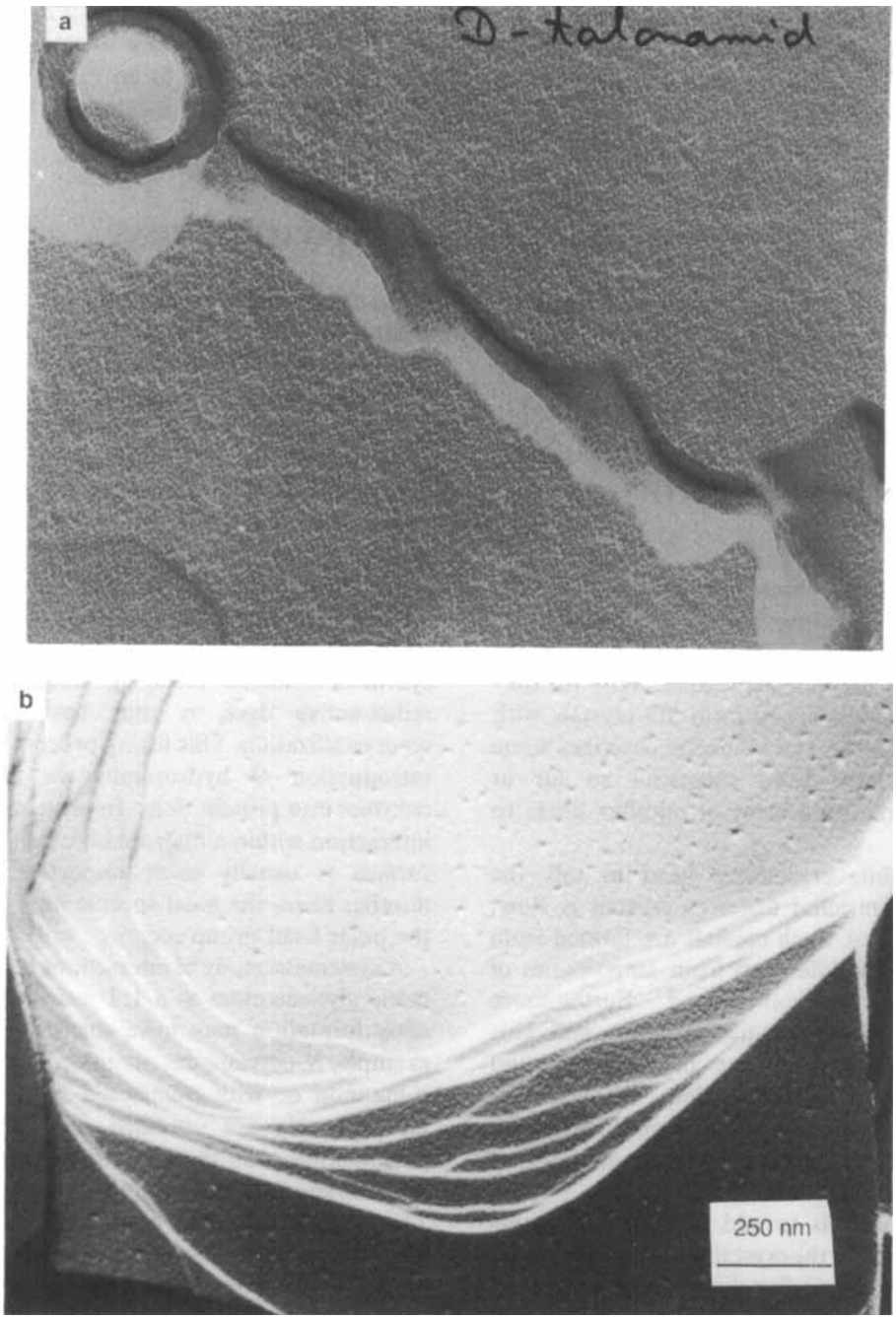

Figure 13 Electron micrographs of (*a*) gulonamide **3** bilayer platelets and (*b*) ill-defined talonamide **4** assemblies. These should be compared with the gluconamide rods in Figures 8–10 and the differentiations in corresponding crystal structures noted (Figs 3 and 4). Bilayer crystals correspond to bilayer assemblies of low curvature. Head-to-tail crystals correspond to assemblies of high curvature.

and the corresponding quadruple micellar helix (Fig 8), for example, give the same melting point (342 K). Both the crystal and the fibres lose their amide hydrogen bond chains at this temperature and dissolve in the form of spherical micelles. The same binding forces are thus active in crystals and highly curved micellar fibres. Other glyconamides behave similarly, although curvature is very different. No important repulsive forces become evident, which differentiate micellar structures from crystals.

Solid state ^{2}H-NMR spectroscopy of **1b** in crystalline and micellar form show the same type of Pake spectrum;[20,24,25] the methylene groups are immobile. Similar experiments with gulonamide **3** show mobility of the same CD_2 group in both crystals and micellar fibres.[20] CPMAS ^{13}C-NMR spectra show broader line

widths for the CH_2 carbons in fibres than in crystals. The core of the solid fibre is thus less well ordered than the crystal. The head group spectra, however, were again quite similar.

Infrared spectra of fibres and crystals of **1b** show the amide I peak, which is sensitive to hydrogen bonding[26] at 1650 cm^{-1}. Above 353 K the same band occurs at 1690 cm^{-1}. Similar observations have been made with other fibrous aggregates. It is thus clear that the same strong amide hydrogen bonding that has been characterized in crystal structures, is also present in micellar fibres of 4 nm thickness and high curvature.

STABILIZATION OF FIBRES WITH SOLID SURFACES

Ultrathin, bimolecular fibres in which all parts are held together by binding forces are, of course, problematic. They do not harmonize with any of the current models of micellar aggregates. Why do they not rearrange immediately to form 3D crystals with much smaller surfaces? The following describes some methods which have been successful so far at preventing such rearrangement of micellar fibres to crystals.

If the amphiphile crystallizes head to tail, the rearrangement of micellar fibres to crystals is slow; the fibre is long-lived. Such crystals are formed from certain chiral amphiphiles and from amphiphiles of low polarity, e.g. terminal esters.[27] Furthermore charged amphiphiles often do not crystallize well. This is especially true if a mixture of loosely bound counterions, such as potassium ions, is present in solution. Hydrogen-bonded ammonium counterions, in particular from diamines and ammonia, on the other hand, support crystallization.

Another possibility is to add charged surfactants which do not penetrate the crystalline fibres. They may cover the surfaces of micellar discs or other particles which dissociate from the fibres. Such particles then remain small and eventual rearrangements of a few molecules to head to tail oriented assemblies does not lead to crystallites. On the other hand only tail to tail arrangements are present in mixed micelles.[20]

Elevated temperatures also retard crystallization. The micellar fibres survive as long as the melting point of the amide hydrogen bond is not surpassed.[20]

Another means of stabilizing ultrathin fibres which are rapidly formed involves their coverage with a thin, inorganic, glass film. Addition of phosphotungstate at pH 7 or below has been very successful.[3] Phosphotungstate films do not disturb solid state NMR spectroscopy.[20] At low temperature, e.g. 5°C, it becomes more difficult to stabilize micellar fibres with solid surfaces. Solid state reactions of unknown mechanisms often lead to an uncontrollable collapse of the fibres and to the formation of small ill-defined platelets.

CO-CRYSTALLIZATIONS

It should be obvious that micellar fibres with solid crystal-like surfaces and densely packed hydrophobic cores cannot be used as dissolving particles in the same way as their spherical analogues in a liquid state. Guest molecules can only be introduced into the host fibres if the guests are also amphiphilic. Space which is occupied at the hydrophobic centre must also be filled at the head group region. Furthermore the amide hydrogen bond chain and other strong binding interactions must not be interrupted by the guest. Otherwise the guest will be expelled out of the micelles upon fibre formation or the fibre will not form. The synthesis of mixed fibres, e.g. containing photo- and redox-active dyes, is thus best carried out by co-crystallization. This fitting process is similar to the introduction of hydrophobic or amphiphilic co-enzymes into protein clefts. In proteins, dipole–dipole interaction within a hydrophobic cleft on the polymer surface is usually most important,[28] whereas in micellar fibres the most specific interactions occur in the polar head group regions.

A systematic study of interactions between diastereomeric glyconamides in a 1:1 ratio[16] has shown that alloy formation may have surprising effects. If, for example, *N*-octylamides are mixed with D-glucon and D-mannon or with D-galacton head groups, planar platelets only are obtained. The curvature of the gluconamide rods, the galactonamide ribbons and the mannonamide scrolls, disappear altogether (Fig 14*a*). This is not the case with homologue *N*-dodecylamides. Here well-defined micellar rods made of 1:1 mixtures of D-gluconamide and D-mannonamide are found (Fig 14*b*). Complete separation of diastereomeric fibres was, however, also found: *N*-octyl-L-galactonamide twisted ribbons (Fig 14*c*) or *N*-octyl-L-mannonamide scrolls form next to *N*-octyl-D-gluconamide quadruple helices (Fig 14*d*). The terminal chiral centre next to the bulk water usually makes all the difference. If this centre has the same configuration, alloy formation is observed; if it has the opposite configuration, separation is favoured. Curvature seems to be more persistent when the hydrocarbon chains grow longer.

Attempts to co-crystallize *N*-octyl-D-gluconamide fibres with dyes were successful with the bixin gluconamide **12**. As stated in the Molecular and Crystal Structures section, the methyl groups of

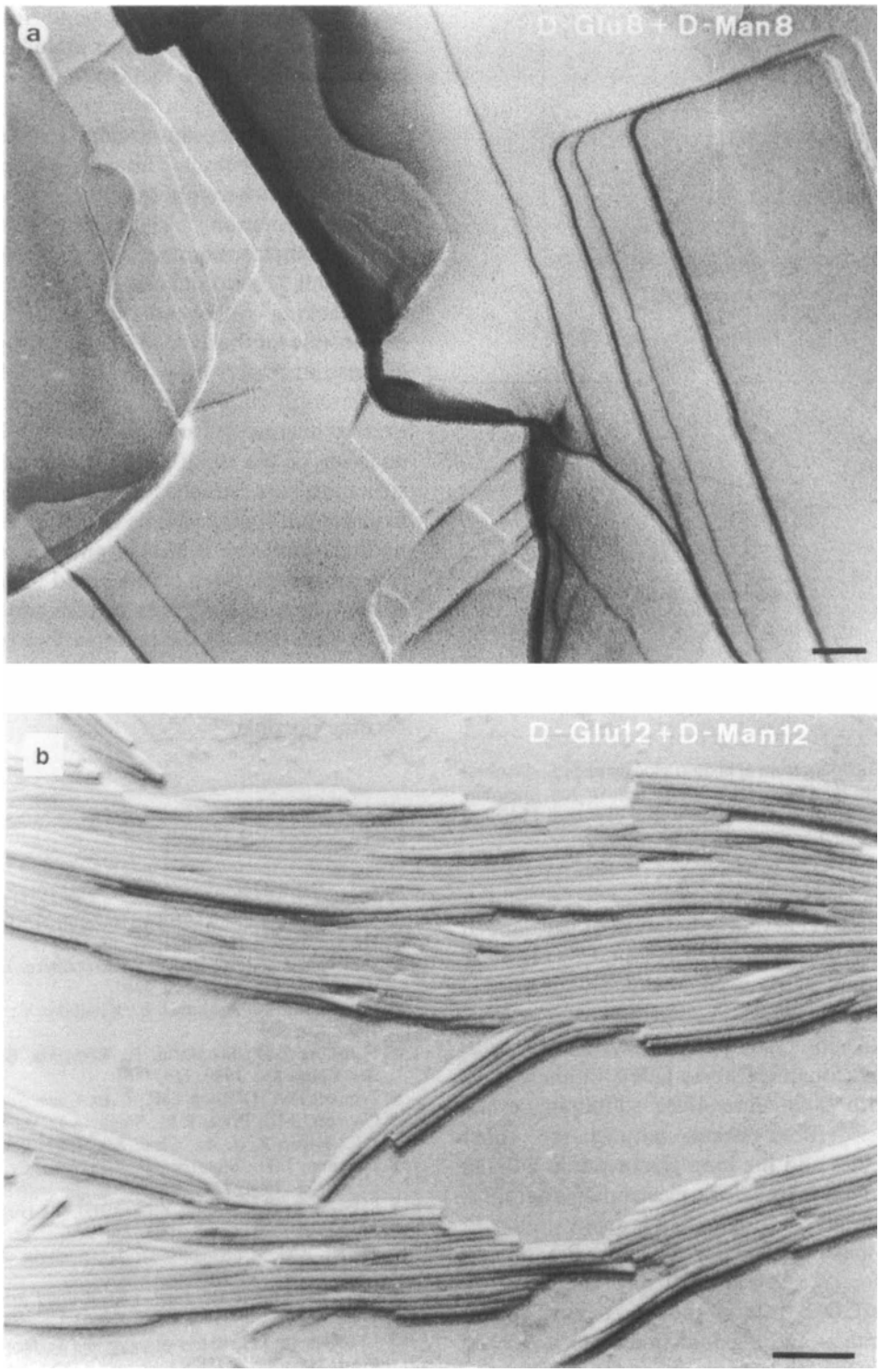

Figure 14 Electron micrographs of molecular assemblies (co-crystals) of 1:1 mixtures of (*a*) *N*-octyl-D-glyconamides and -mannonamides and (*b*) the corresponding *N*-dodecylamides. For a comparison see the electron micrographs of pure *N*-octyl-D-gluconamide (Fig 8, quadruple helices) and mannonamide (Fig 11*b*, scrolls).

amphiphilic carotenoids hinder the formation of domains. It was indeed found that spherical gluconamide micelles dissolved the bixin derivatives at above 80°C and that the same amount of monomeric bixin remain dissolved at 20°C (Fig 15*a*). No circular dichroism (CD) was observed at above 80°C in micellar solution. Upon fibre formation the bixin chromophore became CD active: in right-handed

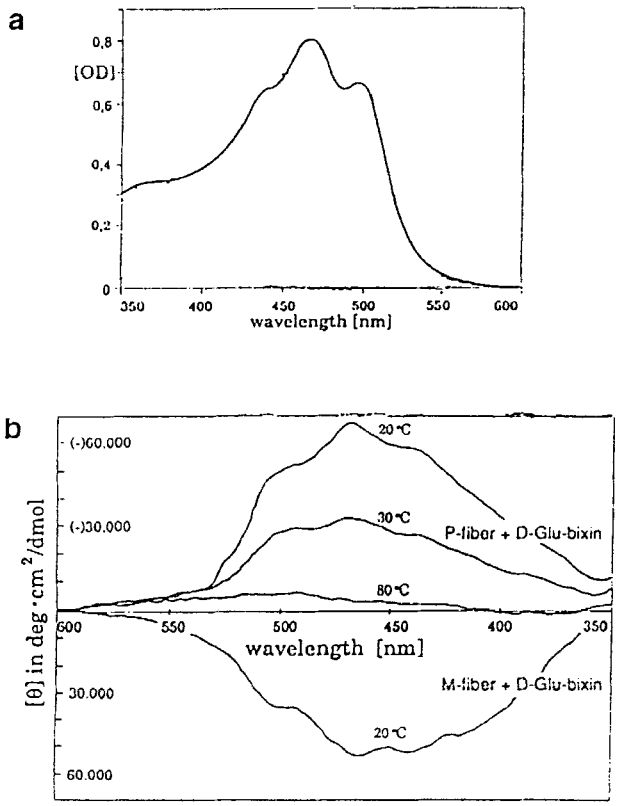

Figure 15 (*a*) Visible spectrum of bixin-D-gluconamide **12** dissolved in D-gluconamide **1b** fibres. It is characteristic for immobile monomers. (*b*) The induced circular dichroism of P- and M-helical fibres made of **1b** and **2** and co-crystallized with **12**.

fibres a positive CD curve was induced; in left-handed fibres a negative mirror image was found[29] (Fig 15*b*). The methyl groups of the carotene thus do not destroy the crystalline order of the head groups.

Attempts to co-crystallize porphyrin **10a** with *N*-dodecyl-D-gluconamide fibres failed, in analogy to the results with bixin derivatives containing cyclic carbohydrates.[29] Both fibres, namely the short porphyrin needles and the long gluconamide bulging helices, appeared side by side on electron micrographs. The open-chain gluconhydrazide **11**, again similar to the bixin case, may integrate into the fibres. Preliminary CD measurements showed relatively small effects. Mirror image CD curves in the Soret band region were observed in D- and L-gluconamide fibres, but the molar ellipticities were only in the order of 10^4.

RELATED FIBRES

The glyconamide head groups explored in this paper are analogous to amino acid head groups. Kunitake,[30] Yamada,[31] Imae,[32] and other Japanese researchers have produced twisted ribbons from glutamate, aspartate, alaninate, and other amino acid derivatives containing one or two hydrophobic chains and amide bonds. To the best of our knowledge none of the reported chiral supramolecular structures is as thin as a molecular bilayer. The same is true for nucleotide amphiphiles, where phosphate chains are responsible for fibre formation.[33] There exists also an intriguing cetyltrimethylammonium salicylate fibre of infinite length and 12 nm thickness.[2] This fibre is achiral and the stacking of phenolate counterions could be responsible for the formation of quadruple rods. Many of these structures may also have solid state surfaces with strongly binding head group interactions. Detailed electron microscopic and solid state NMR spectroscopic analyses of the isolated molecular bilayers in these structures are needed to verify this generalizing assumption. It may well be that in some cases a loose hydrocarbon core is hidden under a crystalline crust of head groups. Such a fibre could then dissolve dyes. It might be predicted that electrons and protons would easily pass through the polar surface region, whereas molecules and large ions could not. Rapid charge separation across polar monolayers might then become possible.

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