Molecular Recognition directed Self-assembly of Ordered Supramolecular Strands by Cocrystallization of Complementary Molecular Components

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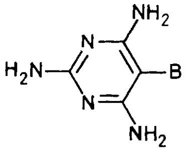
The interaction of two suitably designed complementary ditopic molecular components (**1**, **2**) and (**3**, **4**) generates spontaneously an organized supramolecular architecture displaying molecular sorting and orientation.

The spontaneous generation of organized structures requires the design of molecular components capable of self-assembling into supramolecular species presenting the desired architectural and functional features. The nature of the species obtained will depend on the information stored in the components. In particular, the self-assembling process may be directed by molecular recognition between two or more complementary subunits so as to form a given supramolecular architecture. If these molecular units incorporate specific optical, electrical, magnetic, binding, *etc.* properties their ordering may induce a range of novel features. Among the means to realize molecular organization are the use of molecular backbones (such as polymers, the natural double helix of DNA, or the self-assembled inorganic double helix of helicates[1]), liquid crystalline phases, molecular films and layers, or solid state lattices. Thus, the formation of mesophases may be induced by molecular recognition between suitable components.[2]

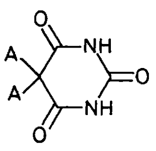
We present here a simple and general concept for generating molecular order. It is based on the recognition directed spontaneous assembling of a supramolecular strand from complementary molecular components each of which presents two identical recognition sites (Figure 1). The interaction of two such units may generate organized polymolecular strands in solution, in a mesomorphic phase, or in the solid state by cocrystallization. In the latter case, recognition based crystal engineering may allow the design of the structure of organic solids. It is seen (Figure 1) that all residues of the same type are located on the same side of the strand, thus providing spontaneous like/unlike *sorting* (into two substrands) and *orientation* of the molecular components in the supramolecular arrangement.

Molecular interactions in the solid state or at surfaces play a basic role in controlling the growth and dissolution of organic crystals,[3,4] the generation of solid state structures,[3,7] and the formation of crystalline inclusion complexes.[5,7]

The formation of a triply hydrogen bonded molecular complex between units of the 2,6-diaminopyridine and uracil type is well documented.[8] Therefore, one may expect 2,4,6-triaminopyrimidine and barbituric acid derivatives, each of



(**1**) B = Bu
(**2**) B = C_8H_{17}



(**3**) A = Et
(**4**) A = Bu

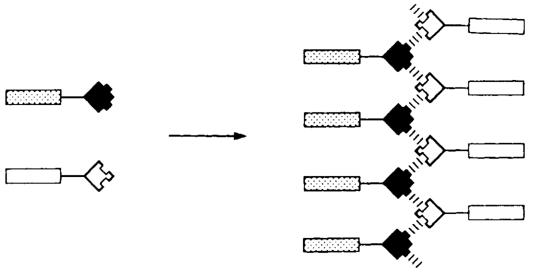
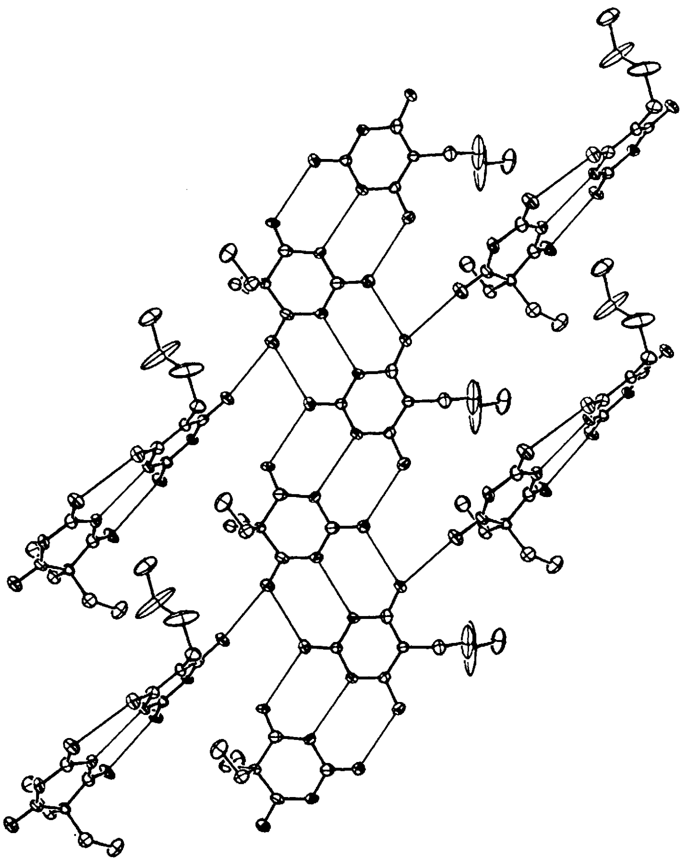
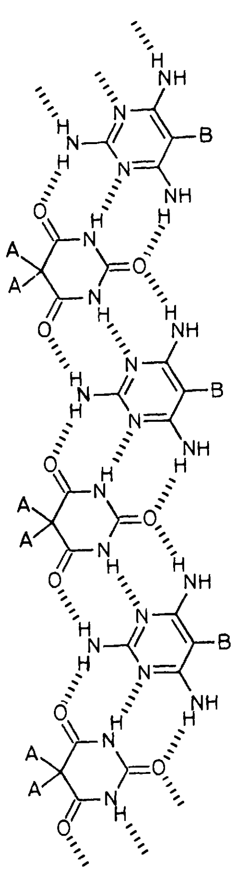


Figure 1. Schematic representation of the formation of an ordered supramolecular strand by the molecular recognition induced association of two different molecular units. Each unit contains a group that possesses two identical binding sites complementary to those of the other unit.





(5)

Figure 2. *X*-Ray structure of the cocrystal of the 1/1 species (5) formed by the components (1) and (3).

which contain two identical subunits of these types, to be able to form extended arrays of three hydrogen bonds. This should lead to the self-assembling of either a cyclic hexamer or a linear oligomeric strand depending on the relative orientation of the components.[6] Each of these supramolecular species has characteristic features and it was therefore of interest to study the interaction between such components both in solution and in the solid state.

The substituted triaminopyrimidines (1) and (2) were obtained by alkylation of malononitrile [NaH, RBr, dimethylsulphoxide (DMSO)] followed by condensation with guanidine.[9] The barbituric acid derivatives (3) and (4) were prepared in the usual way, by condensing the corresponding disubstituted diethylmalonate with urea.[10]

Whereas all four materials (1)—(4) are soluble in chloroform, mixing (1) with one equivalent of (3) or (4) led to the rapid precipitation of a solid that contained equimolar amounts of each component. The same species was formed by mixing non-equimolar quantities of the starting compounds. Solids were also obtained by concentration of 1/1 solutions of (2 + 3) and (2 + 4). All of these cocrystalline solids had significantly higher melting points [215—216 °C for (1 + 3); 268—269 °C for (1 + 4); 207—208 °C for (2 + 3); 215—216 °C for (2 + 4)] than the individual components (1) (200—201 °C), (2) (132—133 °C), (3) (191—192 °C), and (4) (159—160 °C). The 1/1 mixtures of (2 + 3) and (2 + 4) were soluble in $CDCl_3$ and showed appreciable downfield shifts for the NH ^1H NMR signals with respect to the pure compounds. The IR spectrum (KBr) of the (1 + 3) compound contained a very broad N–H stretching band shifted to lower frequencies around 2600 cm^{-1}, which was absent in the components. Both spectral features correspond to what is expected if association by hydrogen bonding occurs.[8,11] The ^{13}C NMR relaxation times of the ring carbons C-4 and C-6 are much shorter for the (2 + 3) mixtures [1.8 s in (2), 3.2 s in (3)] than in the components [14.6 s, for (2), 22.2 s for (3)] indicating a marked increase in molecular size (conc. 6 mM in $CDCl_3$).

Tonometry determinations showed that the apparent molecular weight of the species formed averaged 544 in the 6—24 mM range (in CH_2Cl_2) indicating molecular association. Measurements at higher concentrations require more soluble materials (work in progress).

The crystal structure of the mixed compound (1 + 3) was determined and is shown in Figure 2.† It can be seen that the components (1) and (3) are arranged in mixed supramolecular strands in which each unit forms six hydrogen bonds with its

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† *Crystal data* for (5): $C_{16}H_{27}N_7O_3$, $M = 365.44$, monoclinic, space group *Cc*, $a = 16.230(5)$, $b = 10.088(3)$, $c = 13.554(4)$ Å, $\beta = 124.08(2)°$, $U = 1838$ Å^3, $D_c = 1.321$ g cm^{-3}, $Z = 4$, $\mu(\text{Cu-}K_\alpha) = 7.12$ cm^{-1} (graphite monochromated). A total of 1105 reflections were collected using a Philips PW1100/16 automatic diffractometer. Quantitative data were obtained at −100 °C using a local-build gas flow device. The resulting data set was analysed using an Enraf-Nonius SDP/VAX package.[15] Three standard reflections measured every hour during the data collection period showed no significant trend. The raw step-scan data were converted to intensities using the Lehmann–Larsen method[16] and corrected for Lorentz and polarization factors. The structure was then solved using MULTAN[17] and refined to $R(F) = 0.064$. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

two complementary neighbours, as represented schematically by structure (**5**).[12] Each ribbon-like flat strand is flanked by (**1**,**3**) pairs (belonging to perpendicularly oriented ribbons) that are connected to the strand by a single hydrogen bond and are all oriented in the same direction. Thus, as a consequence of molecular recognition, expressed by the hydrogen bonding pattern between (**1**) and (**3**), *all like residues* A and B are respectively located on the same side of the strand, as represented in Figure 1 and in structure (**5**). This therefore amounts to a spontaneous separation and a parallel orientation of the A and B groups. For a given strand, this arrangement corresponds in one dimension to the two-dimensional organization induced by the formation of oriented molecular layers. One may also consider that the species formed represents a kind of self-assembled 'ladder' polymer[13] of supramolecular nature. Of special significance is the fact that these features should hold not only in the solid state but also in (concentrated) *solution* or in a *mesophase*. The crystal packing consists of sheets of polar molecular strands related to each other by translation. As a result the entire three-dimensional structure becomes polar.

Thus, the recognition interaction between the present complementary components spontaneously induces molecular sorting of like/unlike species and generates long range order, orientation, and left/right differentiation at the molecular level. The process may be considered as the operation of a programmed molecular system that contains the information required for the self-assembling of an organized supramolecular architecture (see also ref. 1).

The arrangement produced may confer specific properties on the material at the macroscopic level. Considering the barbituric unit as the 'assembler' component, mixing it with a triaminopyrimidine derivative should automatically lead to the generation of an *oriented series* of B groups along a strand,‡ thus offering the opportunity of inducing novel properties (optical, electronic, ionic, magnetic, *etc.*). For instance, such a process may allow the designed engineering of (non-centrosymmetric) cocrystals of organic molecules possessing non-linear optical,[14] electron transfer, or energy transfer properties.

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‡ This, of course, only holds if the recognition interactions directing the process are stronger than other interactions in the various species that may be formed.

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