Supramolecular Chirality: Chiral Hydrogen-Bonded Supermolecules from Achiral Molecular Components

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Chiral supermolecules may be obtained from suitable achiral molecular constituents associated through a dissymmetrizing interaction mode. This is the case for the supermolecules **I–IV** formed by hydrogen-bonding association between the achiral complementary components **1a,b** and **2a,b,c**. The crystal structures of the supermolecular pairs **I–III** and of the homochiral aggregate of two ternary supermolecules **IV** have been determined. The structural data are discussed.

1. Introduction. – The three-dimensional arrangement of atoms in molecules characterizes *molecular stereochemistry*. Similarly, the spatial arrangement of molecules held together be weak interactions to create a supermolecule is the realm of *supermolecular stereochemistry* [1a]. Like a molecule, a supermolecule may exist in enantiomeric or diastereoisomeric forms. Supramolecular chirality results both from the properties of the components and from the way in which they associate. Thus, a supermolecule may be chiral when *i)* at least one component is asymmetric, or *ii)* an interaction between achiral components is dissymmetrizing, yielding a chiral association.

The first case is self-evident. The second case, which involves the generation of chirality from achiral components, has not only intriguing implications with respect to the emergence of optical activity on earth [2], but is also central to the understanding of how molecular interactions may lead to the generation of supramolecular entities possessing novel features that are not present in their components.

Chiral symmetry breaking in achiral organic compounds is known to occur in crystals [2–4], in *Langmuir* films [5], and in an aggregate in solution [6]. It is of much interest to extend such events to multicomponent systems and to devise general approaches to the generation of chiral species from achiral components.

The present work is part of a broader investigation on the directed formation of chiral supramolecular species from achiral molecular constituents. Specifically, it concerns the stereochemical features of the supermolecules **I–IV** formed by H-bonding

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of complementary partners (pleromers [1b]), the glutarimides **1a,b**, and the aminoadenine **2a** or diaminopyrimidine **2b,c** derivatives (*Fig. 1*).

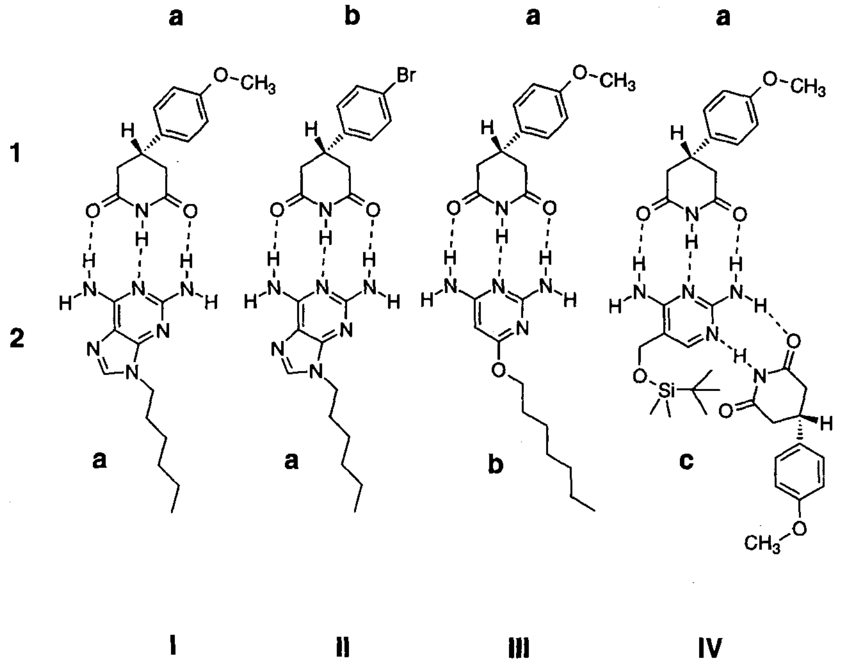

Fig. 1. *H-Bonded pairs* **I**, **II**, **III**, *and capped H-bonded ternary species* **IV** *formed from the complementary components* **1a,b**, *and* **2a,b,c**

2. Results and Discussion. – Compounds **1a,b**, and **2a,b,c** were synthesized by unexceptional procedures and presented spectral and analytical properties in agreement with their structure. The achiral pleromers **1** and **2** have been selected so that their in-plane association through three H-bonds (see, *e.g.*, [7]) is dissymmetrizing and may be expected to generate a chiral supermolecule. Thus, the glutarimide component has a plane of symmetry perpendicular to its ADA (H-bond *a*cceptor-*d*onor-*a*cceptor) recognition sequence, whereas the DAD (donor-acceptor-donor) centers of the other complementary components lie in the molecular plane of symmetry. As a consequence, in the triply H-bonded pairs **I**–**IV**, the symmetry planes of the components are perpendicular, making the association chiral and generating two enantiomeric supermolecules (*Fig. 2*). The formation of supramolecular diastereoisomers may also be considered along similar lines [1].

Chirality creation from achiral components requires *i*) the ability to form a chiral association, *ii*) a reversible interconversion between the enantiomers, and *iii*) a preference for homochiral assembling. All three features are of supramolecular nature and may, in principle, be present in supermolecules such as **I**–**IV**. The formation of a chiral phase from **I**–**IV** requires, that, in the condensed state, two- or three-dimensional packing favor homochiral over heterochiral species.

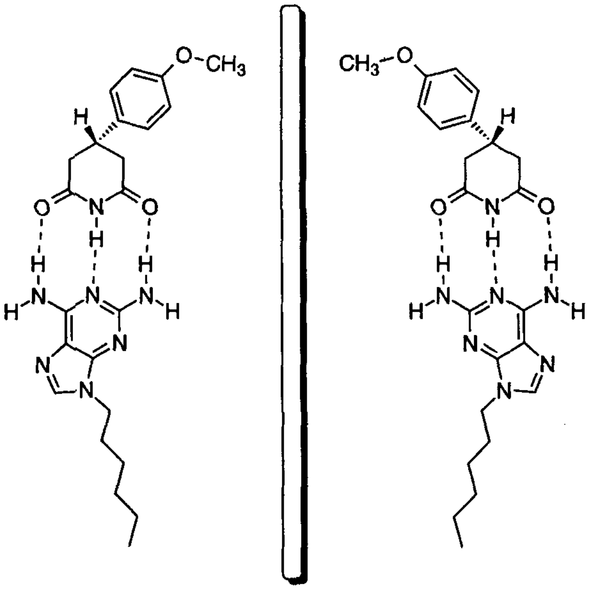

Fig. 2. *Generation of two enantiomeric supermolecules* I *through H-bonding of the two achiral complementary components* **1a** *and* **2a**

To this end, the crystal structures of the three different pairs **I**–**III** and of the capped three-component entity **IV** (*Fig. 1*) have been determined.

2.1. *Solid-State Structure of Pair* **I**. Single crystals of the pair **I** were grown by slow diffusion of hexane into a CH_2Cl_2 solution of the two components **1a** and **2a**.

The crystal structure can be described as consisting of pairs **I** of triply H-bonded pleromers **1a** and **2a**, interconnected through the amino-adenines *via* two sets (of *Hoogsteen* and α-aminopyridine-dimer type) of two H-bonds, forming long supramolecular amino-adenine ribbons (*Fig. 3*). The orientation and the chirality of the pairs alternate along the ribbon, thus making the ribbon heterochiral. Furthermore, the parallel ribbons interdigitate generating crinkled layers, which stack on top of each other through the ribbons running in the same direction. A ribbon in a layer is offset with respect to the ribbons in the layers above and below (*Fig. 4*).

2.2. *Solid-State Structure of Pair* **II**. Single crystals of the pair **II** were grown by slow diffusion of cyclohexane into a dioxane solution of the two components **1b** and **2a**. Replacing MeO by Br in the glutarimide does not change the crystal structure of the pair. **II** is iso-structural in the solid state to **I** showing the same type of heterochiral amino-adenine ribbons (*Fig. 5*) and the interdigitation of the ribbons in two dimensional crinkled layers. No Br,Br interaction is apparent.

2.3. *Solid-State Structure of Pair* **III**. Single crystals of **III** were grown by slow diffusion of Et_2O into a CH_2Cl_2 solution of the two components **1a** and **2b**. The last three C-atoms of the aliphatic chain of the pyrimidine unit **2a** show disorder and are difficult to localize.

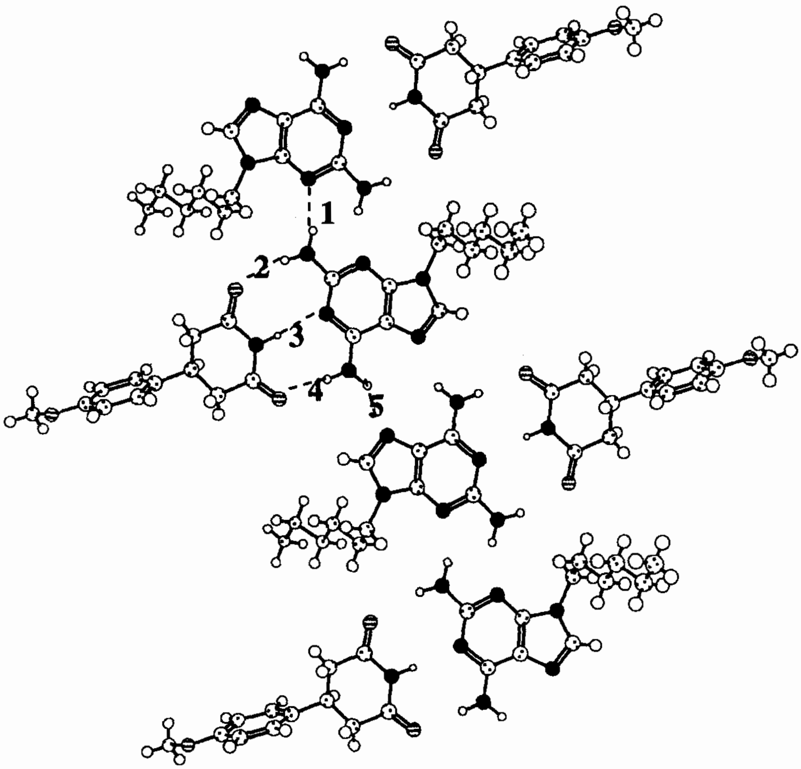

Fig. 3. *Crystal structure of the heterochiral ribbon formed by the supermolecular pair* **I**. H-Bonding distances [Å]: **1**(N,N) = 2.88; **2**(N,O) = 2.98; **3**(N,N) = 2.98; **4**(N,O) = 3.15; **5**(N,N) = 2.91.

The crystal structure can be described as constituted by pairs of enantiomeric species **III** interconnected *via* H-bonds between the pyrimidine groups. These heterochiral units further associate into a long ribbon (*Fig. 6*). Just as in the case for crystal structures **I** and **II**, the ribbons interdigitate in parallel forming pleated layers that stack on top of each other (*Fig. 7*).

2.4. *Solid-State Structure of the Capped Ternary Species* **IV**. Single crystals of the ternary species **IV** were grown by slow diffusion of hexane into a dioxane solution of the two components **1a** and **2c**.

The structure of **IV** differs from those of **I**–**III** in several ways. Even though crystallization was carried out in a solution containing a 1:1 mixture of DAD (2,4-diaminopyrimidine) and ADA (glutarimide) components as in the previous cases, the crystal contains a 1:2 ratio of these units. The structure does not present H-bonded ribbons, but instead the molecules associate into a discrete aggregate of six components: two pyrimidines **2c** and four glutarimides **1a** (*Fig. 8*). An important point is that this entity is chiral, being composed of two ternary supermolecules **IV** of same chirality.

The crystal structure can be described as formed by squares of four homochiral aggregates with neighboring squares sharing corners (*Fig. 9*). The squares extend in two

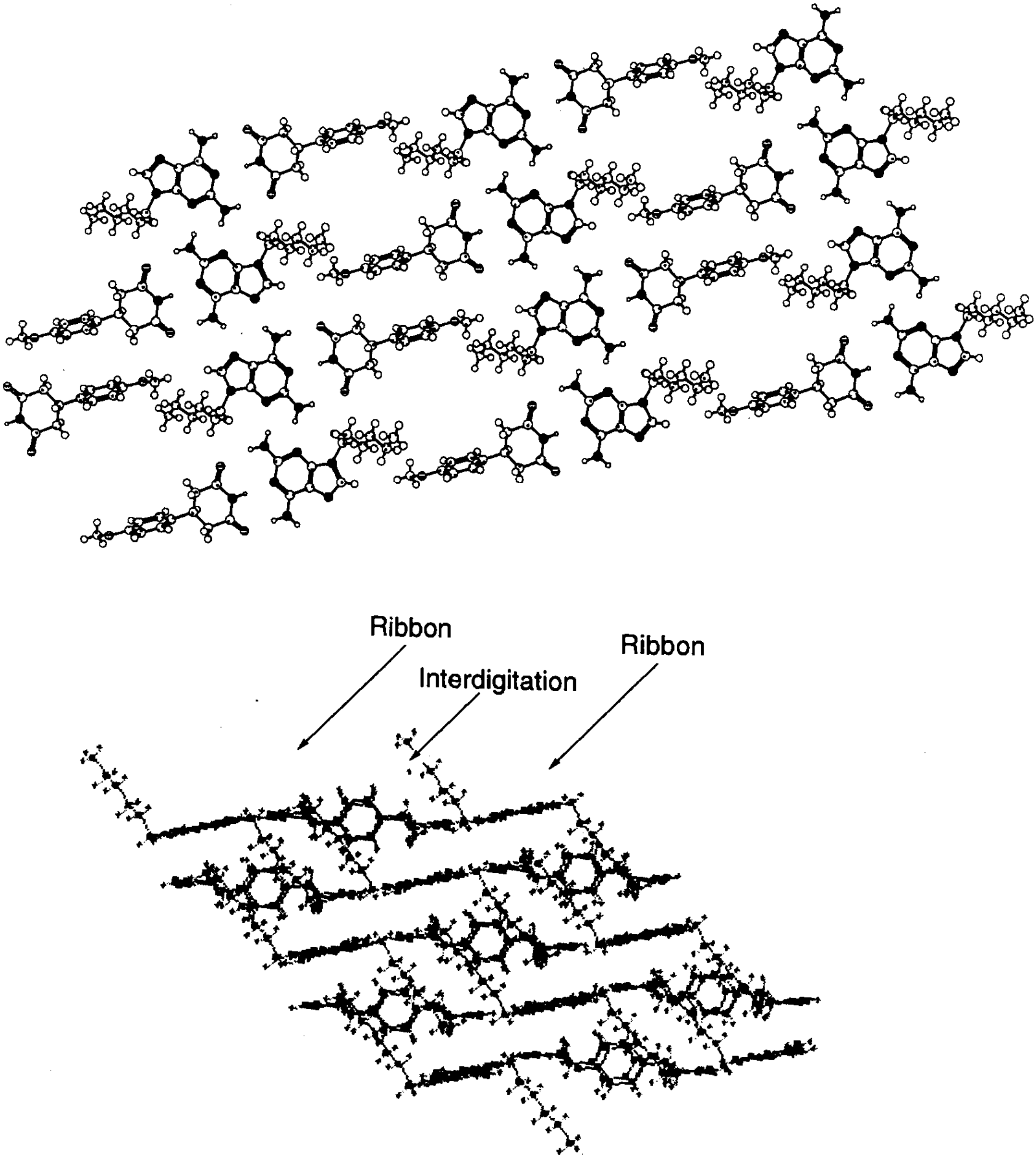

Fig. 4. Top: *Interdigitation of ribbons formed by supermolecule* **I**. Bottom: *Side view along the axis of the ribbons showing the packing of the crinkled layers*

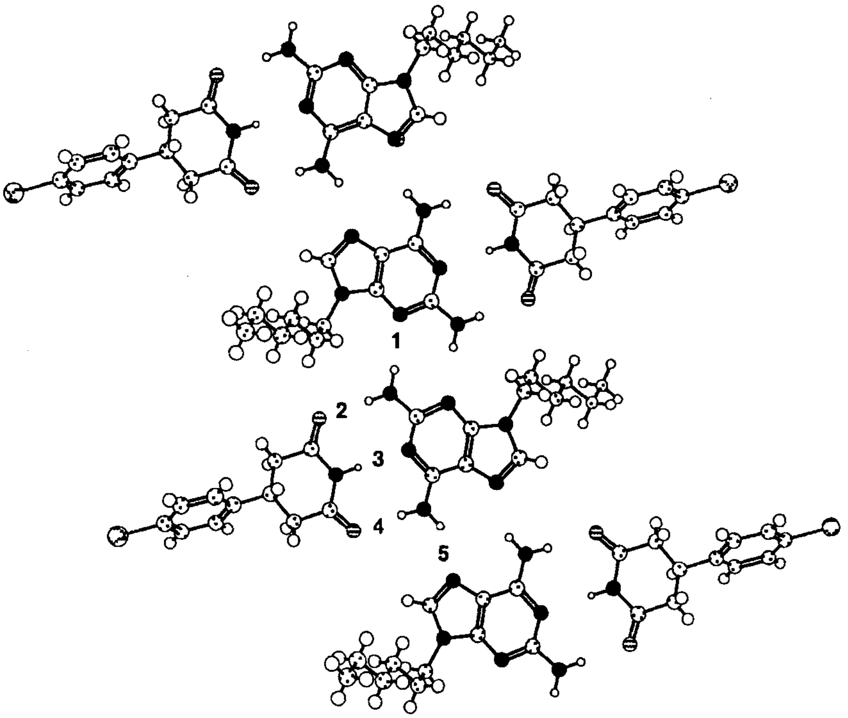

Fig. 5. *Crystal structure of the heterochiral ribbon formed by the supermolecular pair* **II**. H-Bonding distances [Å]: **1**(N,N) = 3.08; **2**(N,O) = 2.90; **3**(N,N) = 3.01; **4**(N,O) = 2.98; **5**(N,N) = 2.97.

dimensions forming a homochiral sheet. Two homochiral sheets of opposite chirality interdigitate to form a heterochiral bilayer (*Fig. 10*). The bilayer motif repeats itself throughout the crystal (for recent reviews, see [8]).

It is interesting to note that the four glutarimides that form the corners of the squares (*Fig. 8*) protrude out of the plane and arrange themselves in a circular fashion defining a hole of 5.76 Å diameter. These cavities are not blocked by the interdigitation, and the registry between different bilayers produces a hollow tube. Seen through the *c*-direction the crystal appears as a honeycomb with cylindrical voids running through it (*Fig. 11*). These tubes are filled with disordered solvent molecules.

2.5. *H-Bonding Features.* The H-bonding distances found in the present crystal structures of **I**–**IV** (N,N = 2.88 to 3.36 Å; N,O = 2.84 to 3.30 Å; see captions to *Figs. 3, 5, 6*, and *8*) fall within the ranges reported for this type of interaction [9]. As has been pointed out [10], a packing scheme is selected which optimizes H-bonding, all strong donor and acceptor sites being H-bonded. The arrangement of the supermolecular components **I**–**IV** in the crystal lattice is maintained by secondary H-bonding interactions between these species.

3. Conclusion. – The present results present general features of supramolecular chirality. They illustrate the view concerning the formation of chiral supermolecules from

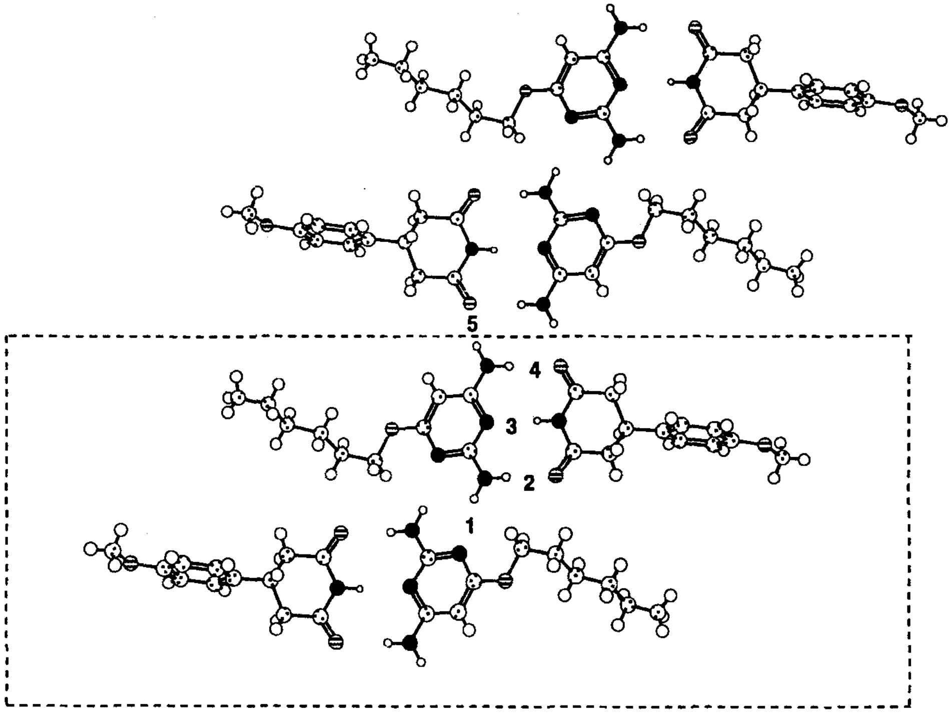

Fig. 6. *Crystal structure of the heterochiral see-saw ribbon formed by the supermolecular pair* **III**. A heterochiral unit containing two enantiomeric species **III** is shown encased. H-Bonding distances [Å]: **1**(N,N) = 3.36; **2**(N,O) = 2.98; **3**(N,N) = 3.15; **4**(N,O) = 3.30; **5**(N,O) = 3.16.

achiral components through dissymmetrizing interaction arrangements. The crystals themselves formed by the species **I**–**IV** are not chiral, being rather a racemic mixture of these supermolecules, as a result of preferential packing in the solid state. However, this approach to the generation of chiral supramolecular entities may, in addition to its significance with respect to the general features of supramolecular chirality, also have impact on the chemistry of molecular assemblies and on solid-state technology (*e.g.*, non-centrosymmetric crystals).

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Experimental Part

Preparations of Compounds **1a**, **1b**, *and* **2a**, **2b**, *and* **2c**. *3-(4-Methoxyphenyl)glutarimide* (**1a**) and *3-(4-bromophenyl)glutarimide* (**1b**) were prepared as described in [11]. *9-Hexyl-9*H*-purine-2,6-diamine* (**2a**; m.p. 188–190°) was obtained by the same procedure as reported for *9-(3-phenylpropyl)-9*H*-purine-2,6-diamine* [12]. *6-(Heptyloxy)pyrimidine-2,4-diamine* (**2b**; m.p. 194–196°) was prepared by the same procedure as described for the

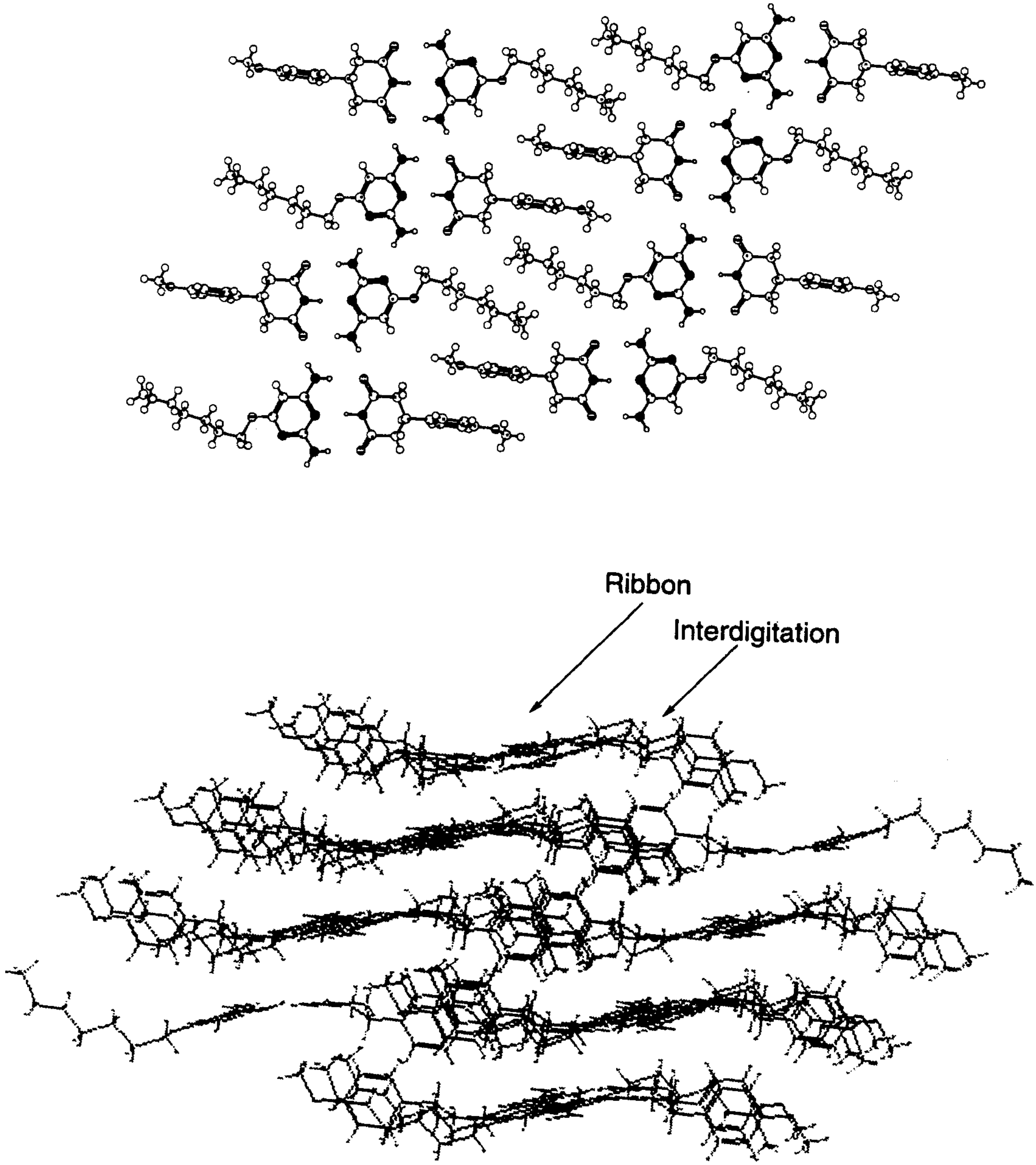

Fig. 7. Top: *Interdigitation of the see-saw ribbons formed by supermolecule* **III**. Botton: *Side view parallel to the axis of the ribbons showing the packing into pleated layers*

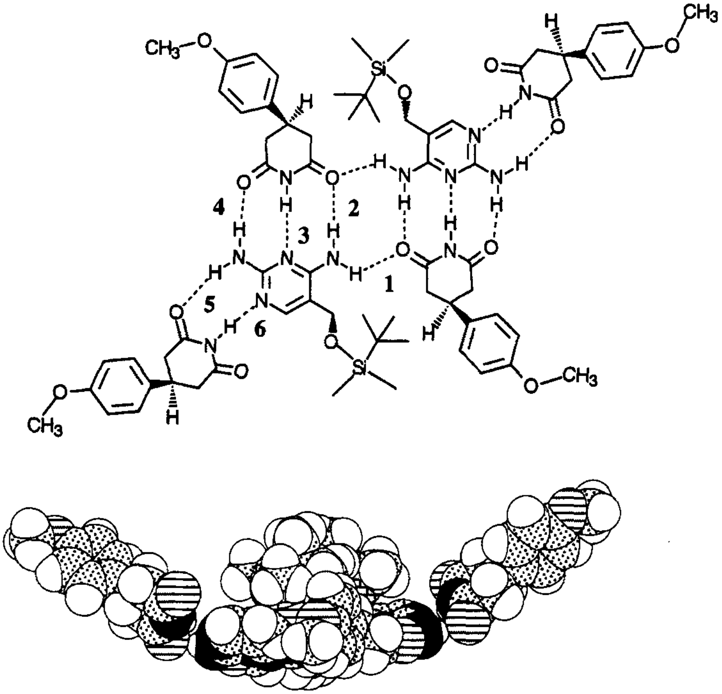

Fig. 8. Top: *Homochiral aggregate of two ternary supermolecules* **IV**. H-Bonding distances [Å]: **1**(N,O) = 2.85; **2**(N,O) = 3.13; **3**(N,N) = 2.99; **4**(N,O) = 2.91; **5**(N,O, = 2.91; **6**(N,N) = 3.11. Bottom: *Side view in space-filling representation; the glutarimides that cap the triply H-bonded supermolecules* (**1a**, **2c**) *H-bond to the pyrimidines with an angle of 20.4°, giving the aggregate a bowl shape*

corresponding 6-butoxy analog [13]. *5-[(*tert*-Butyl)dimethylsilyloxy]pyrimidine-2,4-diamine* (**2c**; m.p. 174–176°) was obtained from (2,4-diaminopyrimidine-5-yl)methanol [14] by silylation [15].

The spectral (^{1}H-NMR, MS) data for **2a**, **2b**, and **2c** agreed with the structure, which is confirmed by the crystallographic data.

Crystallographic Data Collection and Structure Determination for the Supramolecular Species **I**, **II**, **III**, *and* **IV**. Single crystals of **I**–**IV** were obtained as described above. Crystal data are given in the *Table*. For all compounds, three standard reflections measured every hour during the data collection period showed no significant trend. For **I** and **III**, the raw step-scan data were converted to intensities using the *Lehmann-Larsen* method and corrected for absorption using DIFABS. For **II** and **IV**, absorption corrections from psi scans of 4 reflections were applied. The structures were solved using direct methods and refined by full-matrix least-squares against F. H-Atoms were introduced as fixed contributors (C–H = 0.95 Å, B(H) = 1.3*$Beqv$(V) Å^2). For **III**, the two terminal C-atoms of the alkyl chain are disordered over two positions. For **IV**, one C-atom of the solvate lies on a fourfold axis, the other C- and the O-atom are disordered around this axis. For all computations, the *Nonius MolEN* package was used [16].

Supplementary Material. ORTEP Plots with the numbering schemes used for **I**–**IV**. Tables of atomic positions, thermal parameters, bond distances and angles, and structure factors are available. CIF Files have been deposited at the *Cambridge Crystallographic Data Centre.*

Table. *X-Ray Crystallographic Data*[a])

Compound	I	II	III	IV
Formula	$C_{23}H_{31}N_7O_3$	$C_{22}H_{28}N_7O_2Br$	$C_{23}H_{33}N_5O_4$	$4(C_{35}H_{48}N_6O_7Si)\cdot C_2H_5OH$ $4[(C_{11}h_{22}N_4OSi)\ (C_{12}H_{13}NO_3)_2]$ $\cdot C_2H_5OH$
Molecular weight	453.55	502.42	443.55	2817.65
Crystal system	triclinic	triclinic	triclinic	tetragonal
Space group	*P*-1	*P*-1	*P*-1	*P*4/*n*
a[Å]	13.198(4)	7.8581(5)	10.106(3)	22.692(2)
b[Å]	13.409(4)	13.235(1)	13.151(4)	–
c[Å]	7.667(2)	13.225(1)	9.050(3)	15.651(2)
α[deg]	106.14(2)	63.095(9)	91.36(2)	90
β[deg]	92.99(2)	89.045(7)	101.11(2)	90
γ[deg]	61.94(2)	72.202(7)	95.70(2)	90
v[Å^3]	1145.2(9)	1155.8(2)	1173(1)	8059(1)
Crystal dimension [mm]	0.15·0.12·0.10	0.60·0.50·0.40	0.30·0.30·0.20	0.25·0.20·0.15
D_{calc} [gcm^{-3}]	1.31	1.44	1.26	1.16
F(000)	484	520	476	3012
μ[mm^{-1}]	0.698	1.791	0.675	0.104
Trans. min and max	0.70/1.00	0.79/1.00	0.55/1.00	0.93/1.00
Temp. [K]	173	294	173	294
Wavelength [Å]	1.5418	0.71073	1.5418	0.71073
Radiation	CuK_α	MoK_α	CuK_α	MoK_α
Diffractometer	*Philips PW1100/16*	*Enraf Nonius CAD4*	*Philips PW1100/16*	*Enraf Nonius CAD4*
Scan mode	$\theta/2\theta$ step-scan	$\theta/2\theta$	$\theta/2\theta$ step-scan	$\theta/2\theta$
hkl Limits	−13,13/−14,11/0,8	−9,0/−16,15/−16,16	−10,10/−13,13/0,9	0,23/0,23/0,16
θ Limits [deg]	3.0/54.08	2.5/26.29	3.0/54.05	2.5/21.97
Number of data meas.	2643	5049	2815	5562
Number of data with $I<3\sigma(I)$	2024	2657	2375	1901
ρ	0.0064	0.0064	0.0025	0.0004
Number of variables	298	289	307	452
$R(F)$	0.039	0.044	0.069	0.086
$R_w(F)$	0.057	0.065	0.104	0.095
GOF	1.266	1.343	1.617	1.225
Largest peak in final difference [eÅ^{-3}]	0.15	0.974	0.812	0.592

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[a]) In common : color : colorless, $Z=2$, weighting scheme $=4F_o^2/(\sigma^2(F_o^2)+pF_o^4)$.

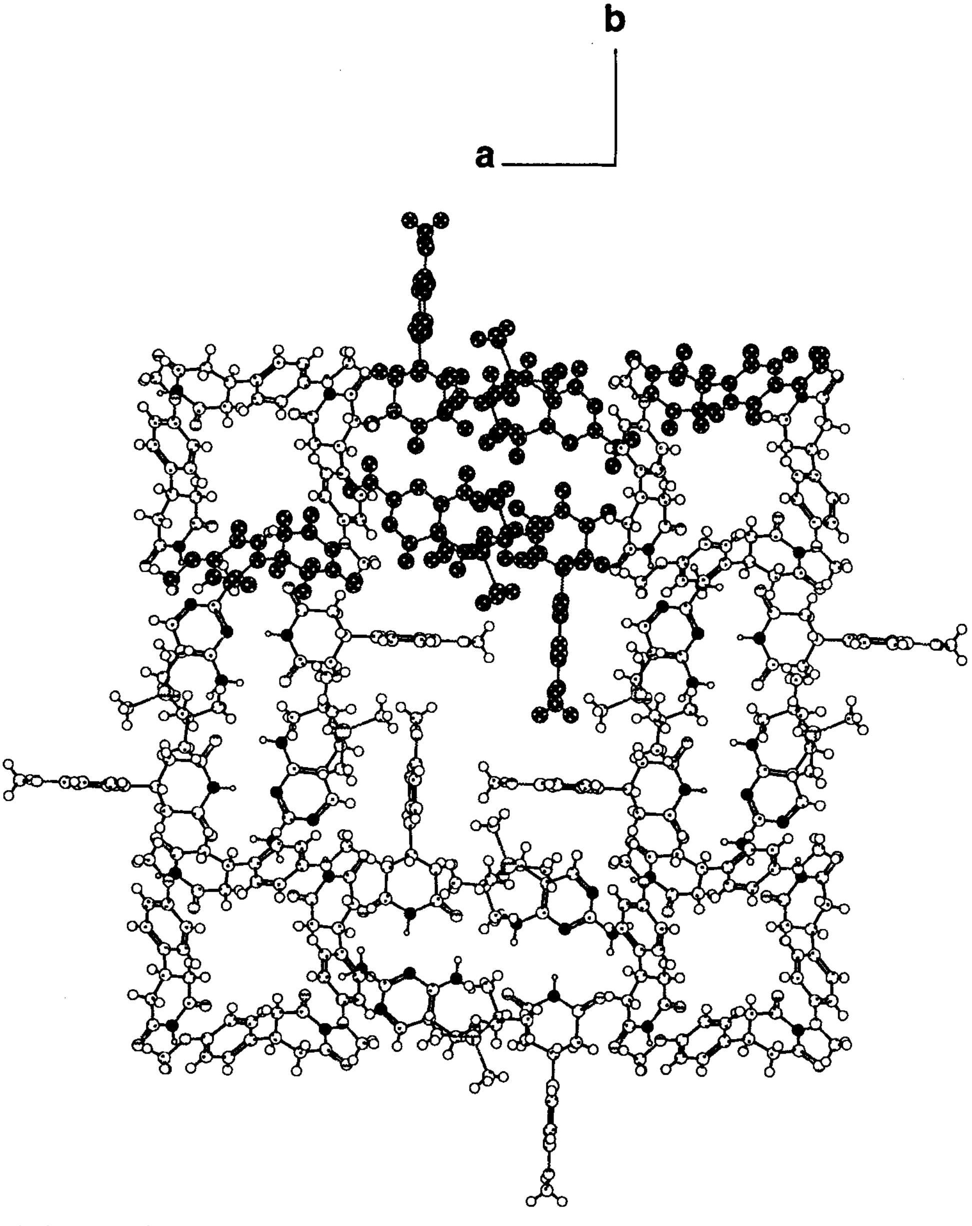

Fig. 9. *A view of the crystal structure of* **IV** *through the* a-b *plane showing the square arrangement formed by four homochiral supermolecular aggregates.* The top one has been highlighted for clarity.

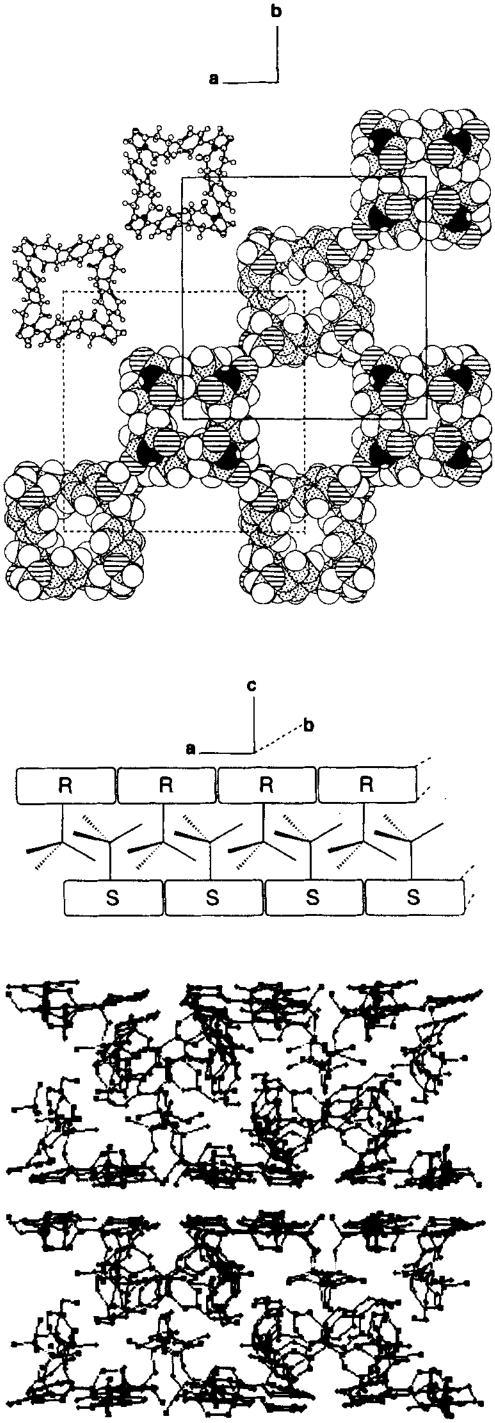

Fig. 10. *Representations of the crystal structure of* **IV**. Top: *Top view* (through the *a-b* plane) *of a bilayer arrangement.* Only the corners of the squares are shown for clarity; the solid lines unite the corners of the square closer to the observer while the dotted lines show the square further away. Center: *Schematic side view* (through the *a-c* plane) *of the heterochiral bilayer. R* and *S* represent supermolecular aggregates of opposite chirality. Bottom: *Side view* (through the *a-c* plane) *showing two bilayers*

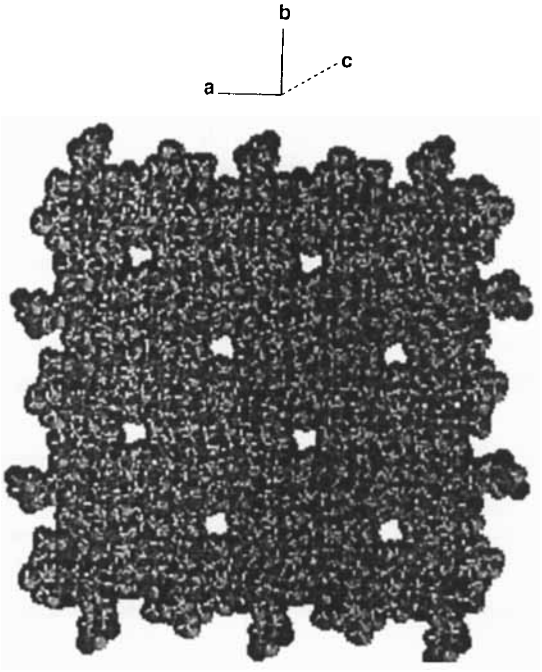

Fig. 11. *Crystal structure of* **IV** *viewed through the* c*-direction traversing two bilayers* (space-filling representation) *showing the tubular voids present in the lattice*

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