Interlacing molecular threads on transition metals

Jean-Claude Chambron, Christiane Dietrich-Buchecker, Catherine Hemmert,
Abdel-Kader Khemiss, Dennis Mitchell, Jean-Pierre Sauvage, Jean Weiss

Laboratoire de Chimie Organo-Minérale, UA 422, Institut de Chimie,
67000 Strasbourg, France

Abstract – Copper(I) is ideally adapted to a three-dimensional template
effect allowing interlacing of 1,10-phenanthroline based molecular
threads. By using appropriate cyclization procedures, interlocked
macrocyclic ligands, the **catenands**, were prepared via the intermediate
synthesis of their corresponding copper(I) complexes, the **catenates**.
Systems containing two and three interlocked rings were made.
Catenands display very special coordinating properties, allowing in
particular to strongly stabilize low formal oxidation states (for
instance, a Ni(I) catenate is air stable) and photo-excited states. A
[3]-catenand (consisting of three interlocked coordinating rings)
contains two potential complexing sites. Hetero-dinuclear compounds
have been made : Cu(I)-Ag(I) and Cu(I)-Co(II). Electrochemical studies
show the two complex subunits to strongly interact, the mode of
interaction probably involving intramolecular stacking between aromatic
rings of the ligands rather than direct communication between the
metals. If directed rings are employed, the catenands and catenates
synthesized present novel properties : the systems obtained are
topologically chiral. By using two copper(I) centers as templating
species and by entwining two bis-chelating threads around them in the
proper fashion, a double helix is obtained. It leads after cyclization
to a dicopper complex **molecular trefoil knot** which can be demetalated
to a knotted free macrocyclic ligand.

The synthesis of **catenanes** (interlocked rings) and **knots** has been a highly challenging
problem to chemists for several decades (ref. 1,2). Such molecular systems (Figure 1) are
fascinating both for their aesthetic aspect and for their intriguing topological
properties.

Chemical topology was initiated in 1961 by the publication of an important article in which
the notion of topological isomers was introduced (ref. 1). The archetypal system of
topological isomerism is that of the trefoil knot and the unknotted ring, as depicted in
Fig. 2.

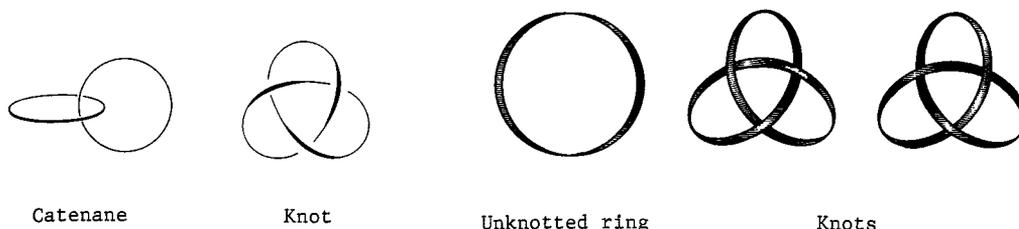| Catenane | Knot | Unknotted ring | Knots |

Fig. 1   Fig. 2. Topological stereoisomers.

As discussed more recently (ref. 3), the three hypothetical molecules of Fig. 2 are

topological stereoisomers : they have identical bond connectivities but their molecular graphs are distinct when embedded in 3-space. In other words, the three objects of Fig. 2 are different since they cannot be interconverted by any continuous deformation without breaking and reforming a chemical bond, although their description in terms of vertices (atoms) and edges (bonds) is the same. In addition to catenanes and knots, very few molecules having a non-planar molecular graph have been made. They consist either of K_5, the complete graph obtained from 5 vertices (ref. 4-6), or of a Möbius strip (ref. 7).

The directed synthesis of catenanes, using the methodology of classical organic chemistry, represents a remarkable accomplishment (ref. 2). Also noteworthy is the ability of Nature to construct highly knotted and raveled systems. Duplex circular DNA can be converted to multi-catenanes and knots by the action of specific enzymes (topoisomerases) (ref. 8).

1) TEMPLATE SYNTHESIS OF INTERLOCKED MACROCYCLIC LIGANDS: SYNTHESIS OF [2]-CATENANDS

Transition metals, with their ability to gather and dispose ligands in a given predictable geometry, can induce a "template effect". This specific property of transition metals has been widely used for the two-dimensional template synthesis of various single macrocycles (ref. 9). Early examples of such syntheses are given by the copper(II) and nickel(II) aliphatic Schiff base complexes first obtained by Curtis in 1961 (ref. 10). In contrast, literature reports only a few syntheses based on a three-dimensional (or generalized) template effect. Recent examples of such syntheses are given by the cobalt(III) sepulchrate and the iron(III) bicapped TRENCAM due respectively to A.M. Sargeson (ref. 11), K.N. Raymond (ref. 12) and their coworkers.

For our part, we used a generalized template effect in order to construct a catenane structure. To obtain interlocked rings, two strategies, given in Fig. 3, were possible : both of them require that the ligands set around the metallic center are adequate molecular threads which can be converted into rings in later stages.
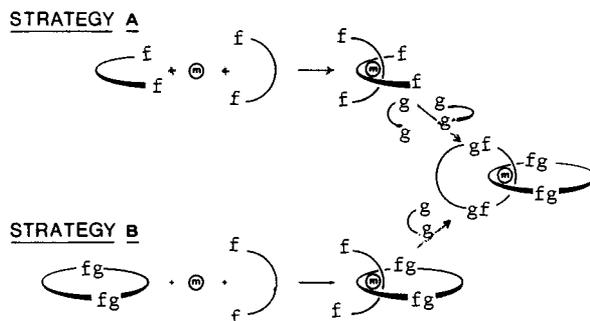

Fig. 3. Synthetic strategies based on a three-dimensional template effect induced by a transition metal.

The straightforward or direct strategy A, which involved simultaneous pairwise connection between eight reacting centers appeared, from a statistical point of view, less favorable than the longer strategy B, which involved, in the final cyclization step leading to a catenane, only connection of four reacting centers. However, the latter implied the preliminary synthesis of a chelating macrocycle. It was difficult to decide which strategy should be first attempted, but in fact not crucial. Much more important was the choice of the different subunits : nature of the coordinating fragment f-f, nature of the transition metal (m), nature and length of the link g-g.

At the time of commencement of this work, we had already developed an efficient synthesis of 2,9-disubstituted phenanthrolines (ref. 13) and shown that such ligands form very stable pseudotetrahedral complexes with copper(I) (ref. 14). The special topography of this type of copper(I) complexes in which the two ligands are entwined around the metallic center is depicted in Fig. 4 for the 2,9-dianisyl-1,10-phenanthroline 1. Complex $[(1)_2Cu(I)]^+$ appeared the ideal precursor for a template catenane synthesis as described in Fig. 3, the only requirement being functionalization of the ligands beyond the coordination sites.

Although strategy B was longer than strategy A, it offered the advantage of a step by step procedure and for this reason we tried that less risky route first.
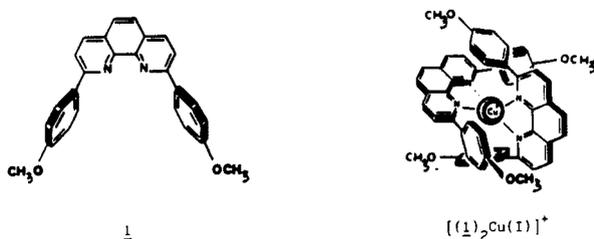
Fig. 4. In the copper(I) complex $[(\underline{1})_2Cu(I)]^+$, the two highly rigid coordinating subunits $\underline{1}$ fit together while encaging the metal atom.

a) Template synthesis of catenate $[(\underline{4})Cu(I)]^+$

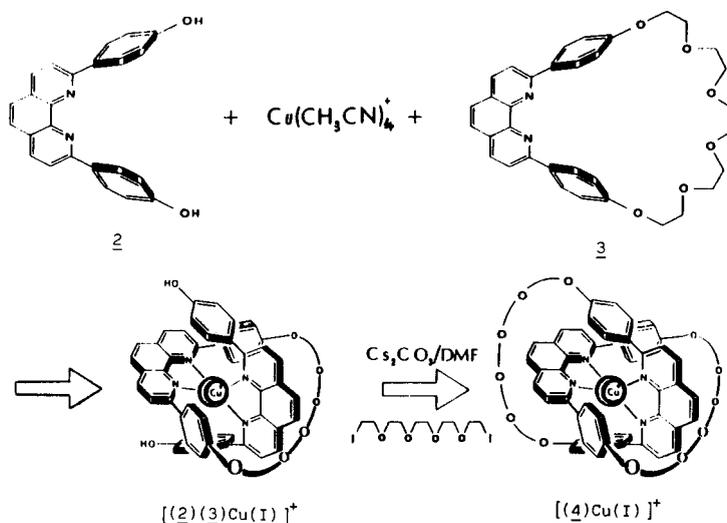Precursors and synthetical pathway followed for strategy B are given in Fig. 5.

Fig. 5. Template synthesis of the copper(I) catenate $[(\underline{4})Cu(I)]^+$ via strategy B.

It was possible to identify by high resolution NMR, step by step, all the intermediates produced along the synthetic pathway described in Fig. 5 and thus to obtain evidence for the catenate structure of $[(\underline{4})Cu(I)]^+$ (ref. 15, 16).

Shortly after the first encouraging result, we succeeded also in the preparation of catenate $[(\underline{4})Cu(I)]^+$ by the shorter strategy A (ref. 17) (27% yield from the precursor $\underline{1}$).

b) Demetalation of catenate $[(\underline{4})Cu(I)]^+$: obtention of the free ligand 4

Once the synthesis of catenate $[(\underline{4})Cu(I)]^+$ was achieved, the crucial question of removal of Cu(I) without destroying the entire catenane structure built around it arose. After several attempts, complex $[(\underline{4})Cu(I)]^+$ could be quantitatively demetalated by treatment with potassium cyanide, affording the free ligand $\underline{4}$ (Fig. 6).
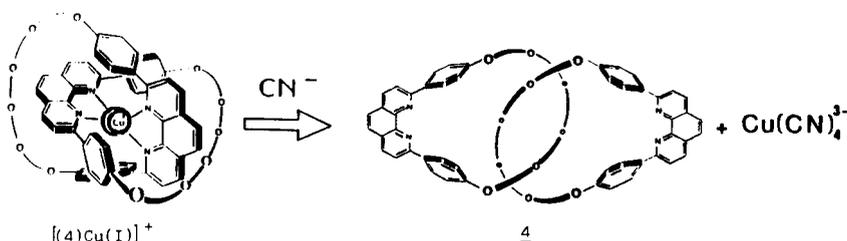

Fig. 6. Demetalation of $[(\underline{4})Cu(I)]^+$, leading to the [2]-catenand $\underline{4}$.

Detailed NMR analysis showed us that the molecular shapes of $[(\underline{4})Cu(I)]^{+}$ and $\underline{4}$ were totally different despite the fact that both molecules presented identical bond connectivity in their organic skeleton.   Interconversion of $[(\underline{4})Cu(I)]^{+}$ to $\underline{4}$ occurred without breaking of any bond of the ligand, but merely by free gliding of one ring into the other.

Compound $\underline{4}$ was the first member of a new family of ligands that we named : the catenands.

The [2]-catenand $\underline{4}$ was used to prepare a series of catenates, containing various complexed cationic species : H^{+}, Li^{+}, Zn^{++}, Cd^{++}, Fe^{++}, Co^{++}, Ni^{++}, Ni^{+}, Cu^{+}, etc... Detailed photochemical, electrochemical, and kinetic studies have been carried out, showing that low formal oxidation states and Metal-to-Ligand Charge Transfer (MLCT) excited states (for Cu(I) and Ni(I)) are highly stabilized in the catenate structure (ref. 18-20).

2) [3]-CATENENDS

This part of the work could be considered as an extension of the three-dimensional template effect. It has led to new [3]-catenates and catenands. Due to their novel topology, they display interesting coordination properties.   The two strategies used to reach [3]-catenates are depicted in Fig. 7.
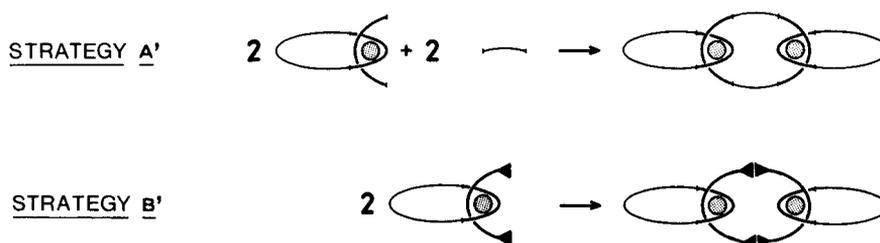

Fig. 7. Principles of template syntheses of [3]-catenates.

Strategy B'evolved as a direct result of the lower efficiency obtained from strategy A'. It is statistically more favorable than A' since 4 reacting centers are involved whereas strategy A'requires 8 reaction centers to participate in the same cyclization reaction.

The three types of reactions actually performed (ref. 21, 22) in our group are represented in Fig. 8 and the results obtained are summarized in Table 1.
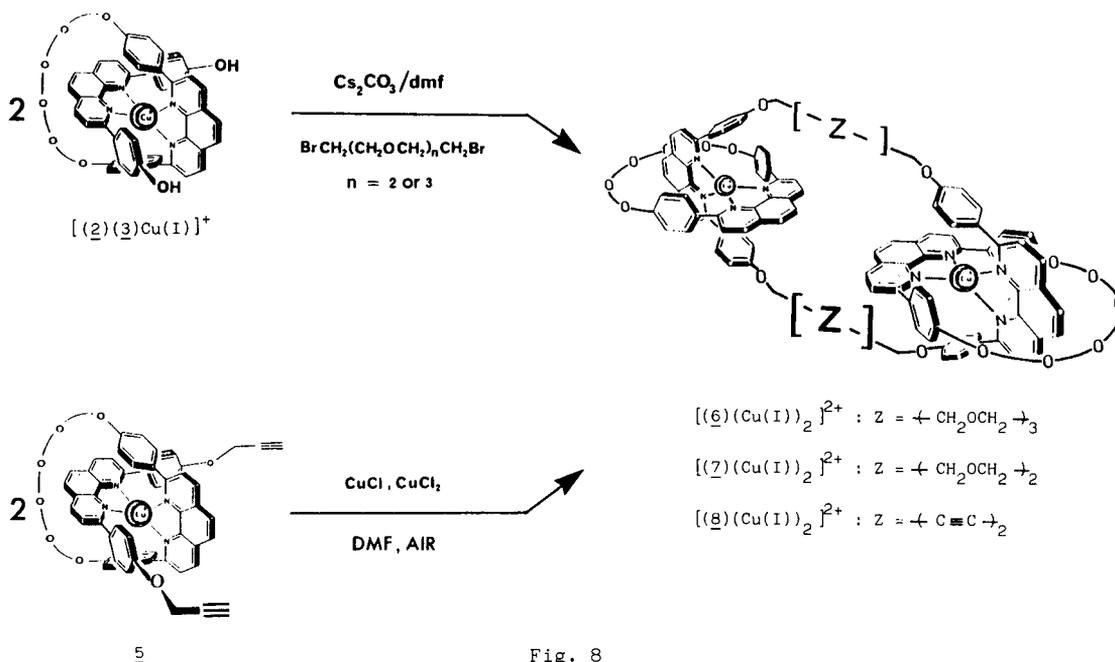

$[(\underline{6})(Cu(I))_{2}]^{2+}$: $Z = +CH_{2}OCH_{2}+_{3}$

$[(\underline{7})(Cu(I))_{2}]^{2+}$: $Z = +CH_{2}OCH_{2}+_{2}$

$[(\underline{8})(Cu(I))_{2}]^{2+}$: $Z = +C\equiv C+_{2}$

Fig. 8

TABLE 1. Synthesis of [3]-catenates.

Entry	Precursor	Link	Compound	Yield (%)	Byproducts (%)
1	$[(\underline{2})(\underline{3})Cu^I]^+$	$BrCH_2(CH_2OCH_2)_3CH_2Br$	$[\underline{6}(Cu^I)_2]^{2+}$	2	free cycles central (5) lateral (60)
2	$[(\underline{2})(\underline{3})Cu^I]^+$	$BrCH_2(CH_2OCH_2)_2CH_2Br$	$[\underline{7}(Cu^I)_2]^{2+}$	6	free cycles central (5) lateral (45)
3	$\underline{5}$	no	$[\underline{8}(Cu^I)_2]^{2+}$	58	Dimer (22) free cycles (none)

The evolution of the yields clearly depends on the nature of the <u>strategy</u> and/or the <u>rigidity</u> of the whole system. The enhancement of efficiency is spectacular from entry 1 to entry 3.

The corresponding ligands <u>6</u>, <u>7</u>, and <u>8</u> were readily obtained by demetalation of the copper(I) complexes with an excess of KCN. The coordination chemistry of <u>8</u> has been explored.

Due to its controlled geometry, holding two coordination sites at a distance of ca. 8.0 Å (ref. 23), the [3]-catenand <u>8</u> seemed to be an appropriate ligand to synthesize heterobimetallic complexes. These complexes may be able to exhibit electron transfer from one site to the other. Photoinduced electron transfer reactions could occur from the $[(\underline{1})_2Cu(I)]^+$ subunit of the bimetallic [3]-catenate. Such a subunit exhibits a (MLCT) excited state with $E(Cu(II)/$ $Cu(I)) = -1.443$ V vs. SCE ($\xi_{0-0} = 2.05$ eV, $\lambda max = 439$ nm, $\varepsilon = 3200$ $M^{-1}xcm^{-1}$)(ref. 24). The lifetime of the excited state (300 ns) should be sufficient to allow electron transfer towards an appropriatly selected electron acceptor such as $[(\underline{1})_2Co(II)]^{++}$ $(E(Co(II)/Co(I)) = -0.600$ V vs. SCE) or $[(\underline{1})_2Ag(I)]^+$ $(E(Ag(I)/Ag(0)) = 0.185$ V vs. SCE)(ref. 19). They could be built on the second coordination site of the [3]-catenand <u>8</u>. The heterobimetallic complexes $[(\underline{8})(Cu(I),Ag(I))]^{++}$ and $[(\underline{8})(Cu(I),Co(II))]^{+++}$ were obtained.

The results obtained from electrochemical studies are collected in Table 2.

TABLE 2. Electrochemical data on bimetallic [3]-catenates.

Entry	Ligand	M	M'	Redox Couple	$E_{Ox/Red}$ (V/SCE)[a]	Values for $[(\underline{4})M']^{n+}$
1	<u>6</u>	Cu^I	Cu^I	Cu^{II}/Cu^I	+0.620	+0.540
2	<u>7</u>	Cu^I	Cu^I	Cu^{II}/Cu^I	+0.620	+0.540
3	<u>8</u>	Cu^I	Cu^I	Cu^{II}/Cu^I	+0.670	+0.540
4	<u>8</u>	Cu^I	Ag^I	Cu^{II}/Cu^I	+0.668	+0.540
				Ag^I/Ag^0	$-0.480^{(*)}$	$-0.700^{(*)}$
5	<u>8</u>	Cu^I	Co^{II}	Cu^{II}/Cu^I	+0.785	+0.540
				Co^{II}/Co^I	-0.360	-0.600
				Co^I/Co^0	-1.180	-1.315

[a]All values were obtained from cyclic voltammetry except (*) values obtained from polarographic measurements. All the systems observed were fully reversible.

In dinuclear complexes the oxidation potentials of Cu(I) and the reduction potentials of Co(II), Co(I) and Ag(I) are higher than the values obtained for the corresponding [2]-catenates. These observations are consistent with electrostatic interactions between the two metals in [3]-catenates.

3) TOPOLOGICALLY CHIRAL CATENANES

As topological stereoisomers (ref. 25), catenanes provide a way to build topologically chiral molecules. Very few examples have appeared in the literature so far (ref. 3). Topological chirality requires that mirror images be topologically distinct, that is, cannot be converted into one another by continuous deformation in 3-space (ref. 3). Chirality of catenanes can be realized if both rings are made unidirectional (Fig. 9). One method to accomplish this is to synthesize catenanes from asymmetrically substituted 1,10-phenanthroline. In this study, catenates $[(9)Cu(I)]^+$ and $[(10)Cu(I)]^+$ (Fig. 10) containing two interlocked directed rings were synthesized in the usual manner from 4-phenyl-1,10-phenanthroline and 4-p-tolyl-1,10-phenanthroline (ref. 26) respectively. They were both obtained in ca. 12% yield. Their demetalation afforded the catenands $\underline{9}$ (ref. 27) and $\underline{10}$.
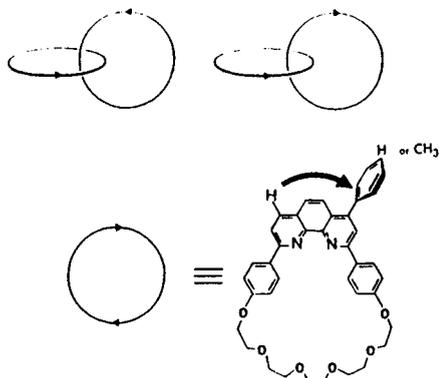

Fig. 9. Principle of construction of topologically chiral [2]-catenands and structure of the individual rings showing their directed nature.
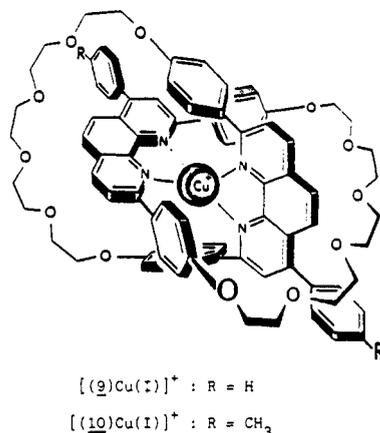

$[(\underline{9})Cu(I)]^+$: R = H

$[(\underline{10})Cu(I)]^+$: R = CH_3

Fig. 10

The chirality of $[(\underline{9})Cu(I)]^+$ and $[(\underline{10})Cu(I)]^+$ was demonstrated by ^{1}H NMR spectroscopy. Their spectrum was almost completely split, in the presence of Pirkle's chiral reagent (ref. 28). In contrast, the free catenands $\underline{9}$ and $\underline{10}$ did not show clear interactions with this reagent, presumably due to their intramolecular flexibility, but their topological chirality is obvious from the asymmetric nature of the starting compounds and the synthetic routes followed.

Owing to the kinetic stability (ref. 20) and the photoredox properties (ref. 19) of copper(I) catenates, the chiral copper(I) catenates might be used efficiently in asymmetric photoinduced electron transfer reactions as well as in studies of their interaction with DNA helices (ref. 29).

4) SYNTHESIS OF A MOLECULAR TREFOIL KNOT (ref. 30)

The strategy envisaged to reach the fascinating trefoil knot (Fig. 2) was based on a double three-dimensional template effect induced by two transition metals (Fig. 11).
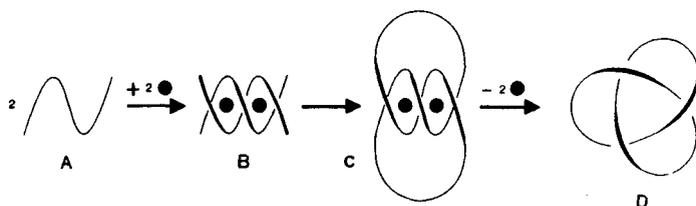

Fig. 11. Strategy towards a trefoil knot using two transition metals as templating species.

Two bis-chelating molecular threads (A) entwined around two copper(I) centres should lead to a double helix (B). After cyclization, the di-nuclear complex (C) already exhibits the topological features characteristic of a trefoil knot. After demetalation these same topological features will be maintained in the free ligand (D).

After many attempts with various linkages, we found that 1,10-phenanthroline nuclei connected via their 2-positions by a $-(CH_2)_4-$ tie, do indeed form a double helix when complexed to two copper(I) centers. The precursors used and the synthetic reactions are represented in Fig. 12.
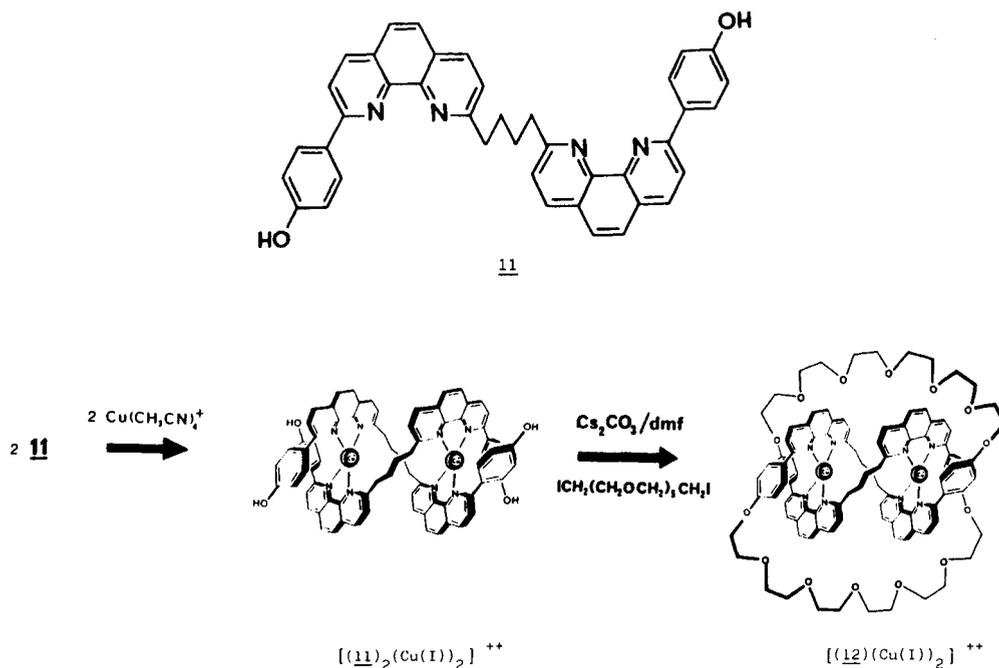

11

$[(11)_2(Cu(I))_2]^{++}$ $[(12)(Cu(I))_2]^{++}$

Fig. 12. Template synthesis of the knotted copper(I) complex $[(12)(Cu(I))_2]^{++}$.

The double helix $[(11)_2(Cu(I))_2]^{++}$ was prepared by addition of $Cu(CH_3CN)_4 \cdot BF_4$ to 11. Crude $[(11)_2(Cu(I))_2]^{++}$ was reacted under high dilution conditions (ref. 18) with two equivalents of the diiodo derivative of hexaethyleneglycol. After tedious work-up and separations, a small amount (3%) of the knotted system $[(12)(Cu(I))_2]^{++}$ was isolated. Compound $[(12)(Cu(I))_2]^{++}$ had ^{1}H NMR and mass spectra (FAB) consistent with its structure. As expected, complex $[(12)(Cu(I))_2]^{++}$ was chiral : Pirkle's reagent (ref. 28) induces splitting for most aromatic signals.

Quantitative demetalation of the copper(I) complex $[(12)(Cu(I))_2]^{++}$ afforded the corresponding free ligand represented in Fig. 13.

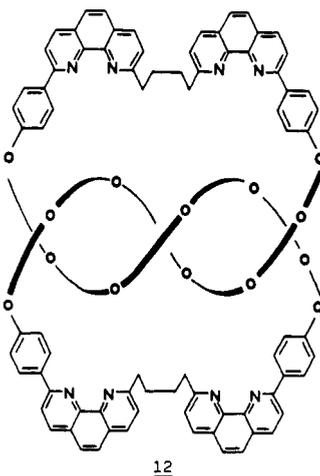The knotted topology of 12 was fully confirmed by the chirality of its potassium complex.

12

Fig. 13. Demetalation of $[(12)(Cu(I))_2]^{++}$, leading to the molecular trefoil knot 12.

In conclusion, the interplay between the novel topological properties of the molecular systems described and their ability to complex transition metals has led to a new type of coordination chemistry.

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