Self-assembly and generation of complexity

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Supramolecular synthesis, by combining molecules through non-covalent interactions, makes it possible to build up extremely sophisticated supramolecular assemblies in the solid state and offers endless architectural possibilities.

Among various openings brought about by supramolecular chemistry, supramolecular synthesis is a domain attracting an increasing number of researchers.[1] Molecular synthesis, the preparation of molecules through interconnection of atoms or groups of atoms by strong covalent bonds, is at the heart of chemistry. By application of synthetic knowledge gathered over the last hundred years, chemists are able to prepare extremely sophisticated biotic molecules found in nature or abiotic molecules designed by man. When taking into account the number of different atoms available and their possible combinations, synthetic chemists have endless possibilities in their hands. Since the beginning of supramolecular chemistry in the late sixties, another synthetic approach based on the use of weak and reversible interactions has been developed. This strategy makes it possible to build up complex supramolecular architectures and is called supramolecular synthesis (Fig. 1). The latter, by combining molecules through non-covalent interactions, also offers endless possibilities.

Self-assembly is a process generating supramolecular entities from molecular components capable of mutual interactions. In that sense, self-assembly may be regarded as a branch of supramolecular synthesis.[2] Self-assembly is a very powerful strategy for the generation of structural and functional complexity. Indeed, in the living world, both structural and functional features of biological assemblies are mainly generated through self-assembly processes.

Self-assembly is a vast domain and covers many different areas. Because of the restricted space available here, we shall only focus on self-assembly processes taking place in the crystalline phase. We will mention a few supramolecular syntheses in the solid state by describing some selected examples, mainly published in *Chemical Communications*, from our group.

The approach we have explored for some 15 years is called molecular tectonics.[3,4] This approach is based on the self-assembly in the solid state of molecular tectons[5] or active construction units bearing in their framework recognition sites. Since we only focus on the generation of molecular networks[6] which are infinite assemblies in the crystalline phase presenting translational symmetry, in order to permit repetition of recognition events to take place, tectons presented in the following examples are programmed units bearing assembling sites oriented in a divergent manner.

In the seven selected examples shown hereafter, we describe how complex architectures have been obtained upon combining rather simple tectons. The main inter-tecton interactions responsible for the formation of networks reported here are either coordination or hydrogen bonds.
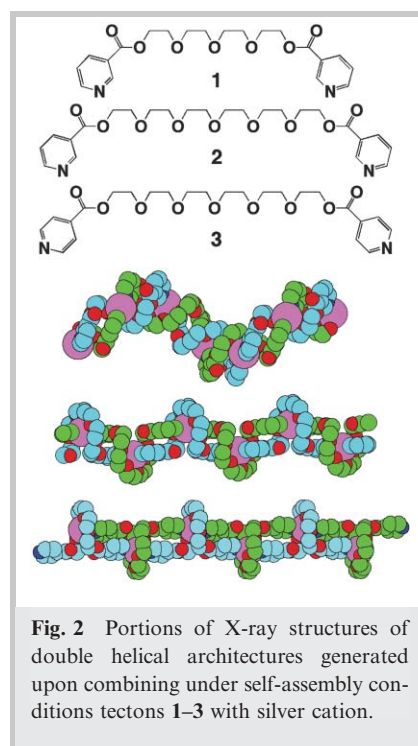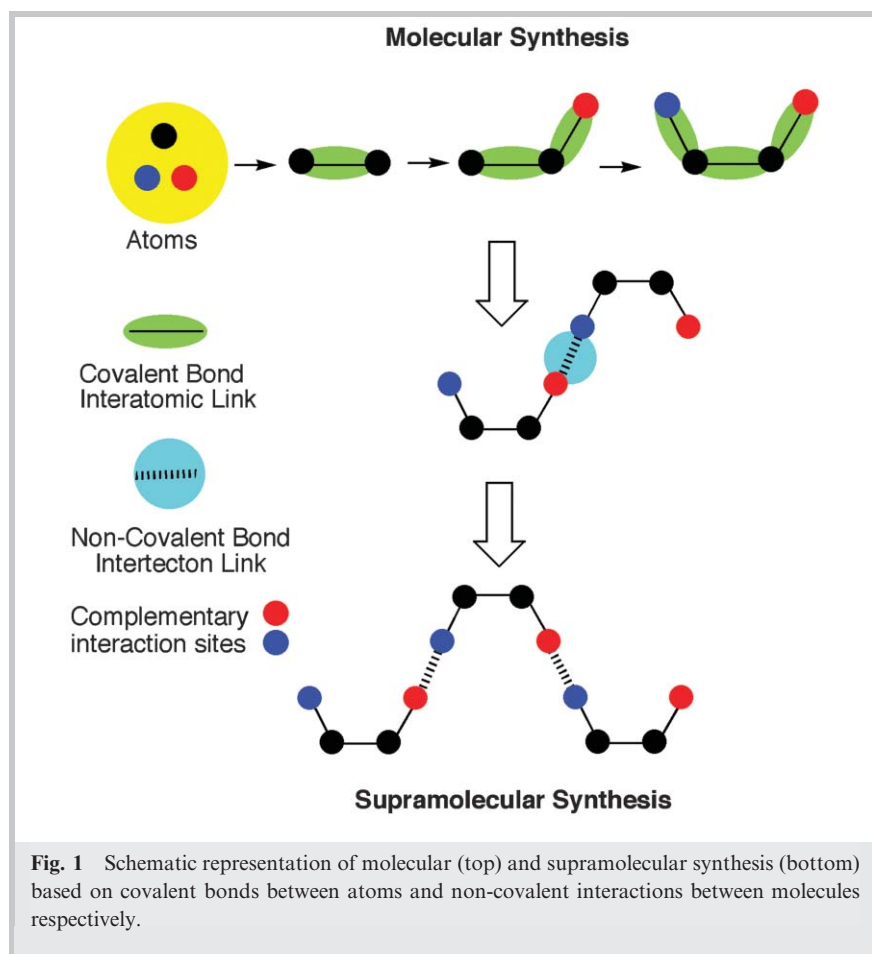
Helical assemblies are fascinating molecular architectures which have attracted considerable interest since the 1950's. Among purely organic helical systems, DNA is certainly the most well known one. The DNA double helix is

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Fig. 1 Schematic representation of molecular (top) and supramolecular synthesis (bottom) based on covalent bonds between atoms and non-covalent interactions between molecules respectively.

Fig. 2 Portions of X-ray structures of double helical architectures generated upon combining under self-assembly conditions tectons **1–3** with silver cation.

formed upon self-assembly of two complementary helical strands. The driving forces for the formation of the DNA double helical arrangement are the establishment of H-bonds between complementary nucleic bases, π–π stacking of the base pairs and hydrophobic effects. However, in principle, any type of attractive interactions may be used to generate double helical architectures. In particular, one may use coordination bonds for the formation of such structures. The design of helical coordination networks is a subject of current interest. Although examples of single stranded helical coordination networks are available in the literature, double helical metalloorganic architectures are rather rare.

For demonstration reasons, let us consider three very simple bis monodentate tectons such as **1**, **2** and **3** (Fig. 2 top) bearing both primary (pyridine derivative) and secondary (oligoethyleneglycol fragments) coordination sites. These homologous tectons differ either in the location of the nitrogen atom on the

pyridine ring or in the length of the spacer. Upon combining the silver cation with these tectons, rather complex helical architectures may be generated under self-assembly conditions (Fig. 2 bottom).[7,8] These structures are double stranded interwoven infinite linear networks formed in the crystalline phase. The formation of these architectures results from the loop type conformation adopted by the polyethyleneglycol spacer which leads to the formation of pseudo crown ethers. The tectons are interconnected by silver cations through coordination bonds formed between Ag$^+$ cation and the nitrogen atom of the pyridine moieties leading to the formation of cationic 1-D coordination networks.

Two adjacent linear networks are interwoven, leading thus to double stranded helical networks (Fig. 3). The driving force for the formation of this peculiar arrangement is related to the loop type disposition of the oligoethyleneglycol units leading to interactions between silver cations belonging to one strand and ether oxygen atoms of the

other strand. Taking into account these interactions, the coordination sphere around the silver cation may be described as comprising two nitrogen (primary sites) and five oxygen atoms (secondary sites).

The fact that topologically equivalent arrangements may be obtained for all three homologous tectons **1–3** clearly demonstrates the robustness of the approach and the non-accidental aspects of the process. Furthermore, by varying either the connecting point on the pyridine ring or the length of the oligoethyleneglycol spacer, the metrics of the double helical strand may be tuned with great precision (Fig. 2 bottom).

The above mentioned example demonstrates the power of self-assembly to generate complex architectures starting from rather simple units.
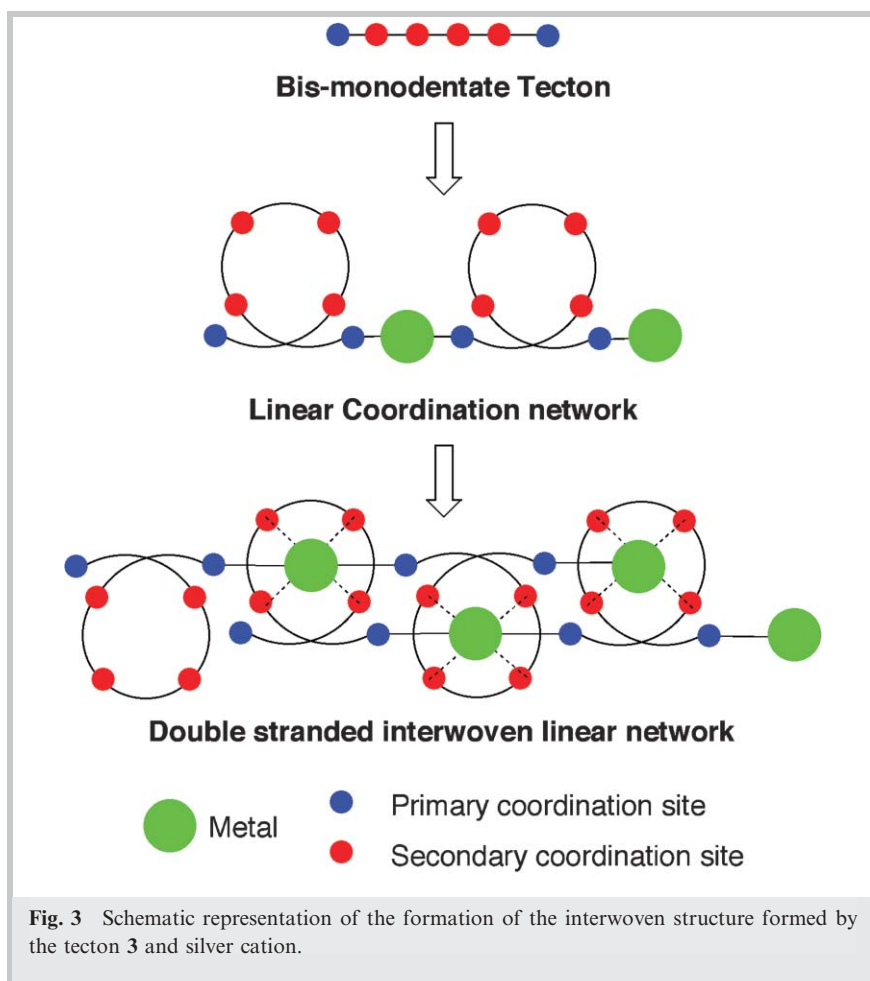
In an isotropic medium, the control of the handedness of helical architectures is of prime importance and a matter of intense investigation. Like those mentioned above, the majority of helical molecular assemblies generated in the crystalline phase are obtained as racemates (a mixture of both P and M helices). This is due to the use of achiral tectons. Indeed, for all three non oriented tectons **1–3** mentioned above, the left and right orientations of the oligoethyleneglycol fragments are equiprobable

Fig. 3 Schematic representation of the formation of the interwoven structure formed by the tecton **3** and silver cation.

Fig. 4 Portions of X-ray structures of single stranded (top) and triple stranded (bottom) helical architectures generated under self-assembly conditions upon combining tectons **4** and **5** respectively with HgCl$_2$.
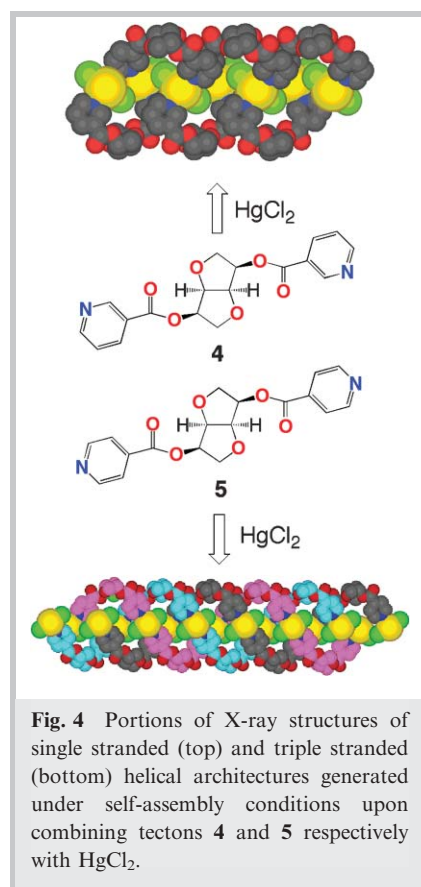
and thus in all three cases both the left- and right-handed helices are formed.

In order to control the spatial orientation of the helical strand, one may use enantiomerically pure tectons such as **4** and **5** (Fig. 4).[9,10] These two building blocks are based on an enantiomerically pure *iso*mannide backbone to which two pyridines as coordination sites have been connected. The two tectons **4** and **5** differ only in the position of the ester junction between the sugar and the pyridine ring. Owing to the *cis*-junction of the two five-membered rings, both tectons **4** and **5** adopt a ''roof''-type shape thus leading to a divergent orientation of the two coordination sites on the same face of the backbone.

Under self-assembly conditions and in the presence of HgCl$_2$, the tecton **4** generates an enantiomerically pure 1-D coordination network of the helical type in the solid state (*C2* space group, monoclinic system). As expected, the mutual interconnection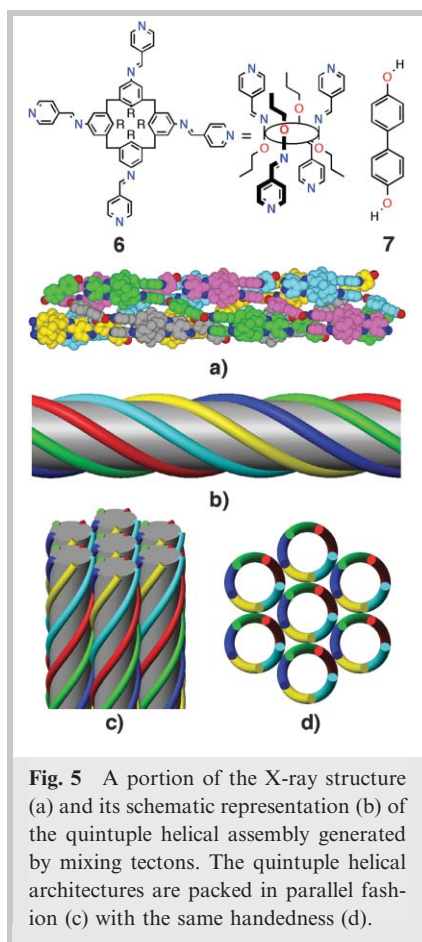 between the tecton **4** and HgCl$_2$ leads to an enantiomerically pure neutral single stranded infinite helix with P helicity (Fig. 4 top). The observed P helicity results from the defined stereochemistry of the *iso*mannide unit and consequently of the tecton **4**. Furthermore, the *syn*-parallel packing of the single stranded helices leads to the formation of a polar crystal. Interestingly, when combining HgCl$_2$ with the tecton **5**, which differs from the tecton **4** only in the orientation of the nitrogen atom of the two pyridine rings, under the same conditions, again an enantiomerically pure helical architecture is obtained in the crystalline phase (Fig. 4 bottom). However, in marked contrast with the case of **4** mentioned above, three infinite helical strands with P chirality self-assemble into a triple stranded non-cylindrical architecture through aromatic/aromatic interactions. The triple stranded helices are packed parallel to each other and are further interconnected through O–Hg interactions.

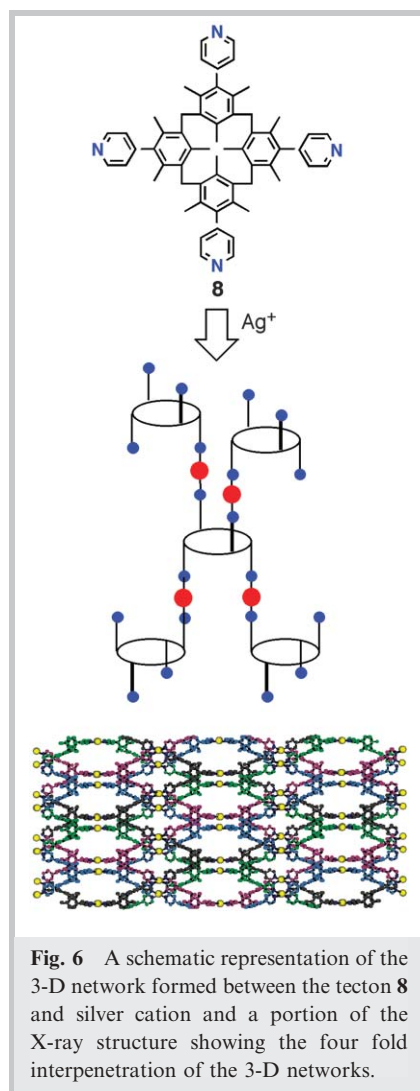Let us consider an even more relevant case of generation of complexity from rather simple tectons. A molecular unit possessing four H-bond acceptor sites occupying the apices of a pseudo-tetrahedron was used for the formation of helical networks in the presence of H-bond donors possessing two divergently oriented polarised hydrogen atoms. The design of such a tecton is based on the calix[4]arene backbone. By first functionalising all four hydroxy groups with *iso*propyl groups, the 1,3-alternate conformation is imposed. The amination of the upper rim followed by the introduction of four pyridines using imine junctions leads to the tecton **6** (Fig. 5). Because of the 1,3-alternate blocked conformation of the calix backbone, the four pyridine moieties behaving as H-bond acceptors are located in an alternating mode below and above the main plane of the calix skeleton.[11]

Upon combining the tetra-H-bond acceptor tecton **6** possessing an *S4* screw axis with the di-H-bond donor unit **7**, a quintuple helical arrangement is obtained in the crystalline phase (Fig. 5a and b). The formation under self-assembly conditions of this complex architecture

Fig. 5 A portion of the X-ray structure (a) and its schematic representation (b) of the quintuple helical assembly generated by mixing tectons. The quintuple helical architectures are packed in parallel fashion (c) with the same handedness (d).

may be described as resulting from four different levels of molecular organisation. First level: the formation of a single stranded H-bonded helical network through the establishment of H bonds between the acceptor **6** and donor **7**. Second level: the formation of the quintuple helical braided network through the packing of the single stranded helical networks (Fig. 5c). Third level: the lateral association of quintuple helical networks into the compacted solid (Fig. 5c). Finally the fourth level of organisation is associated with the spontaneous resolution. Indeed, for a given crystal, all helical strands are oriented in the same direction (Fig. 5d). However, the overall mixture of crystals is a racemate.

Interpenetration is another interesting example of structural complexity. Although many examples of interpenetrated networks have been reported,[12] the mechanism of the formation of these architectures remains unclear. In other words, in general, we are lacking a stepwise scenario. The [1,1,1,1]metacyclophane is an interesting backbone.

Fig. 6 A schematic representation of the 3-D network formed between the tecton **8** and silver cation and a portion of the X-ray structure showing the four fold interpenetration of the 3-D networks.

Indeed, this skeleton, for steric reasons, is blocked in the 1,3-alternate conformation over a vast range of temperature. Furthermore, this unit presenting an S_4 axis of symmetry offers the possibility of anchoring four pyridine units in the alternating fashion *i.e.* two above and two below the main plane of the cyclophane (Fig. 6).

Upon combining the tecton **8** with Ag^+ cation, a 3-D cationic coordination network is obtained.[13] This network results from interconnection of consecutive tectons **8** by silver cation adopting the linear coordination geometry. The assembling node responsible for the formation of the architecture is based on coordination bonds established between the nitrogen atom of the pyridine and the silver cation. The 3-D network results from two translations of the assembling node into two perpendicular directions of

space (Fig. 6 middle). Interestingly, the cationic 3-D networks are interpenetrating each other with a fourfold interpenetration order (Fig. 6 bottom). For the case mentioned here, it seems that the interpenetration does not only take place in order to occupy the empty space generated by individual 3-D networks, but results also from silver–silver interactions (dAg^+–Ag^+ of 3.08 Å).

The design and generation of robust hybrid porous crystalline materials with controlled pore size still remains a challenge. The interest in this type of material results from numerous applications such as specific sorption, gas storage and separation, ion exchange and catalysis that such architectures may offer. One of the major difficulties associated with porous crystalline solids is the loss of structural integrity upon removal and/or exchange of guest molecules occupying the pores.

The metallaporphyrin **9-Zn** (Fig. 7)[14] is a self-complementary tecton containing both a metal centre capable of further coordination and two pyridines as extra coordinating sites. This tecton self-assembles in the crystalline phase into a 3-D coordination network presenting hexagonal channels. The formation of this architecture results from the self-interconnection of the tectons through the formation of Zn–N bonds between the metal centres adopting a distorted octahedral geometry and pyridine units.

The hexagonal channels are filled with solvent molecules. What seems to be remarkable for this complex arrangement is the fact that the structural integrity of both the empty and solvent inclusion frameworks is maintained. Furthermore, the guest exchange between different solvates and empty framework takes place both in solution and through the vapour phase *via* single-crystal-to-single-crystal transformations.

Finally, a last example of the generation of complexity by self-assembly processes. In this example, a further step consisting of bridging the gap between microscopic and macroscopic levels is achieved. Forming composite crystals, *i.e.* growing further crystalline layers on preformed crystals, is a topic of current interest because of potential applications in optics and magnetism for example.

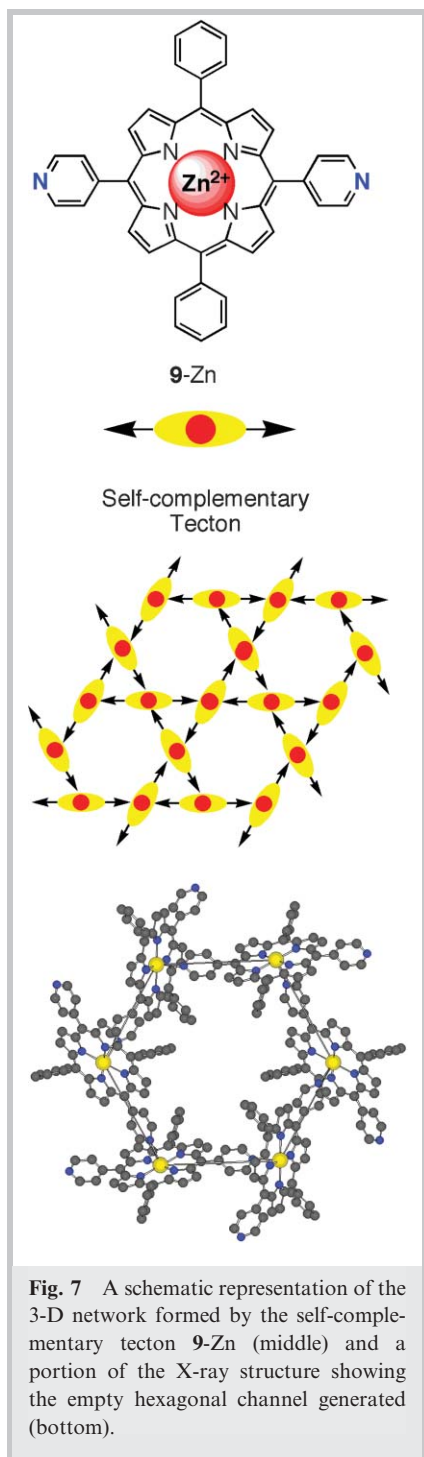Upon combining cationic H-bond donor tectons[15] such as **10** with

Fig. 7 A schematic representation of the 3-D network formed by the self-complementary tecton 9-Zn (middle) and a portion of the X-ray structure showing the empty hexagonal channel generated (bottom).
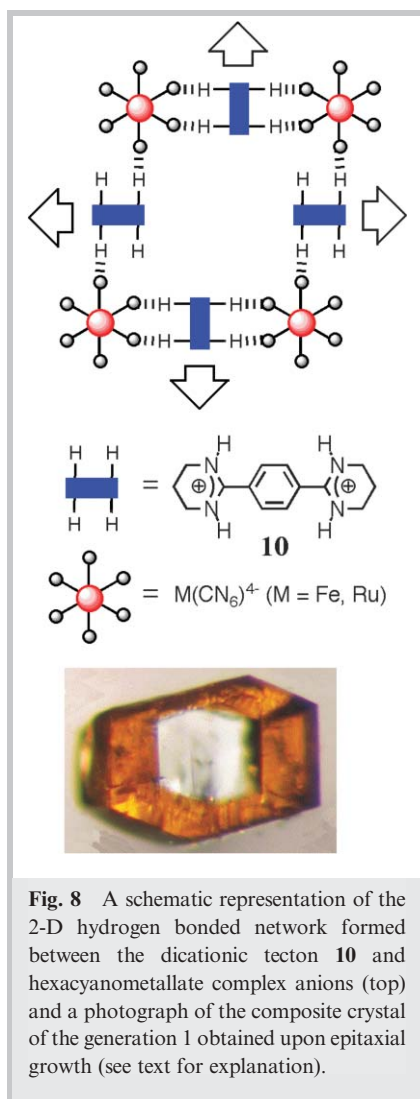

Fig. 8 A schematic representation of the 2-D hydrogen bonded network formed between the dicationic tecton 10 and hexacyanometallate complex anions (top) and a photograph of the composite crystal of the generation 1 obtained upon epitaxial growth (see text for explanation).

$[M^{II}(CN)_6]^{4-}$ (M = Fe or Ru) complex anions, two analogous 2-D H-bonded networks resulting from the interconnection of octahedral anionic units by two dicationic tectons 10 through both a chelate and a monohapto mode of H-bonding (Fig. 8 top) are obtained. Interestingly, both crystalline materials

are isomorphous (same crystal system, space group and almost identical unit cell metrics). This analogy was explored for the formation of crystals of crystals through epitaxial growth of crystalline layers on preformed crystals. For example, starting with crystals of $[10\text{-}Ru(CN)_6]$ considered as generations $G_0(Ru)$, the next generation $G_1(Ru,Fe)$ was obtained upon immersing the preformed crystals G_0 into a solution containing the same tecton 10 and $[Fe(CN)_6]^{4-}$ (Fig. 8 bottom).[16] Interestingly, the reverse, i.e. fabricating $G_1(Fe,Ru)$ from $G_0(Fe)$, was also achieved. Furthermore, by repeating the epitaxial growth process, higher generations (up to four) were obtained.[17]

Through a restricted selection of examples, we brushed some aspects of the self-assembly approach based on supramolecular synthesis in the crystalline phase. These representative examples were taken for demonstration purposes. They clearly demonstrate the power of self-assembly to generate complex architectures from rather simple informed and active molecular building blocks. Understanding abiotic self-assembly is an important challenge for molecular and supramolecular chemists. Mastering self-assembly processes will, without doubt, lead to extremely sophisticated molecular architectures. Furthermore, through the incorporation of specific physical and/or chemical properties, this approach will lead to functional architectures presenting collective properties which will be exploited in specific applications such as separation, decontamination, sensing, catalysis and the fabrication of optical, magnetic and electronic devices.

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