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# Supramolecular Control of Structure and Reactivity

*Perspectives in  
Supramolecular Chemistry  
Volume 3*

*EDITED BY ANDREW D. HAMILTON*

*University of Pittsburgh, USA*

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# **Supramolecular Control of Structure and Reactivity**

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# Contents

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<b>Contributors</b>	vii
<b>Preface</b>	ix
<b>1 Metal Template Control of Self-Assembly in Supramolecular Chemistry</b> John R. Fredericks and Andrew D. Hamilton	1
<b>2 A Survey of Supramolecular Chemistry (1993–1994)</b> Uday Maitra	41
<b>3 Control of Reactivity in Aggregates of Amphiphilic Molecules</b> Paolo Scrimin	101
<b>4 Models of Hemoprotein Active Sites</b> Michel Momenteau	155
<b>5 Recent Developments in the Design of Self-Replicating Systems</b> Edward A. Wintner and Julius Rebek Jr	225
<b>6 Synthetic Control of DNA Triplex Structure Through Chemical Modifications</b> Krishna N. Ganesh, Vijayanti A. Kumar and Dinesh A. Barawkar	263
<b>Cumulative Author Index</b>	329
<b>Cumulative Title Index</b>	331
<b>Index</b>	333





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# Preface

In recent years there has been an explosion of interest in the burgeoning new field of supramolecular chemistry. Building on the pivotal work of Pedersen, Cram and Lehn, scientists from many nations have been investigating the chemistry of noncovalent interactions. Particular focus has been placed on the design of synthetic molecules that can mimic biological systems and achieve significant recognition or catalytic activities. Crucial for success in this endeavor is an understanding of the interplay between different binding interactions and how they contribute to the recognition of ground state or transition state structures. What can be learned from or achieved with artificial receptor molecules and why is this study important in the context of biochemical processes? This is a critical question at the heart of all modern supramolecular chemistry research and the answer is manifold. While the study of the natural system may answer “how” an enzyme functions, the study of small synthetic analogs can help us understand “why” it works. Small molecule mimics of biological function provide an opportunity to study the intrinsic chemistry of molecular recognition and catalysis away from the complex environment of a biopolymer. Small molecules provide considerably greater detail and precision in the study of their structure and of the thermodynamics and kinetics of their recognition interactions. Modifications can be easily made to the position, orientation and nature of binding groups as well as the solvent environment, leading to new insights into the underlying chemistry of the biological process. Understanding the “why” of an enzyme function gives us not only increased mechanistic understanding but also the ability to reproduce biological levels of reactivity in synthetic systems.

This book provides a broad view of the different approaches that have been taken to control structure and reactivity in supramolecular systems. Six researchers from around the world describe different approaches to novel supramolecular systems ranging from amphiphiles with catalytic activity to synthetic entities that recognize and bind to the major groove of DNA. Other

contributions describe the use of metal templates to construct synthetic receptors and also the design of molecules with the capacity for self-replication. A comprehensive discussion of the use of small molecule models of heme protein function is also included as well as a review of recent contributions in the general area of supramolecular chemistry.

Andrew D. Hamilton  
Pittsburgh  
May 1996

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# Chapter 1

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## Metal Template Control of Self-Assembly in Supramolecular Chemistry

*JOHN R. FREDERICKS AND ANDREW D. HAMILTON*

*University of Pittsburgh, PA, USA*

### 1. INTRODUCTION

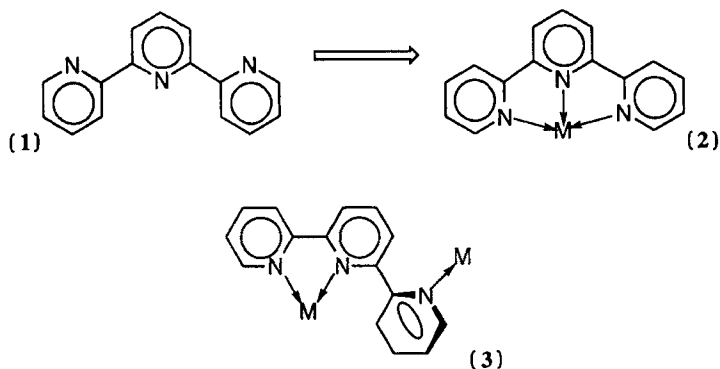
There is enormous current interest in the development of molecules that self-assemble into aggregates of well-defined shape and function [1]. A key to success is the identification of both strong and directional binding forces to hold together the different components of the structure. To this end, extensive use has been made of intermolecular hydrogen bonds [2],  $\pi$ - $\pi$  stacking interactions [3] and metal-ligand coordination (the subject of this review) to build large, multicomponent aggregates. Such structures form the foundation of the burgeoning field of nanoarchitecture. Self-assembled systems have been designed which can act as host molecules for organic guests [4] and enclathrating agents [5]. A molecule has been developed that can act as a molecular abacus [6], and various modular strategies to the formation of molecular building sets have been proposed [7,8]. Although the long-term goal of much of this work is the design of functioning devices, important progress is also being made in understanding the factors that influence the formation of self-assembled aggregates. For example, recent studies have emphasized the role of preorganization [9-11], analyzed the detailed thermodynamics and kinetics of self-assembly [12], incorporated error-checking mechanisms into aggregate formation [13] and demonstrated cooperativity [14].

Metal–ligand coordination has been widely utilized in designing self-assembling aggregates. In this chapter, we will first give an overview of the use of metals to control the formation of novel structures, and then describe their role in the design of some functioning aggregates. There are several factors which influence the self-assembly process for these structures: the nature of and substitution pattern on the ligand, the ability of an aromatic ligand to  $\pi$ -stack with itself or other ligands, and the stereochemical preference of the metal ion. This last factor has been shown to be the most important in determining the final shape and structure of a templated aggregate, though the other two factors certainly have an effect.

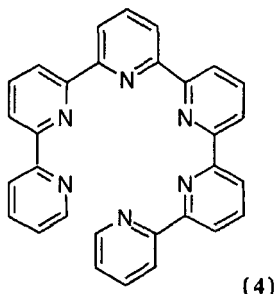
## 2. METAL TEMPLATE CONTROL OF SUPRAMOLECULAR STRUCTURE

### 2.1 Self-Assembly of Double- and Triple-Helical Structures

The ability of certain metal ions to coordinate with pyridine has been used in designing various double-helical structures. Linking three pyridine rings produces the molecule 2,2':6',2''-terpyridine (terpy). In the solid state, terpy takes a planar *trans,trans*-conformation (1). Coordinating terpy with most metal ions causes the ligand to adopt a planar *cis,cis*-conformation (2). To use oligopyridines to form helices, the rings must be induced to take up a nonplanar or “twist” geometry. This type of conformation can be induced by coordinating two metals to the terpy. The steric and electrostatic repulsion of the metal centers leads to a twist geometry as shown in (3) [15].



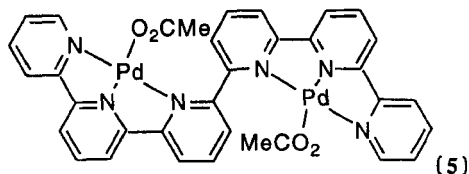
Using the longer oligopyridine ligand 2,2':6',2'':6'',2''':6''',2''':6''''-sexipyridine (spy) (4), Constable *et al.* have shown that some metal ions can induce the formation of double-helical aggregates. In particular, (4) was allowed to complex with six different metal ions and the resultant structure of each aggregate was determined [16].



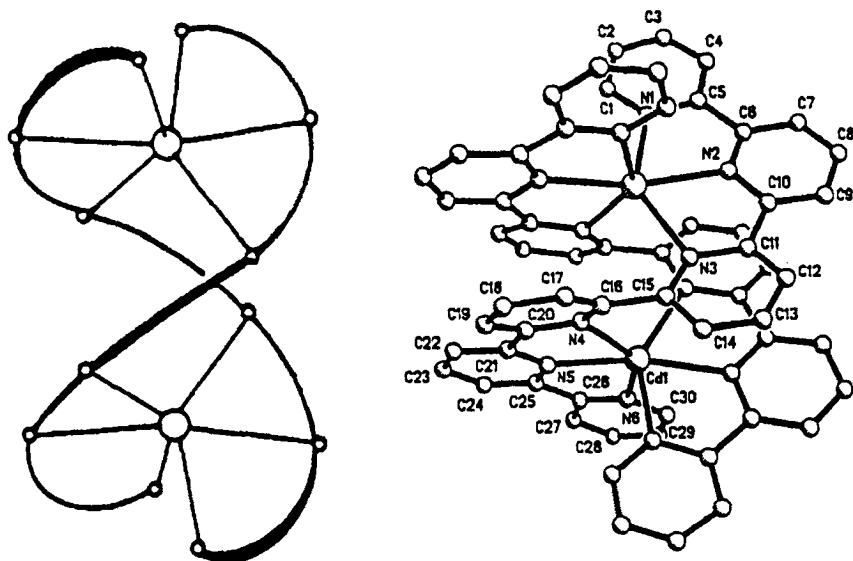
When the ligand was allowed to react with manganese(II) acetate, a complex of formula  $[\text{Mn}_2(\mathbf{4})_2][\text{PF}_6]_4$  resulted. This was determined to be a double helix, with each manganese atom displaying six-coordinate geometry. Evidence for the formation of a double helix was found in the cyclic voltammetry and electron spin resonance (ESR) data. The voltammogram revealed four well-separated reductions, but no oxidation wave. The aggregate may be stabilized with respect to reduction because of the close proximity of the two manganese(II) centers. ESR data suggest that both manganese atoms are in identical environments and that there is a magnetic interaction between them. The complex formed between iron(II) and (4) behaved similarly, though it was not as resistant to oxidation as the manganese complex.

The crystal structure of the complex between (4) and cadmium(II) also shows the formation of a double-helical structure between two equivalents of ligand and two equivalents of metal ion (Figure 1). Both left-handed and right-handed helices form. The two cadmium(II) ions are in identical six-coordinate sites. The metal-metal distance of 4.173 Å (1 Å = 0.1 nm) does not permit direct cadmium-cadmium interactions. It is notable that ligand (4) arranges itself so that stacking interactions are present. Data from the  $^1\text{H}$  nuclear magnetic resonance (NMR) spectra suggest that this complex persists in solution.

The importance of octahedral, six-coordinate geometry in helix formation was established in the reaction of (4) with the normally four-coordinate square planar palladium(II). This forms a 1:2 ligand:metal complex as in (5), with each palladium(II) in a distorted square planar environment.



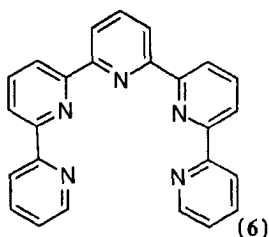
A complex of the formula  $[\text{Cu}_3(\mathbf{4})_2][\text{PF}_6]_3$  results from the reaction of (4) with Copper(I). Molecular models and  $^1\text{H}$  NMR data suggest the structure shown in Figure 2, with each copper (I) ion in a distorted tetrahedral environment.



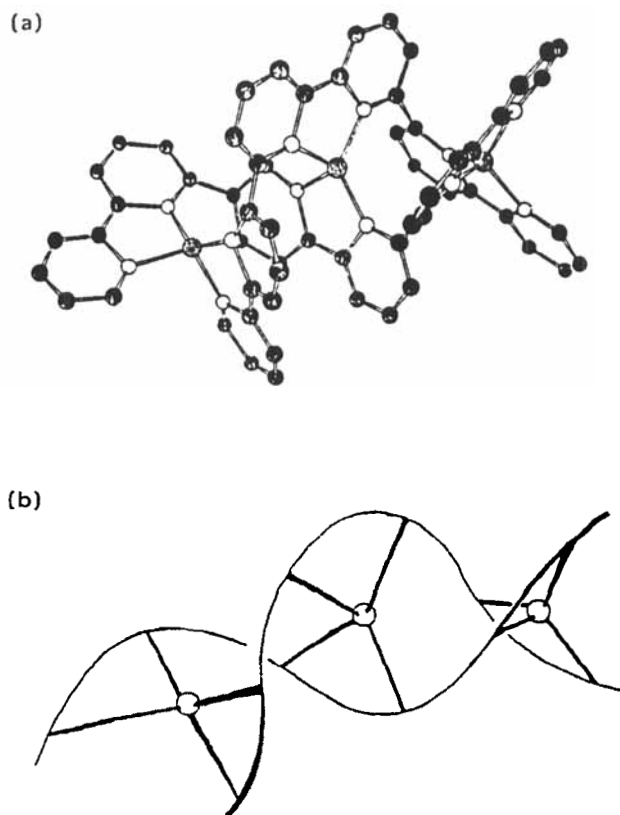
**Figure 1** Structure of the double-helical complex formed between (4) and cadmium(II). Reproduced by permission from *J. Am. Chem. Soc.* **112**, 1256–1258 (1990)

The stoichiometry of the complex formed between silver(I) and (4) is the same as for the copper(I) complex, although the structures are unlikely to be identical. The silver(I) ion has a radius over 30% larger than copper(I), so one ligand must “slip” relative to the others to accommodate three silver(I) ions [17].

Most self-assembled helices have been constructed using only a single type of metal ion. Constable and Walker have designed a helix which contains two different metals using the quinquepyridine (qpy) (6) as the ligand. Two qpy ligands can provide only 10 metal-coordinating sites. Thus, in a double-helical structure one site will be appropriate for a six-coordinate metal with pseudooctahedral geometry and the other for a four-coordinate metal with pseudotetrahedral geometry. When methanolic or ethanolic solutions of  $[\text{Co}(\text{6})(\text{MeCN})_2]^{2+}$  were treated with  $\text{Cu}^+$  or  $\text{Ag}^+$ , complexes  $[\text{CoAg}(\text{6})_2]^{3+}$  and  $[\text{CoCu}(\text{6})_2]^{3+}$  were formed. Cyclic voltammetry, fast-atom bombardment mass spectrometry (FABMS) and  $^1\text{H}$  NMR all gave data consistent with the formation of a heterobinuclear double-helical complex [18].

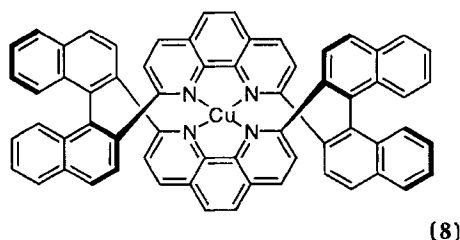
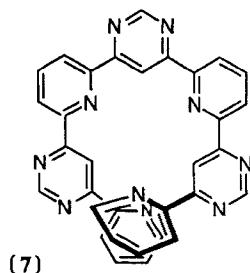




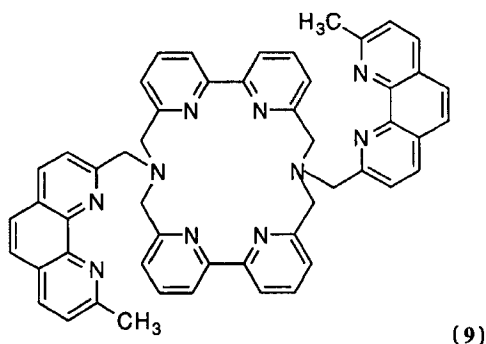


**Figure 2** Proposed structure (a) for the cation  $[\text{Cu}_3(4)_2]^{3+}$  together with a schematic representation (b). Reproduced by permission of the Royal Society of Chemistry

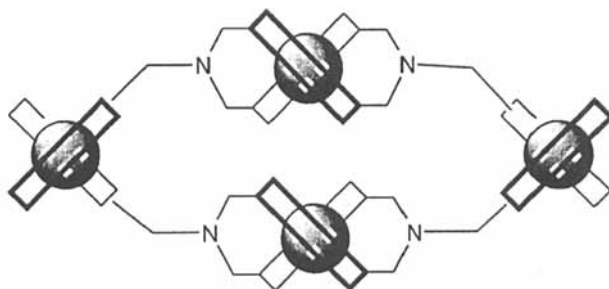
The propensity for double-helix formation in these complexes is so strong that the metals can be used to template the synthesis of the oligopyridine ligands [19]. The combination of one sexipyridine ligand (4) and nickel(II) templates the coupling of two terpyridines. Demetalating the complex using aqueous KCN gives (4) in an overall yield of 50%, much improved over the nontemplated method. Lehn and coworkers have recently shown that incorporation of alternating pyridine–pyrimidine groups into a ligand, such as (7), leads to electrostatic repulsion of the nitrogen atoms and significant stabilization of a helical structure, even in the absence of metal ions [20]. The helical environment for metal coordination can also be imposed by covalent connections, as Cram and coworkers have shown in the combination of phenanthroline and binaphthyl subunits in (8) [21].



All of the helices we have seen to this point have been constructed using ligands which have two or more identical metal-binding sites connected by spacers. A self-assembling double helix has been designed around a ligand (9) which contains two distinct transition metal-binding sites. This ligand can coordinate one metal ion in the central pyridine-based macrocycle, and two more metal ions with its phenanthroline sidearms. The metal ions complexed by the sidearms are then free to complex with another ligand and form a double helix. Reaction of (9) with excess copper(I) gave a helicate structure in the solid state, as shown in Figure 3. Each copper(I) ion is in a distorted tetrahedral environment, and the overall symmetry is  $C_2$ . The structure persisted in solution according to  $^1\text{H}$  and  $^{13}\text{C}$  NMR, FABMS and ultraviolet (UV)-visible spectroscopy. The  $^1\text{H}$  NMR titration data show that the helix is the only species present, indicating positive cooperativity for the helicate formation. A similar helicate was confirmed in solution for the product of ligand (9) and excess silver(I) ion [22].

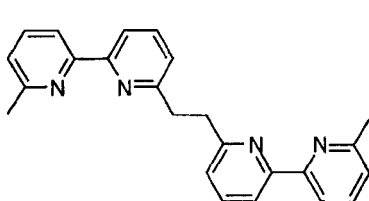


Lehn and coworkers have designed many double-helical compounds. Copper(I), cobalt(II) and iron(II) were allowed to complex with the ethylene-bridged bis(bipyridine) (10) and bis(phenanthroline) (11) to examine the stereochemical preferences of the metal ions. When ligand (10) was treated with copper(I), a complex of 2:2 stoichiometry (molecular weight confirmed by

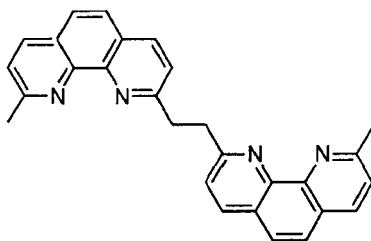


**Figure 3** Schematic structure of the helical aggregate between (9) and Copper(I)

FABMS) with a double-helical conformation was formed (Figure 4). Each copper atom possesses a distorted tetrahedral geometry, and the complex was shown to persist in solution by  $^1\text{H}$  NMR and cyclic voltammetry. In contrast, when ligand (11) was treated with cobalt(II), a 1:1 complex was formed. The crystal structure reveals that the aggregate is not a double helix, and the cobalt possesses a distorted octahedral geometry [23].

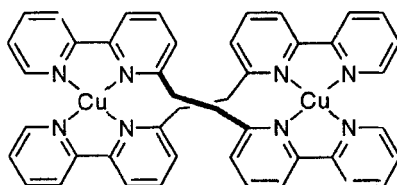


(10)



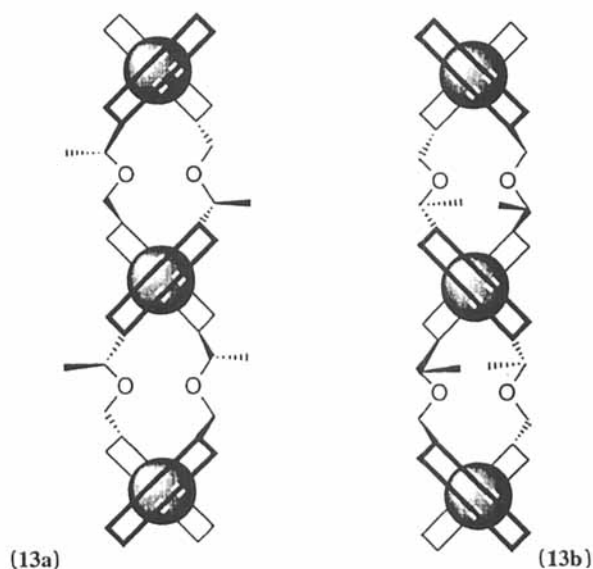
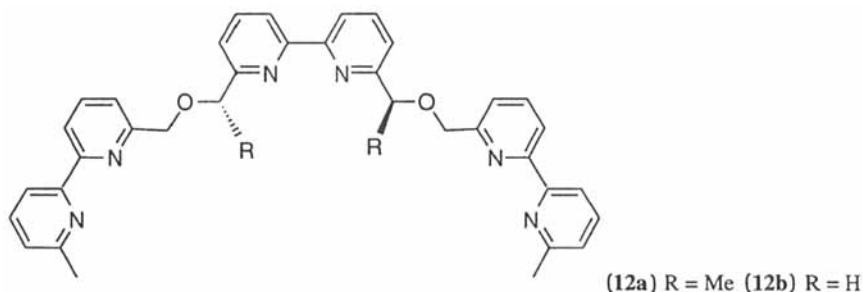
(11)

This metal–bipyridine motif was used to design a self-assembling chiral helix. The strategy was to incorporate stereogenic centers directly on the backbone of the ligand. Ligands (12a) and (12b) were synthesized and allowed to react with copper(I) and silver(I). FABMS and UV–visible spectra showed that both copper(I) and silver(I) formed 2:3 ligand:metal complexes with both ligands. Achiral (12b) gave, as expected, a racemic mixture of right-handed and left-



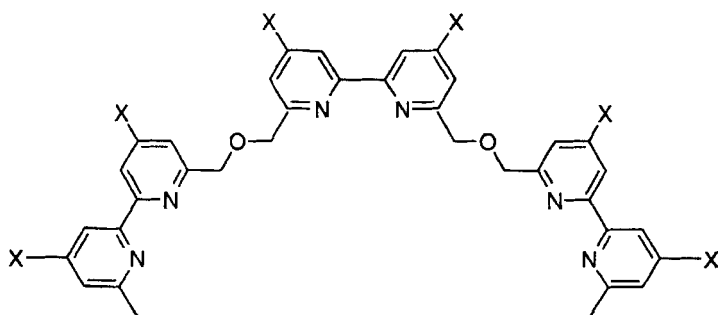
**Figure 4** Representation of the structure of  $[\text{Cu}_2(\text{10})_2]^{2+}$

handed helices. However, chiral (**12a**) would be expected to lead to preferential formation of one diastereomeric helix. The circular dichroism (CD) spectrum of  $[\text{Cu}_3(\mathbf{12a})_2]^{3+}$  displays a strong, positive Cotton effect. This, along with the  $^1\text{H}$  NMR data, points to a very high helical induction (95%). Consideration of space-filling and preliminary molecular mechanics calculations suggested that the complexes take the conformation of a right-handed helix as in (**13a**) rather than the left-handed diastereomer (**13b**) [24].

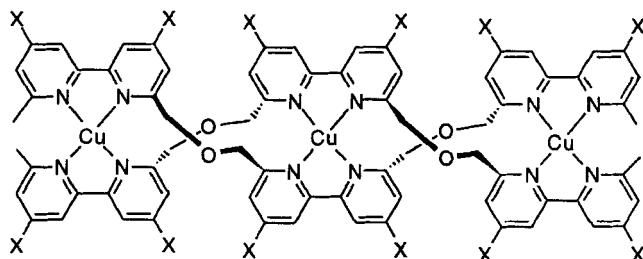


Related double-helical metal complexes have been used to investigate the role of cooperativity in self-assembly. Ligands (**14a**) and (**14b**) were allowed to react with  $\text{CuBF}_4$  to form the corresponding helicates (**15a**) and (**15b**). The formation of helicates (**15a**) and (**15b**) was confirmed in solution by spectrophotometric titration. Two sharp isosbestic points are seen in the spectrum, and the excess absorbance diagram is linear even at a very low

ligand-to-metal ratio, indicating the clean generation of a single species. A Scatchard analysis of this complexation showed the concave downward shape characteristic of a system which displays positive cooperativity. Also, a Hill plot gave a maximum slope of 1.75, which, being greater than unity, provides evidence for positive cooperativity [25]. The approximate values  $\Delta H^\circ = -168 \pm 10 \text{ kJ mol}^{-1}$  and  $\Delta S^\circ = -218 \pm 30 \text{ J K}^{-1} \text{ mol}^{-1}$  indicate that the helicate formation reaction  $3\text{M} + 2\text{L} \rightarrow \text{M}_3\text{L}_2$  displays a large negative entropy. This is presumably owing to the formation of one aggregate from five separate components.



(14a) X = CO<sub>2</sub>Et (14b) X = H

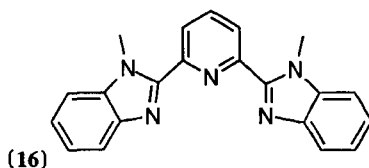


(15a) X = CO<sub>2</sub>Et (15b) X = H

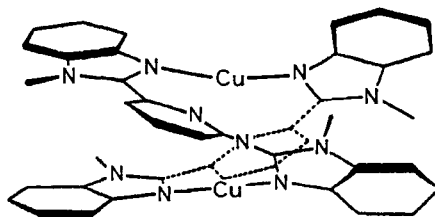
It would be expected that if several different ligands and two different metal ions were all present in solution, the resulting aggregates would contain many different coordination products. Lehn and coworkers have designed self-assembling systems which do not give a mixture of products, but rather only a few well-defined aggregates. These systems show self-discrimination or nonself-discrimination, and exhibit the phenomenon of error checking. Reaction of copper(I) with a solution of several ligands containing different numbers of bipyridine units gave only matched helicates with ligands of the same length. No mixed ligand species were present. Self-recognition can occur even if several different metal ions are present. A mixture of copper(I) (which shows a preference for pseudotetrahedral geometry) and nickel(II) (which shows a

preference for pseudooctahedral geometry) results exclusively in the formation of a copper(I)-based double helix and a nickel(II)-based triple helix with oligobipyridine ligands [13].

The conformations of helices formed between metals and ligands are dictated by the stereochemical preferences of the metal ions. However, structural features of the ligand, such as the ability to position aromatic rings in a  $\pi$ -stacking arrangement, can promote the formation of helices. The relative importance of these factors was examined by Williams and coworkers by investigating complex formation with a range of different ligands [11]. Copper(I) forms a binuclear double helix with ligand (16) as shown in Figure 5. The bridging pyridine places the copper(I) ions in a distorted tetrahedral environment. Removal of the bridging nitrogen should therefore destroy the helicity of the complexes. Stacking interactions can be seen between the benzimidazole moieties. Replacement of the bridging pyridine with a nonaromatic bridge should reveal the importance of these stacking interactions.

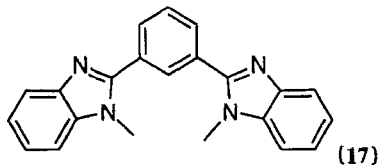


The ligands exist in two different conformations: *cis,cis*, as in (16), and *trans,trans*, as in the phenyl analogue (17). The *cis,cis*-ligand should promote the formation of a helix, while the *trans,trans*-ligand will not. In its complex with copper(I), (16) has taken the *cis,cis*-conformation. In contrast, the copper(I) complex with (17) does not form a helical structure. The structure of the complex  $[\text{Cu}_2(17)_2]^{2+}$  is shown in Figure 6. Stacking interactions are present in this structure between the two bridging benzene rings. It is notable that the Cu–N bond distance is almost identical to that in  $[\text{Cu}_2(16)_2]^{2+}$ . Examination of molecular models of these two compounds reveals that they may be interconverted merely by rotating the Cu–N and benzimidazole–

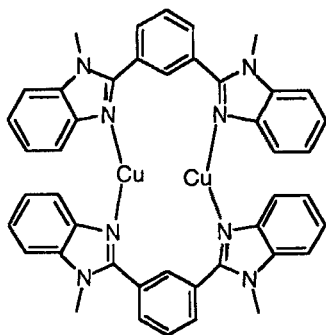


**Figure 5** Representation of the structure of  $[\text{Cu}_2(16)_2]^{2+}$ . Reproduced by permission from *J. Am. Chem. Soc.* **114**, 4230–4237 (1992)

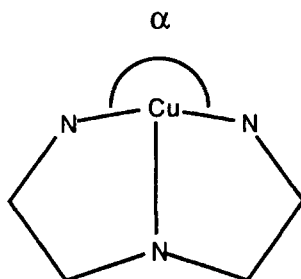
pyridine or benzimidazole–benzene bonds. These two structures may be regarded as pseudostereoconformers of one another. The complex  $[\text{Cu}_2(\mathbf{17})_2]^{2+}$  persists in solution in polar aprotic solvents, as evidenced by data from cyclic voltammetry, UV–visible spectroscopy and  $^1\text{H}$  NMR spectroscopy.



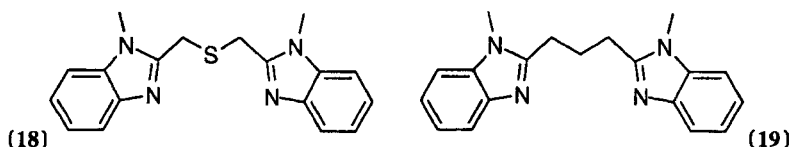
The complex between (18) and copper(I) is revealing in determining which factors encourage double-helix formation. The complex has 1:1 stoichiometry with T-shaped coordination of the copper, even though a double-helical conformation is also possible. The benzimidazole–benzimidazole stacking interactions and bridging groups do not seem in themselves to be sufficient to cause formation of a helical structure. Williams and coworkers suggest that  $[\text{Cu}_2(\mathbf{16})_2]^{2+}$  undergoes double-helix formation because the mononuclear complex is unstable. The geometry of copper(I) would not favor a mononuclear complex because the bite angle  $\alpha$ , estimated to be in the range  $200\text{--}206^\circ$ , would be too large a distortion of the ideal geometry of  $120^\circ$  (Figure 7). In contrast, ligand (19) forms the three-coordinate complex  $[\text{Cu}(\mathbf{19})(\text{MeCN})]^+$  with approximately trigonal coordination of the copper. The extended Hückel molecular orbital (EHMO) method can also be applied to this system, and shows poor orbital overlap as the angle  $\alpha$  increases from  $120^\circ$  to  $180^\circ$  to  $200^\circ$ . These studies support the idea that although the presence of bridging groups and stacking interactions may enhance the stability of metal–ligand helices, the coordination preference of the metal is a greater factor in the determination of the structure [11].



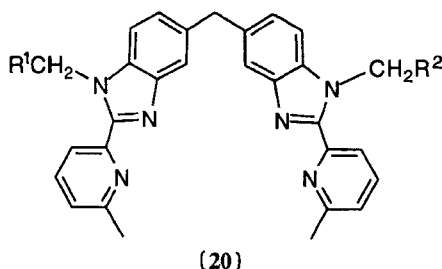
**Figure 6** Representation of the structure of  $[\text{Cu}_2(\mathbf{17})_2]^{2+}$



**Figure 7** Bite angle involved in the formation of tridentate copper(I) complexes

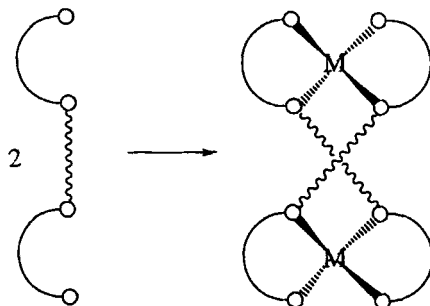


The effect of metal ion stereochemical preference in mediating the final structure of a self-assembling helix was examined by Williams and coworkers using the ligand **(20)** [26]. The formation of a double-helical structure is seen from the reaction of two equivalents of copper(I) and two equivalents of **(20)** (Figure 8). This structure, with pseudotetrahedral geometry around the metal centers, was found to exist in solution by UV-visible spectroscopy,  $^1\text{H}$  NMR and cyclic voltammetry. The double helix does not appear to be the only species existing in solution: mononuclear  $[\text{Cu}(\text{20})_2]^+$  was observed by  $^1\text{H}$  NMR spectroscopy. The  $^1\text{H}$  NMR spectrum of the complex between copper(I) and **(20)** suggests that at room temperature, there may be a rapid equilibrium between the mononuclear complex and the binuclear complex.



In contrast, cobalt(II) and **(20)** (Figure 9) led to the formation of a triple-helical complex with pseudooctahedral geometry around the metal centers. The

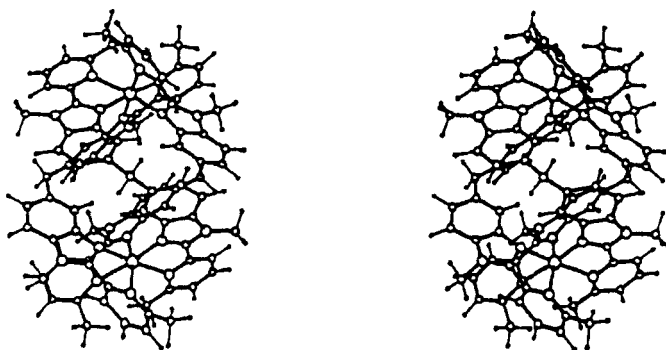




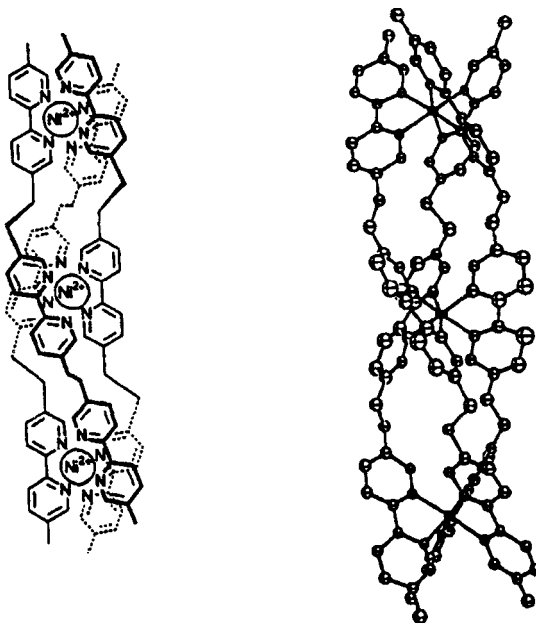
**Figure 8** Schematic structure of the double-helical complex formed from (20) and copper(I)

triple helix was observed in the crystal structure, and also confirmed in solution with UV-visible spectroscopy,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and cyclic voltammetry. This triple-helical structure was the sole species found, suggesting that cooperativity is present with the first cobalt(II) creating a favorable coordination environment for the second. The double-helical species  $[\text{Co}_2(\mathbf{20})_2]^{4+}$  might be expected to form because the cobalt octahedral-tetrahedral transition shows the smallest loss of ligand field stabilization energy. No stacking interactions were observed in the triple-helical complex, and molecular models suggest that stacking interactions are also absent from the double helix. This implies that the self-assembly is directed by the stereochemical preferences of the metal ions and not by interligand interactions. A related triple helix was also seen in the complex of (20) and cobalt(III) [27].

The behavior of zinc(II) is more complicated since it is known to be able to accommodate either a pseudotetrahedral or a pseudooctahedral geometry.



**Figure 9** Stereoview of the triple-helical complex  $[\text{Co}_2(\mathbf{20})_3]^{4+}$ . Reproduced by permission of the Royal Society of Chemistry



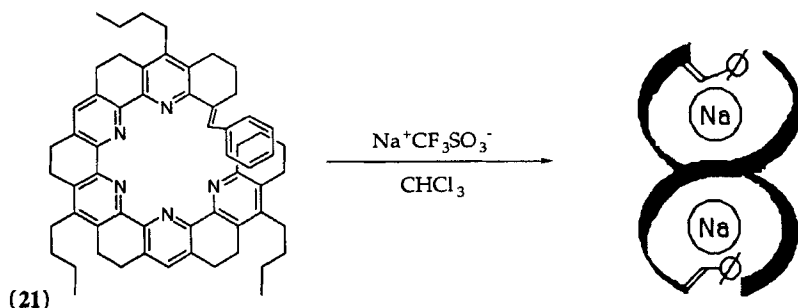
**Figure 10** Representations of the crystal structure of a self-assembled trinuclear triple helix. Reproduced by permission of Angewandte Chemie

UV–visible spectroscopic analysis of the reaction between zinc(II) and (20) shows one complex whose stoichiometry suggests a double-helical structure and one complex whose stoichiometry suggests a triple-helical structure. The complex  $[\text{Zn}_3(\text{20})_2]^{2+}$  is also observed in the analysis, and may have a structure which has a tetrahedral  $\text{Zn}^{2+}$  bridging two  $[\text{Zn}(\text{20})]^{2+}$  units [26].

A related triple-helical structure has been characterized by Lehn and coworkers based on the templating effects of three  $\text{Ni}^{2+}$  ions. A tris(bipyridine) ligand related to (14b) was prepared, with in this case an ethylene spacer linked through the 5-positions of the pyridine rings. The crystal structure of this triple helix is shown in Figure 10, and confirms that no  $\pi$ -stacking interactions are present. The molecule does not display the regular triple-helical symmetry of  $D_3$ , but rather has a  $C_2$  axis perpendicular to the Ni–Ni–Ni axis, crossing through the middle of the central C–C bond of the central bipyridine unit of one strand. This symmetry suggests that the helix is chiral, with two enantiomers possible. Crystals of the complex were studied by CD, though the optical purity of the helix has not been determined [28]. Potts *et al.* have prepared a tricopper(I) triple helix based on a terpyridine ligand with ethynyl group spacers between each pyridine [29].

A helix has been designed which does not involve a transition metal, but rather the alkali metal sodium ion. Because the interaction of  $\text{Na}^+$  with

organic ligands is weak and nondirectional, the formation of the helix is controlled by preorganizing the ligand. Ligand (**21**) is an example of a heterohelicene that is less flexible than oligopyridines, and is preorganized into a helical shape by the ethylene bridges. In solution, (**21**) exists as a racemic mixture of left- and right-handed isomers. The interconversion between the two enantiomers occurs at a rate of  $>100\text{ s}^{-1}$ .

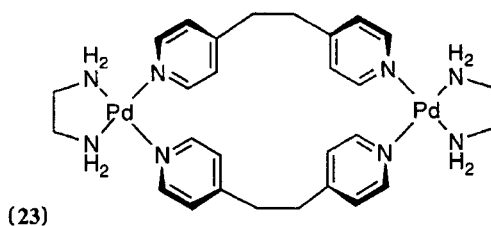
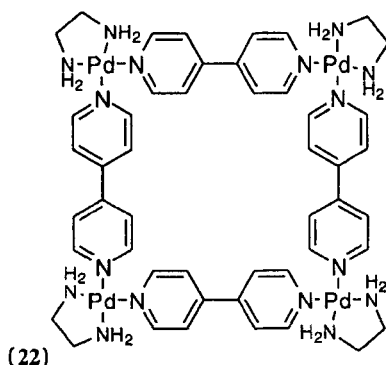


When sodium triflate ( $\text{NaOTf}$ ) is introduced into a solution of ligand (**21**), the double helix  $[\text{Na}_2(\text{21})_2][\text{OTf}]_2$  is formed. The species  $[\text{Na}(\text{21})][\text{OTf}]$  is also detected, but equilibrates to form  $[\text{Na}_2(\text{21})][\text{OTf}]_2$  if allowed to stand in the dark. The stoichiometry of the complex was confirmed by mass spectrometry (MS). Diastereotopic  $\text{CH}_2$  protons are seen in the  $^1\text{H}$  NMR spectrum of the complex as interconversion between left- and right-handed enantiomers is no longer rapid. Shielding effects are observed between benzylidene groups and the pyridine rings of the other ligand strand, showing that they lie above one another in the helical structures. This is an example of a metal–ligand aggregate whose assembly is dictated solely by the conformation of the ligand [30].

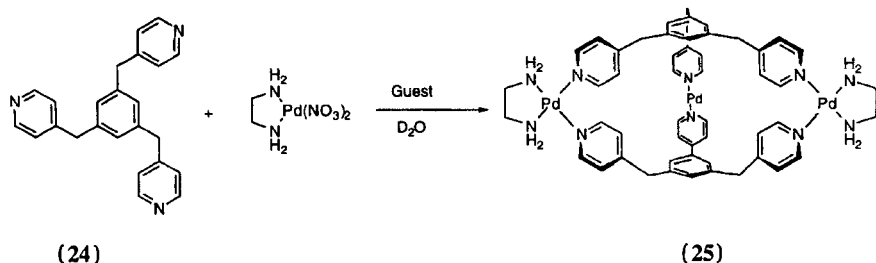
## 2.2 Self-Assembly of Box Structures

Metal ions that form four-coordinate, square planar complexes are inactive in the formation of helices, but show particular value as corner pieces in the construction of cubic or boxlike structures. Fujita *et al.* have elegantly shown that palladium(II) nitrate complexes react with 4,4'-bipyridines to form 4+4 complexes like (**22**) [31]. The bipyridines function as the sides and the palladium(II) ions as the corners of a square macrocycle.  $^1\text{H}$  NMR analysis shows this complex to be the thermodynamically stable product of the reaction with slow exchange between (**22**) and smaller fragments. Moreover, the central cavity in (**22**) is of sufficient size to encapsulate aromatic guests. Addition of 1,3,5-trimethoxybenzene to an aqueous solution of (**22**) leads to upfield shifts of the guest resonances and the measurement of a  $K_a$  of  $750\text{ M}^{-1}$ . By changing the size of the pyridine component (to diazapyrene and diazaperylene), Stang *et al.* have shown that palladium-based boxes of much

larger size can be prepared [32]. Use of 1,2-bis(4-pyridyl)ethane in place of 4,4'-bipyridine leads to the 2:2 complex (23) with a differently shaped cavity [33]. The size and recognition characteristics of the macrocycle could be changed by varying the spacer between the pyridine rings.

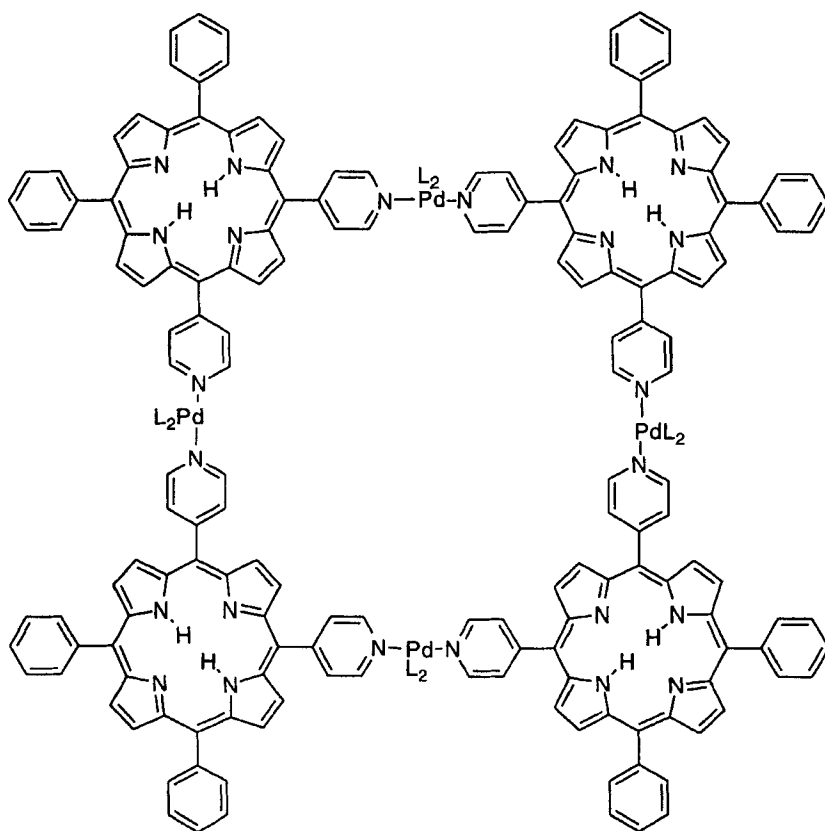


A further refinement of this strategy has recently been shown by the self-assembly of the cage complex (25) formed from the reaction of three palladium(II) ions with 1,3,5-tris(4-pyridylmethyl)benzene (24) [34]. A key feature of this process is the critical role played by aromatic guests (such as 4-methoxyphenylacetic acid) in templating the formation of (25). In the absence of guest, only ill-defined, oligomeric metal complexes are formed.



In an extension of this basic approach, Stang and Zhdankin have prepared molecular boxes with four iodonium ions as corners and four biphenyl groups as sides in a structure directly analogous to (22) [35].

Drain and Lehn have further extended the metal-templated box strategy with the synthesis of 5,10-bis(4-pyridyl)-15,20-diphenylporphine. In the presence of palladium(II) or platinum(II) this self-assembles into the 4:4 complex (26) with four porphyrins occupying the four walls of the box [36].

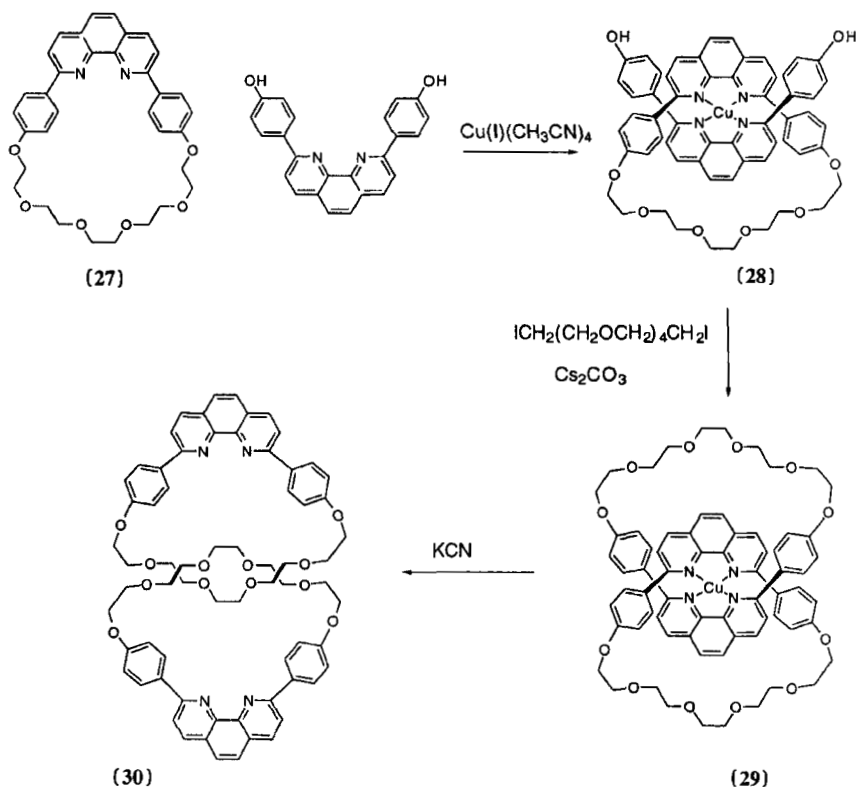


(26)

### 2.3 Self-Assembly of Catenanes

In a seminal series of papers, Sauvage and coworkers have demonstrated the use of transition metals in templating the formation of catenated structures [37]. This area has been extensively reviewed [38–40] and will only be covered briefly here. The central strategy has been to use the perpendicular positioning

of two phenanthroline ligands around a copper(I) center effectively to thread one strand of a macrocycle through a second. Reaction of macrocycle (27) and 2,9-bis(4-hydroxyphenyl)phenanthroline with copper(I) salt leads to the threaded tetrahedral complex (28), which has the two phenolic hydroxy groups positioned above and below the plane of the other phenanthroline ring. These can be linked via a Williamson ether synthesis using the appropriate diiodide. The result is the catenated structure (29) templated around the copper(I) center. Treatment of templated (29) with KCN leads to the metal-free catenand structure (30) containing interlocked macrocyclic rings. This unusual, linked bis(phenanthroline) ligand can be used to bind other transition metals and stabilize normally reactive oxidation states, such as nickel(I) [41]. This strategy has recently been extended to the formation of more complex catenated structures, including a [3]catenane containing two smaller rings threaded onto a larger macrocycle [42].



The metal coordination strategy of Fujita has been used to design a [2]catenane whose behavior is remarkably like that of “magic rings” – able to