Self-assembly of double helical, triple helical and deoxyribonucleo-helicate architectures

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Supramolecular chemistry [1,2], the chemistry of non-covalent intermolecular interactions, is essential for biological processes such as molecular recognition, catalysis and transport. In biology, such interactions rely on the use of more or less preorganized molecular receptors. Can chemists go one step beyond preorganization by designing systems that can undergo molecular self-organization, in other words systems capable of spontaneously generating a well-defined supramolecular architecture by self-assembly from their components in a given set of conditions? To do this the molecular information necessary for the process to take place and the program that it follows must be stored in the components and operate according to an algorithm based on molecular recognition events. Thus, these systems may be termed programmed supramolecular systems [3].

In recent progress toward this goal, molecular information and recognition has been used as a means of controlling the generation of supramolecular species from individual components. Thus, suitable components can be designed to self-organize and spontaneously assemble into the desired final superstructure.

Self-assembly has been implemented in several types of organic and inorganic systems [2–5]. In particular, linear oligobipyridine ligands have been designed so that, in the presence of appropriately selected metal ions (such as $\mathrm{Cu^{I}}$ and $\mathrm{Ni^{II}}$), they spontaneously generate inorganic double [6] and triple [7] helices, termed helicates (Fig. 1a and b). The self-assembly of these components shows positive cooperativity. The type of helix resulting from self-assembly is determined by the structural features (information) of the ligands and the coordination (tetrahedral or octahedral) geometry (algorithm) of the metal ions.

Once components that self-organize into helices were available, the possibility of connecting nucleosides to the oligobipyridine backbone became particularly attractive. In this way artificial oligonucleosides such as oligothymidine could be designed which might interact with natural polynucleotides or nucleic acids. On treatment with $\mathrm{Cu^{I}}$, oligothymidine strands gave double-helical complexes representing inside-out analogues of double-stranded nucleic acids, which we called deoxyribonucleo-helicates (DNH) [8] (Fig. 1c). The DNH complexes are double-helical oligonucleosides formed spontaneously by self-assembly of two suitably designed ligand strands and copper(I) ions. In contrast to DNA, they have positive charges located inside the strands, and the information-bearing nucleobases are on the outer spine of the double helix, pointing away from its axis. They should be able to interact with other species both electrostatically and by hydrogen bonding through the thymidines. In particular they might bind to both single-stranded and double-stranded nucleic acids forming mixed natural-artificial triple- and quadruple-stranded species. Such interactions could be selective, determined both by the overall shape of the DNHs and by the attached recognition groups.

In a study of helicate self-assembly from a mixture of different ligands and metal ions, it has been found that only the 'correct' double or triple helical complexes are formed through self-recognition [9]. This points to a change in paradigm from 'pure compounds' to 'instructed mixtures' — that is, from seeking chemical purity to designing programmed systems composed of mixtures of instructed components capable of spontaneously forming well-defined superstructures without interference or crossover. One might predict that this trend will represent a major line of development of chemistry in the years to come: the spontaneous but controlled buildup of structurally organized and functionally integrated supramolecular systems from a pre-existing 'soup' of instructed components following specific programs and interactional algorithms.

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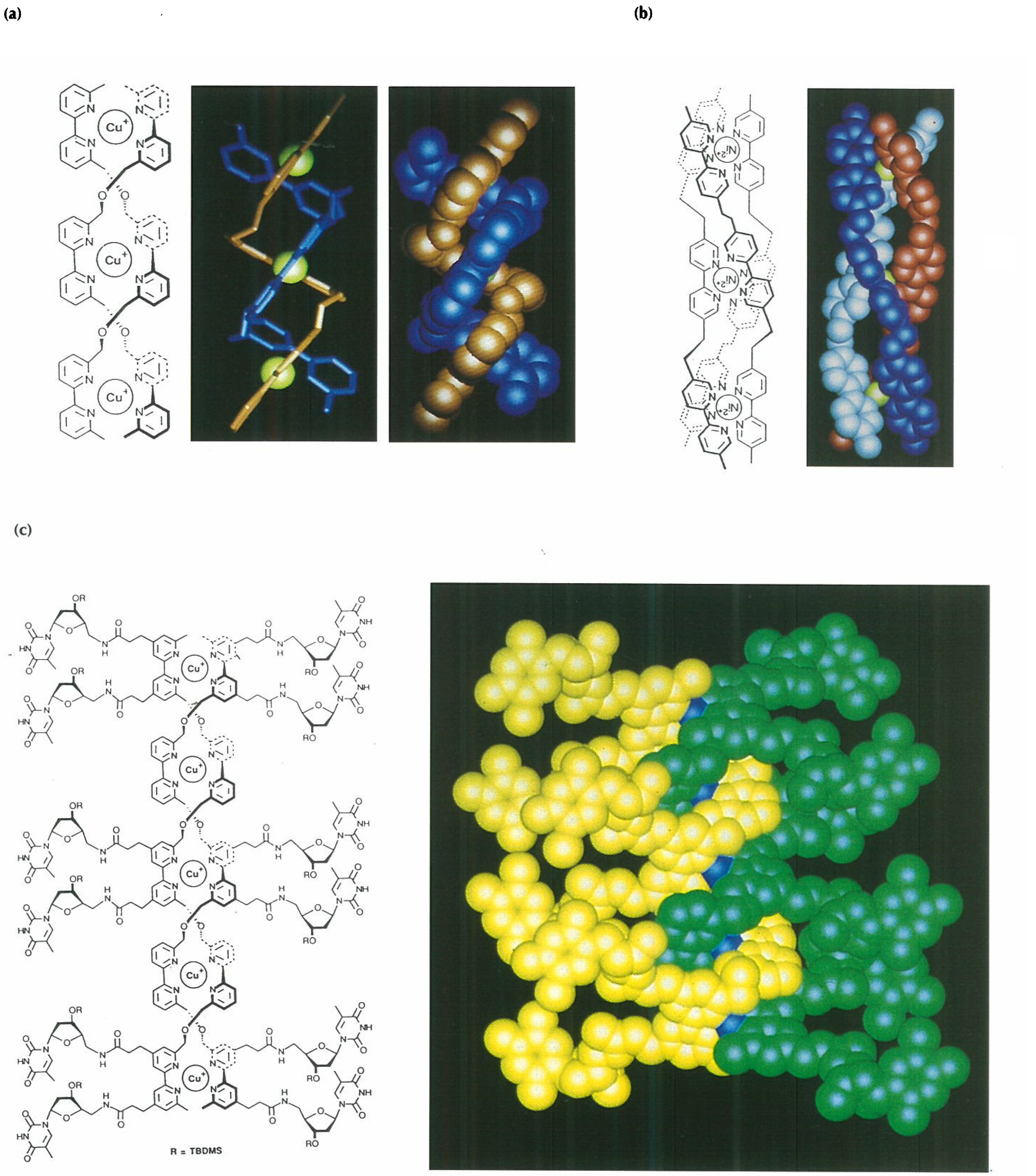

Fig. 1. (a) Double helicate (left) and its crystal structure (center and right), formed from two strands of a specific tris bipyridine ligand and three Cu^{I} ions (yellow). **(b)** Triple helicate (left) and its crystal structure (right), formed from three strands of a modified linear tris bipyridine ligand and three Ni^{II} ions (yellow). **(c)** Structural (left) and computer model (right) representation of the deoxyribonucleo-helicate (DNH) formed from two hexathymidine-pentabipyridine strands and five Cu^{I} ions (blue).