# Transition metals as assembling and templating species: from catenanes and knots to strings threaded through molecular rings

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Abstract

New dicopper(I) knots have been synthesized as well as their face-to-face isomers. The knots range from 80 to 90-membered rings and their preparation yields depend crucially on structural parameters such as number of methylene fragments linking the two chelating units and length of the polyethyleneoxy unit used in the cyclization reaction. The best yield was obtained for an 84-membered knotted ring with a $-(CH_2)_6-$ connector : this relatively long fragment allows pronounced winding of the double helix precursor and is thus favorable to the knotting reaction. The face-to-face complexes were in some instances the major products, being obtained in yields amounting to 24% in the case of the dicopper (I) bis 43-membered ring system. Based on a related three-dimensional template effect, other multicomponent molecular systems have been synthesized. They contain rings, coordinating open-chain fragments and transition metals and can be constructed at will by taking advantage of the strong preference of copper(I) for bis- chelate complexes. The compounds consist of one or two rings threaded by the acyclic subunit, the various organic components being assembled via coordination to copper(I).

## Introduction

DNA is one of the most important molecules of living matter for it contains the genetic information of any organism. The topology of DNA is also fascinating since it can form beautiful and complex catenanes (systems consisting of interlocking rings, like olympics or chains) and knots (single, closed but knotted curves) like the famous trefoil knot.

Using modern synthetic methodologies, consisting of gathering and orienting organic fragments around transition metals prior to incorporating them into cyclic molecules (the so-called "template effect"), many important topologies can be constructed with molecules. An example, which is not only related to DNA but also linked with mathematics and graphic art, is the trefoil knot, recently prepared at the molecular level. The making of topologically and geometrically non-trivial chemical objects, obviously represents a synthetic challenge, which is part of the motivation for their actual preparation.

### Synthesis of dicopper(I) trefoil knots and related unknotted molecular systems.

Although molecular knots were discussed in chemical literature more than three decades ago (ref.1) it is only recently that the first chemical knot was synthesized.(refs.2,3). The use of transition metals as assembling and templating species turned out to be crucial in the development of preparative methods allowing to synthesize macroscopic amounts of catenanes and knots.(refs.4,5). A recent report describes the experimental procedure for making the original di-copper knotted 86-membered ring as well as its face-to-face isomer complex, consisting of two 43-membered rings arranged around two copper(I) centers.(ref.6). In an attempt to improve the very poor yield (the dicopper trefoil knot was obtained in 3% yield only), some of us investigated the effect of structural parameters on the course of the reaction. The results obtained have recently been reported as a preliminary communication (ref.7). The strategy used (ref.2) is indicated in Figure 1. Figure 2 describes in a schematic way the alternative cyclization reaction leading to the unknotted face-to-face complexes and the equilibrium which interconverts the helical and the non helical precursors.
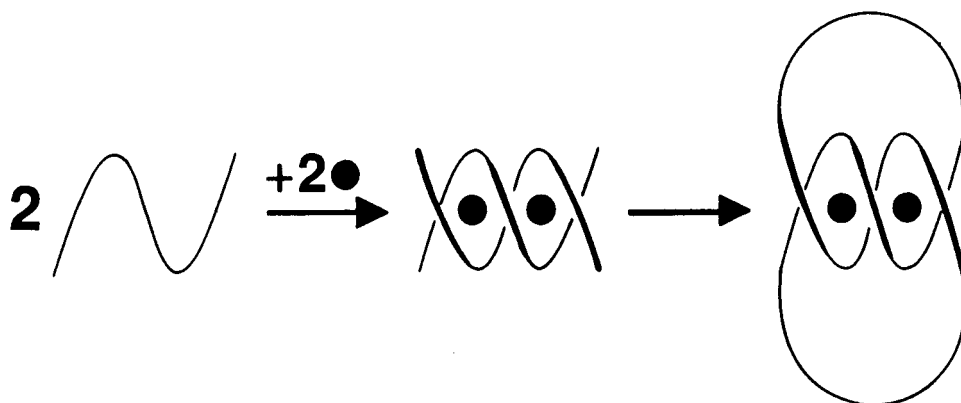
Figure 1.   Principle of the strategy leading to a dimetallic trefoil knot. First step: interlacing of two molecular strings around two transition metal coordinating centers, with formation of a helicoidal precursor. Second step: connection, with the appropriate linkers, between the four ends of the double helix to afford the knot.
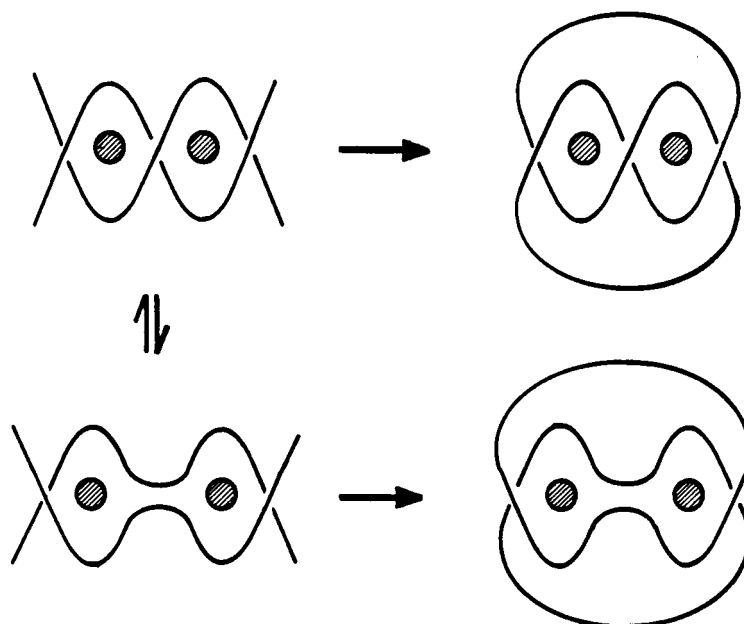


Figure 2.   The equilbrium between the helicoidal interlaced system and its face-to-face analogous complex. Interconversion between the two isomeric cyclic products is of course not possible.

What will be determining is (i) the proportion of double helix precursor formed versus face-to-face open chain complex (Figure 2) and (ii) the spacial arrangement of the four reacting ends of the helicoidal dinuclear complex. This latter factor will reflect the degree of winding of the two molecular strings interlaced around the copper(I) atoms. The chemical structures of the starting compounds and the complexes synthesized and studied are depicted in Figures 3a and 3b.
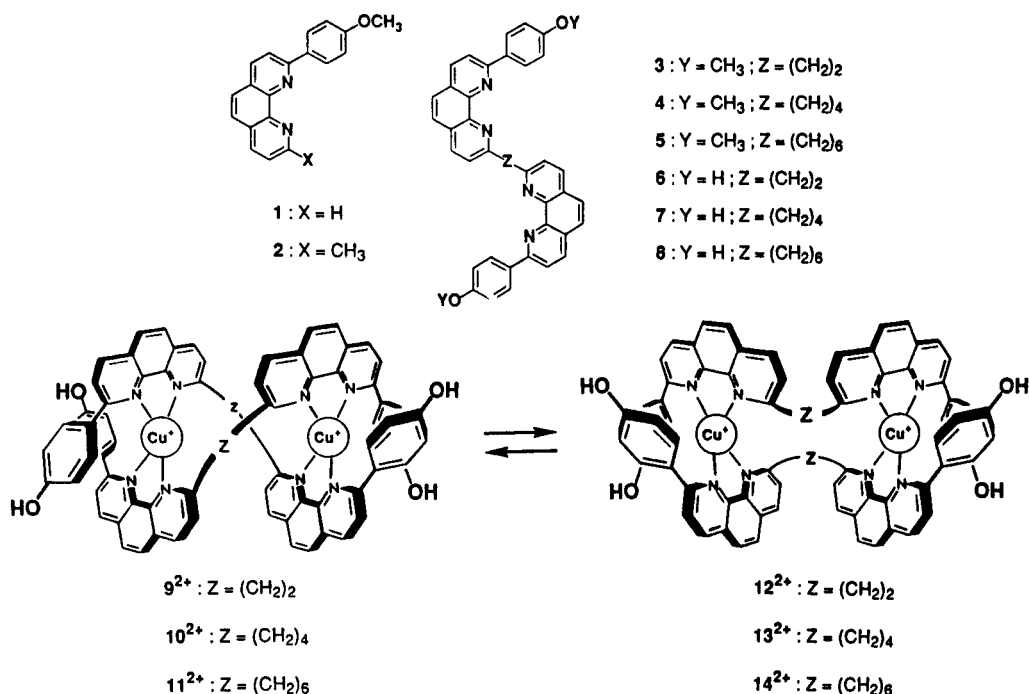
3 : Y = CH$_3$ ; Z = (CH$_2$)$_2$

4 : Y = CH$_3$ ; Z = (CH$_2$)$_4$

5 : Y = CH$_3$ ; Z = (CH$_2$)$_6$

6 : Y = H ; Z = (CH$_2$)$_2$

7 : Y = H ; Z = (CH$_2$)$_4$

8 : Y = H ; Z = (CH$_2$)$_6$

1 : X = H

2 : X = CH$_3$

9$^{2+}$ : Z = (CH$_2$)$_2$

10$^{2+}$ : Z = (CH$_2$)$_4$

11$^{2+}$ : Z = (CH$_2$)$_6$

12$^{2+}$ : Z = (CH$_2$)$_2$

13$^{2+}$ : Z = (CH$_2$)$_4$

14$^{2+}$ : Z = (CH$_2$)$_6$

**Figure 3a.   The acyclic precursors.**

X = CH$_2$(CH$_2$OCH$_2$)$_n$CH$_2$

[Cu$_2$(k-80)]$^{2+}$ : n = 4 ; x = 16 ; Z = (CH$_2$)$_4$

[Cu$_2$(k-82)]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_2$

[Cu$_2$(k-84)]$^{2+}$ : n = 4 ; x = 16 ; Z = (CH$_2$)$_6$

[Cu$_2$(k-86)]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_4$

[Cu$_2$(k-90)]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_6$

[Cu$_2$(m-40)$_2$]$^{2+}$ : n = 4 ; x = 16 ; Z = (CH$_2$)$_4$

[Cu$_2$(m-41)$_2$]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_2$

[Cu$_2$(m-42)$_2$]$^{2+}$ : n = 4 ; x = 16 ; Z = (CH$_2$)$_6$

[Cu$_2$(m-43)$_2$]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_4$

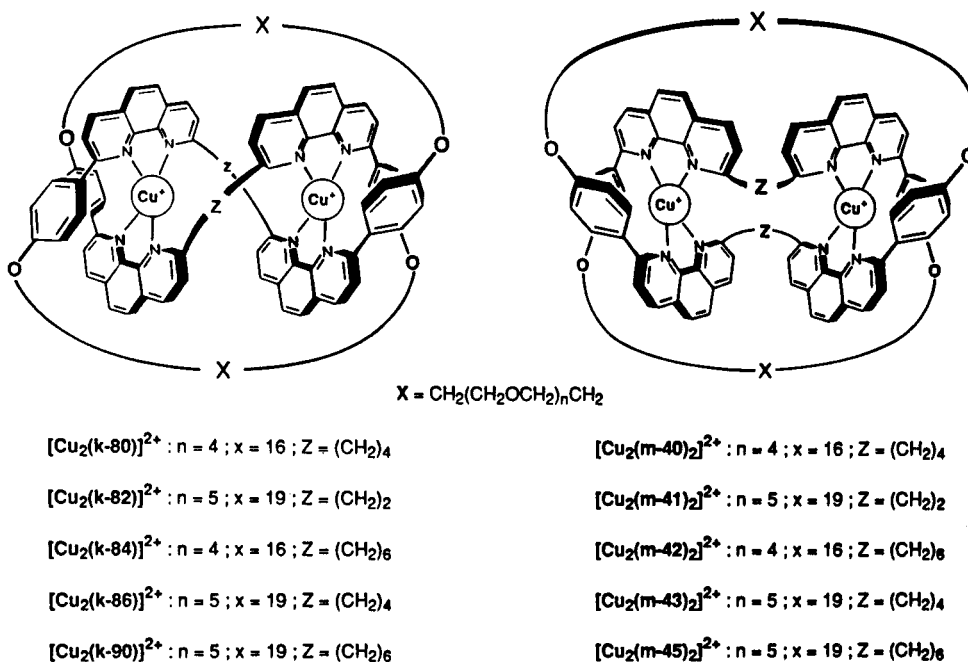[Cu$_2$(m-45)$_2$]$^{2+}$ : n = 5 ; x = 19 ; Z = (CH$_2$)$_6$

**Figure 3b.   The molecules described in the present report. For the cyclic compounds, the total number of atoms x connecting two phenolic oxygen atoms is 16 if n=4 (pentaethyleneoxy fragment) or 19 if n=5 (hexaethyleneoxy linker). Each knot is represented by the letter k accompanied by the overall number of atoms included in the cycle. The face-to-face complexes contain two monocycles (letter m), the number of atoms in each ring being also indicated. It can be noted that each knot has a face-to-face counterpart. For instance, [Cu$_2$(k-90)]$^{2+}$ and [Cu$_2$(m-45)$_2$]$^{2+}$ are constitutional isomers. *They are by no means topological stereoisomers* (ref.8).**

1,10-phenanthroline was treated with *p*-lithioanisole (ref.9) in ether at 0°C to afford **1** in 69% yield after hydrolysis and oxidation by $MnO_2$. **2** was prepared by reacting **1** and methyllithium followed again by hydrolysis and oxidation ; it was obtained as a white solid in 92% yield from **1**. The *bis*-phenanthroline compound **3** was made by the oxidative coupling (iodine) of the deprotonation product generated from **2** with lithium diisopropylamid (LDA). It was obtained in good yield (77%) from **2**. **4** was prepared as previously described.(ref.6)· The bis-chelating ligand **5** was synthesized by reacting **1** with 1,6-dilithiohexane (ref.10) in ether at 0°C, followed by hydrolysis and $MnO_2$ treatment. **5** was obtained as a pale yellow solid in 60% yield.

The three diphenols **6, 7** and **8** were prepared following a demethylation procedure described earlier (refs.4,5,11). The anisyl derivative (**3, 4** or **5**) was heated at ~200°C in pyridinium chloride, followed by work-up and careful drying. The yields were excellent in spite of the brutal conditions used.

The dicopper(I) complexes $9^{2+}$ to $14^{2+}$ were made by mixing $Cu(CH_3CN)_4^+$ with the corresponding diphenol (**6, 7** or **8**). It must be stressed that mixtures of complexes were obtained, corresponding to the equilibrium of Figure 2.

All the cyclization reactions leading to the dicopper trefoil knots $[Cu_2(k-82)]^{2+}$ to $[Cu_2(k-90)]^{2+}$ and the face-to-face dinuclear complexes $[Cu_2(m-40)_2]^{2+}$ to $[Cu_2(m-45)_2]^{2+}$ were carried out under similar conditions, on the crude mixture of precursors (double helix and face-to-face complex). The phenolic complexes $(9^{2+}+12^{2+})$, $(10^{2+}+13^{2+})$ or $(11^{2+}+14^{2+})$ were reacted with the desired diiodo derivative (penta- or hexa-ethyleneglycol) in DMF, in presence of $Cs_2CO_3$, with vigorous stirring. The knotted and the face-to-face complexes were obtained in various proportions, depending on which open chain compounds were used: bis-phenanthroline **6, 7** or **8**, and diiodo derivative. The respective yields are given in Table I.

Table I. Preparation of $[Cu_2(k-80)]^{2+}$ to $[Cu_2(k-90)]^{2+}$ and $[Cu_2(m-40)_2]^{2+}$ to $[Cu_2(m-45)_2]^{2+}$.

| Acyclic precursor | Diiodo fragment | Isolated complexes | Yield |
|---|---|---|---|
| $9^{2+}$ + $12^{2+}$ | hexa | $[Cu_2(m-41)_2]^{2+}$ | 0.5% |
|  |  | $[Cu_2(k-82)]^{2+}$ | 0.5% |
| $10^{2+}$ + $13^{2+}$ | penta | $[Cu_2(m-40)_2]^{2+}$ | 4.6% |
|  |  | $[Cu_2(k-80)]^{2+}$ | 0.7% |
| $10^{2+}$ + $13^{2+}$ (see ref. 7) | hexa | $[Cu_2(m-43)_2]^{2+}$ | 24% |
|  |  | $[Cu_2(k-86)]^{2+}$ | 3% |
| $11^{2+}$ + $14^{2+}$ | penta | $[Cu_2(m-42)_2]^{2+}$ | unstable complex |
|  |  | $[Cu_2(k-84)]^{2+}$ | 8% |
| $11^{2+}$ + $14^{2+}$ | hexa | $[Cu_2(m-45)_2]^{2+}$ | 21% |
|  |  | $[Cu_2(k-90)]^{2+}$ | 2.5% |

It can be noted that all the preparation yields are rather low, except for some face-to-face complexes which can be obtained in more than 20% yield. As far as dicopper(I) knots are concerned, the best results was obtained with $[Cu_2(k-84)]^{2+}$ (8% yield). A possible explanation is that the $-(CH_2)_6-$ fragment linking the two phenanthroline units is particularly favorable either to double helix formation versus face-to-face precursor or to cyclization to the knot. The latter explanation seems reasonable on the basis of a recent X-ray crystallographic study on $[Cu_2(k-84)]^{2+}$ (ref.12). The structure shows the helicoidal core to be very well adapted to the formation of a knot, particularly with a highly twisted helix, owing to the relatively long $-(CH_2)_6-$ fragment.

## Transition metal directed threading of molecular strings into coordinating rings

Transition metals have been used as assembling and templating species in a variety of processes (ref.13).The three-dimensional template effect of one or two copper(I) centres has extensively been used to construct topologically non-trivial molecules like catenanes and knots (refs.2-7), as discussed above.

Another approach, based on the formation of electron acceptor-donor aromatic stacks, has recently led to the preparation of various catenanes and rotaxanes (ref.14).

In order to make more entangled systems and topologically more complex and attractive chemical objects we investigated the behaviour of multi-chelate threads in presence of coordinating rings and copper(I). The principle of the problem is indicated in Figure 4.
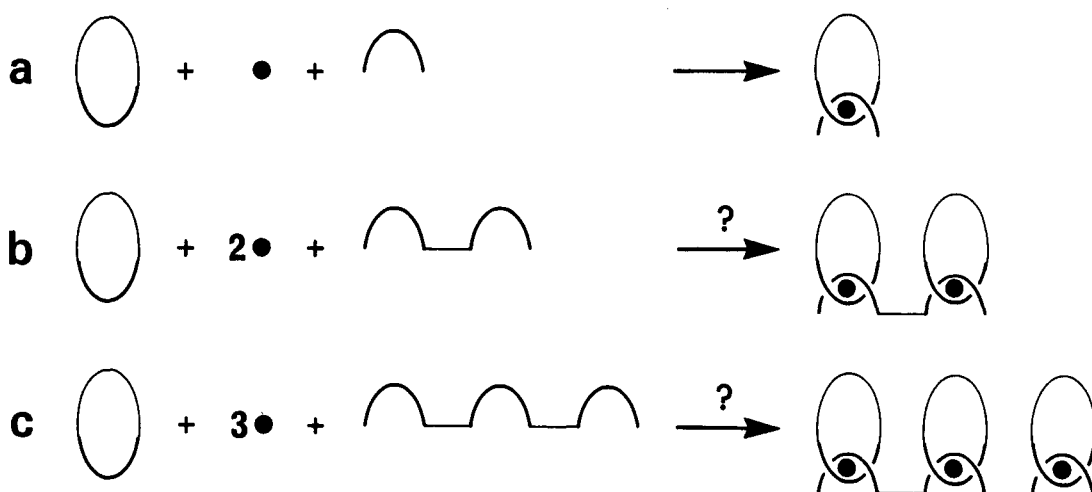


Figure 4.   Principle of the hypothetical multi-threading reaction.   The coordinating fragments are indicated in thick line.   The assembling metal centre is a black circle.
(a) : the well established quantitative threading of a monochelate with formation of a precursor to various catenanes.
(b) and (c) : possible generalisation of the reaction to multi-metallic threaded systems.

The driving force for building these multi-component structures is the formation of a bis-chelate complex. In fact, Cu(I) and 2,9-diphenyl-1,10-phenanthroline (dpp) derivatives form very stable bis-ligand pseudo-tetrahedral complexes whereas monochelates of the type Cu(dpp)+ are much less stable (ref.15). This has been applied in the simplest case ((a) of Figure 4) with unambiguous and quantitative formation of the threaded product (ref.4). If the string contains several coordination sites, the situation may become more complex and less predictable.

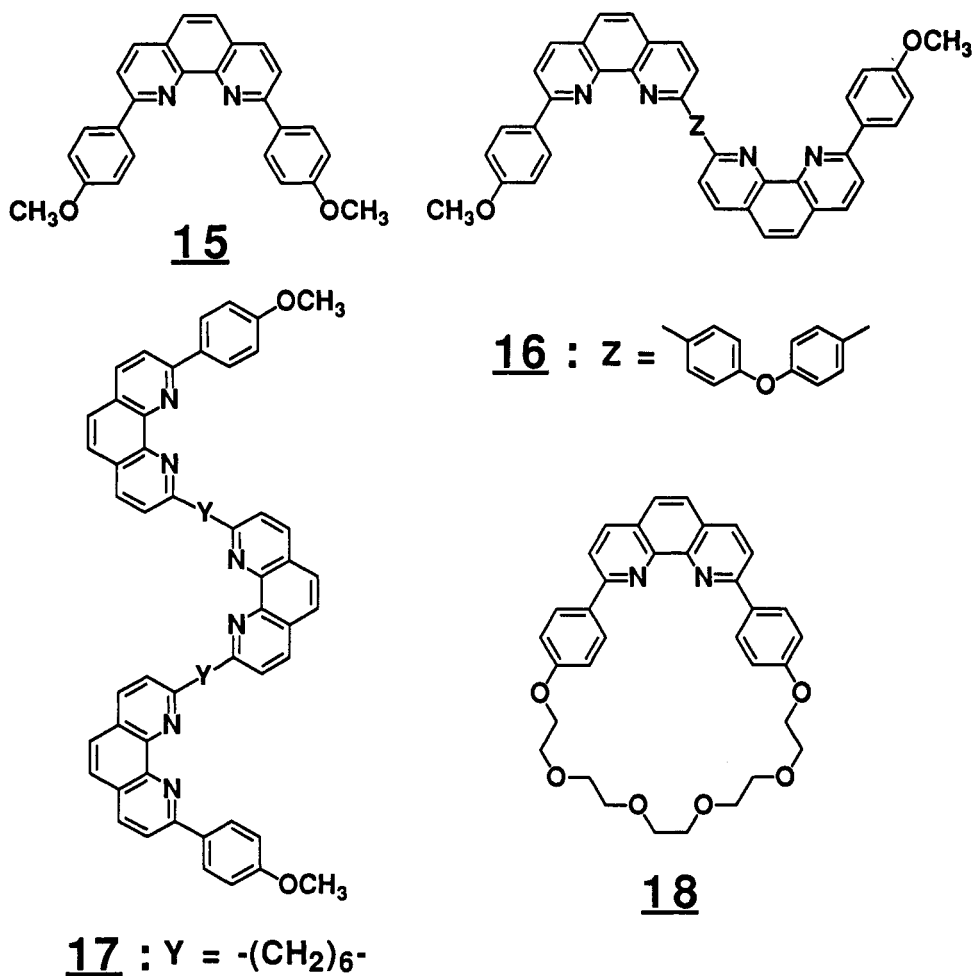The organic compounds investigated in the present study are represented in Figure 5.



Figure 5

The synthesis of **15** and **18** has previously been reported (refs.4,7). **16** is a rigid bis-chelate fragment whereas **17** is a flexible three-coordination site thread.

**15, 18** and copper(I) exactly behave as schematically represented in (a) of Figure 4. The validity of principle (b) has also been experimentally demonstrated. By mixing **16** or **4** (1 eq.), **18** (2 eq.) and Cu(CH$_3$CN)$_4$$^+$.BF$_4$$^-$ in CH$_2$Cl$_2$/CH$_3$CN a single complex was formed in both cases as shown by thin-layer chromatography (TLC) and $^1$H NMR. They correspond to the threaded system (b) of Figure 4. Quantitative formation of these dinuclear compounds is expected since **16** is too rigid and **4** is too short to fold up and form a mononuclear copper(I) complex. The chemical reaction is depicted in Figure 6(a).
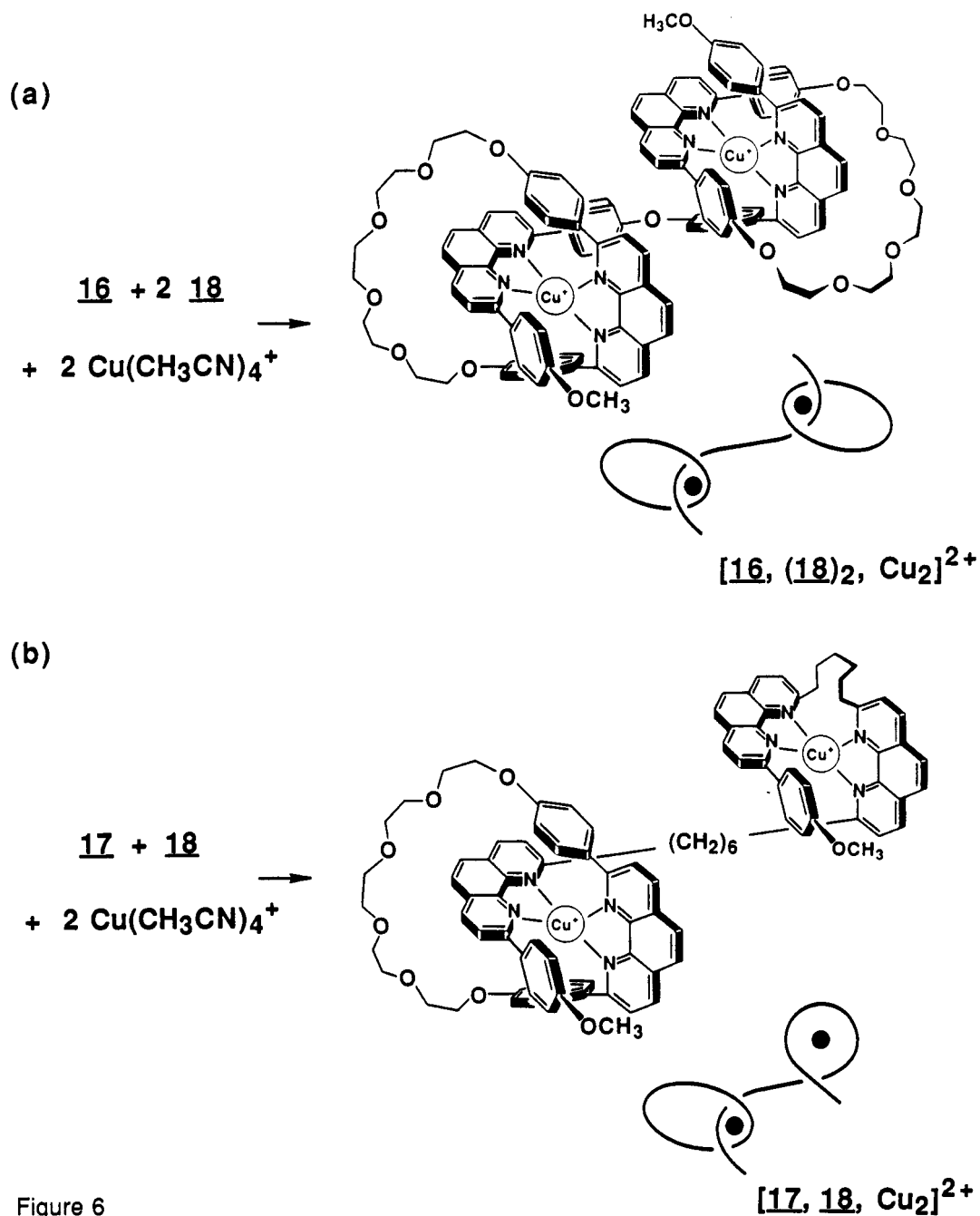
**(a)**

$\underline{16} + 2\ \underline{18}$

$+\ 2\ Cu(CH_3CN)_4{}^+$ $\longrightarrow$

$[\underline{16},\ (\underline{18})_2,\ Cu_2]^{2+}$

**(b)**

$\underline{17} + \underline{18}$

$+\ 2\ Cu(CH_3CN)_4{}^+$ $\longrightarrow$

$(CH_2)_6$

$[\underline{17},\ \underline{18},\ Cu_2]^{2+}$

Figure 6

The level of complexity increases further in the system containing **17, 18** and copper(I). When a 1 : 3 : 3 mixture of **17, 18** and $Cu(CH_3CN)_4{}^+$ was prepared, a mixture of complexes and free ligands was obtained, in contradiction with (c) of Figure 4. **17** is indeed flexible and should easily accomodate a curled-up conformation in which two of the three binding sites

complex the same copper(I) centre intramolecularly. The third 1,10-phenanthroline subunit was then expected to be available for intermolecular reactions. In effect, when **17, 18** and $Cu(CH_3CN)_4^+$ were mixed in a 1 : 1 : 2 proportion, a single compound was formed. It has the formula [**17, 18**, $Cu_2$]$^{2+}$ (ESMS, M-PF$_6$ : obs. 1756.8 (calc. 1755.9); M-2PF$_6$ : obs. 805.8 (calc. 805.5)) and, as indicated in Figure 6(b), it originates from intramolecular bis-chelate copper(I) complex formation <u>and</u> threading of the vacant site into the added ring **18**.

In conclusion, transition metals can govern a large variety of assembling processes, leading to complex multinuclear species. By using multisite molecular strings, double helices or face-to-face edifices can be obtained. The former compounds are precursors to trefoil knots, *the topology of which being particularly attractive.* On the other hand, by combining cyclic organic fragments and coordinating molecular strings with metals, novel threading processes are observed, affording in a totally metal directed fashion, molecular systems consisting of one or two rings threaded by a string. Such assemblies could possibly lead to molecular <u>abacus</u> by selecting appropriate metals and rings of different "colours" (i.e., of different size or bearing different substituents).

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