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Molecular Knots : Template Synthesis of Dicopper(I) Trefoil Knots of various Size

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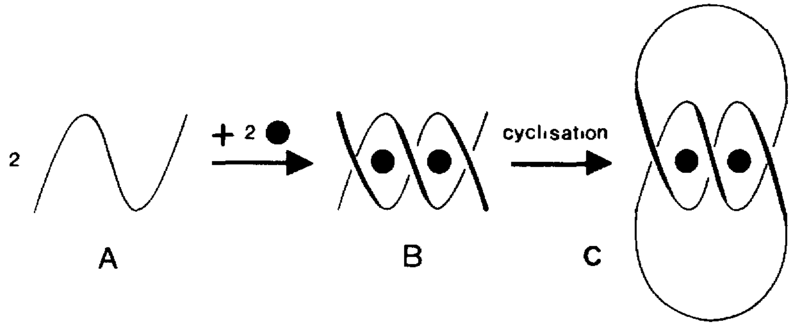
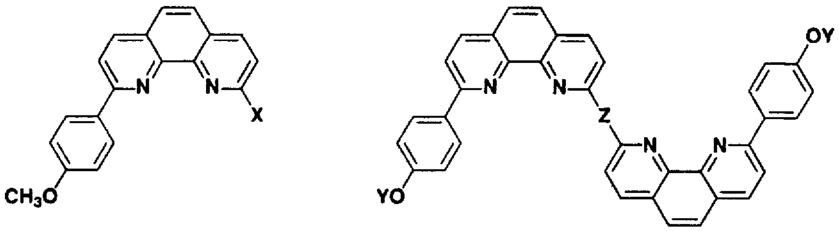
Abstract: In order to improve the template synthesis of our first molecular knot, we examined slightly modified systems and we now report the synthesis of four new dicopper (I) trefoil knots with a ring size ranging from 80 to 90 atoms.

Although the synthesis of catenanes (interlocking rings) has been met with relative success for many years[1], the recently developed template (or pre-organised) strategies[2,3] leading to the most preparative procedures, molecular knots have been much more scarcely considered[1,4,5] or actually synthesised[6]. They do however constitute a whole class of compounds whose importance in chemical topology[1,4,5] is obvious The synthesis of these chemical objects is even made more challenging since the discovery of knotted forms of DNA[7] After our 3% yield synthesis of an 86-membered knotted ring[6], we examined slightly modified systems with the hope of improving the preparation procedures. We now report the synthesis of four new di-copper(I) knots with a ring size ranging from 80 to 90 atoms. The same strategy as the one originally reported[6] has been followed. It is indicated in the scheme.



Scheme - (A) is a bis-chelating molecular thread bearing two end functions. In the presence of a transition metal (black circle) it forms a di-nuclear double-stranded helicoidal arrangement (B), precursor of the complexed trefoil knot (C) obtained by appropriate cyclisation

The combination of copper(I) as templating metal and 2,9-disubstituted-1,10-phenanthroline as chelating brick showed so appropriate in many instances for constructing interlocking rings[2,8] that we wanted to keep on these two species in the modified routes. The only modular parts were thus the **linker** connecting the two chelates before cyclisation and the long end functionalised **fragment used in the cyclisation step.**



1 : $X = H$
2 $X = CH_3$
3 $LiCH_2CH_2CH_2CH_2Li$
4 : $LiCH_2CH_2CH_2CH_2CH_2CH_2Li$

5 : $Y = CH_3$, $Z = (CH_2)_2$
6 . $Y = CH_3$, $Z = (CH_2)_4$
7 $Y = CH_3$, $Z = (CH_2)_6$
8 : $Y = H$, $Z = (CH_2)_2$
9 : $Y = H$, $Z = (CH_2)_4$
10 : $Y = H$, $Z = (CH_2)_6$

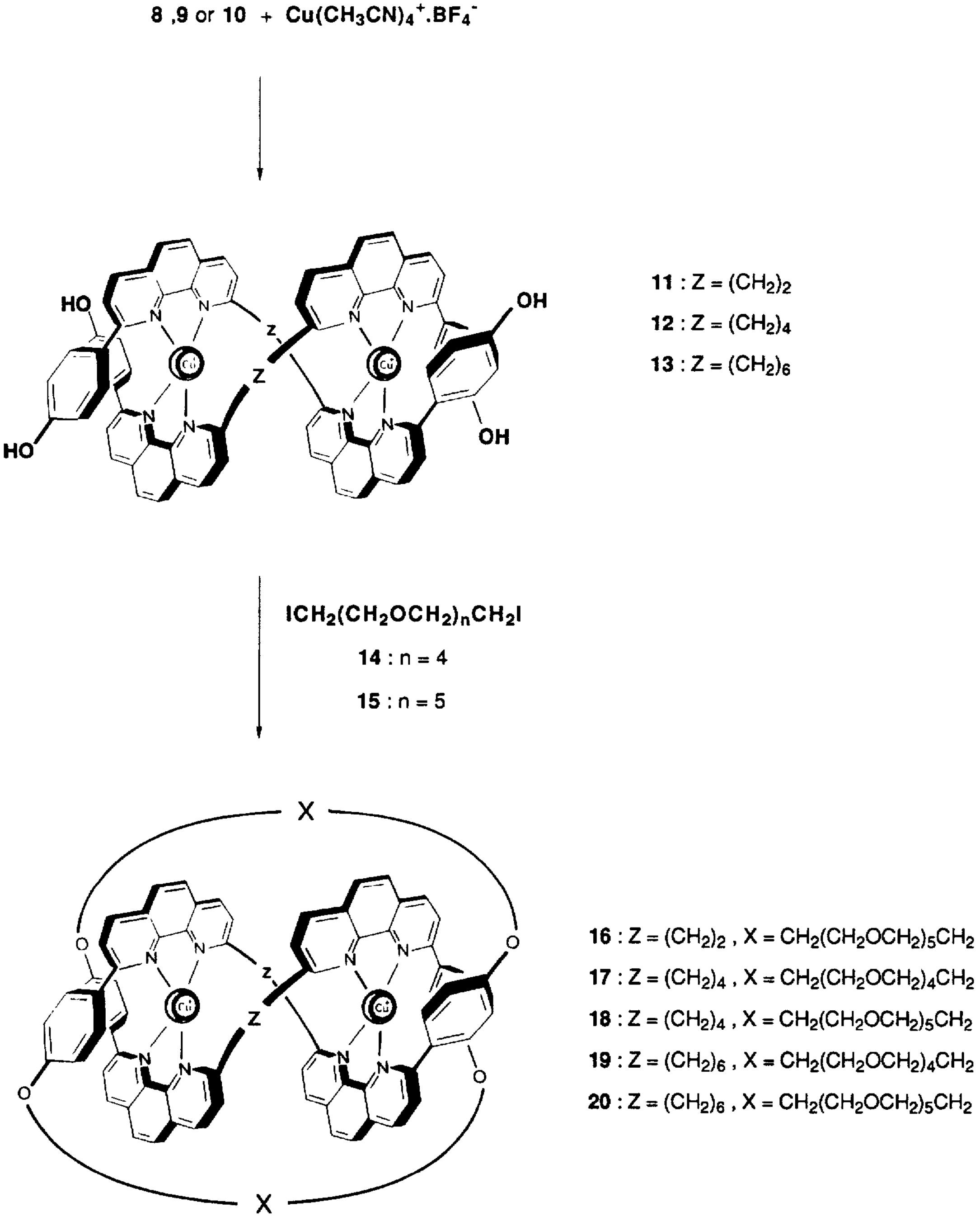
Figure 1

The various precursor compounds are indicated in Figure 1. The "tying reaction" leading to the trefoil knots[9] is represented in Figure 2.

1 was prepared from 1,10-phenanthroline and p-lithioanisole in 58% yield, following a previously published procedure[6,10]. Treatment of **1** by CH_3Li in ether at 0° to 10°C for 6 hours followed by hydrolysis and MnO_2 reoxidation led to a 92% yield of **2** (colourless crystals; mp: 161°C). The coupling reaction[11] affording **5** was carried out as follows: **2** was first treated with lithium di-isopropylamid (LDA) in THF at -78°C for 3 hours. Iodine was subsequently added, followed by hydrolysis, work-up and column chromatography. A 77% yield of **5** was obtained (white solid: m p. > 260°C). **6** and **9** were prepared as earlier described[6]. **7** was synthesised in an analogous way as **6** from $Li(CH_2)_6Li$[12] and **1** suspended in ether at 0°C followed by hydrolysis, MnO_2 oxidation and column chromatography. **7** was obtained as a white solid (mp: 194-195°C) in 54% yield. The diphenols **8**, **9** and **10** were prepared in a quantitative yield by demethylation of **5**, **6** and **7** respectively by heating the corresponding anisyl derivative at 210° for three hours in pyridinium chloride, water treatment, neutralisation and precipitation.

It is essential to be able to control the formation of double helices (B of the scheme) when reacting the bis-chelating molecular threads (A) with the metal centres. This is mainly governed by the nature of the fragment linking the two phenanthrolines. No evidence of double-stranded helicoïdal arrangment was obtained with $-(CH_2)_3$-or $p\text{-}C_6H_4\text{-}O\text{-}p\text{-}C_6H_4$-.

With polymethylene fragments containing even numbers of CH_2's, helices are indeed obtained (as determined by ^1H NMR measurements using methoxy containing compounds **5**, **6** and **7**) although in very variable proportions (~15% for **12**; 50% for **13**) The cyclisation reaction leading to the dicopper(I) knots **16-20** was carried out on mixtures containing the desired helices **11**, **12** or **13** obtained from **8**, **9** or **10** and copper(I). A representative procedure concerning the preparation of **19** is the following. The mixture of copper(I) complexes obtained by mixing stoichiometric amounts of $Cu(CH_3CN)_4^+.PF_6^-$ and **10** in CH_3CN-DMF under argon contains about 50% of the desired double-stranded helical dinuclear complex **13**. This material could not be separated by column chromatography due to fast reequilibration of the various copper(I) complexes contained in the mixture. It was thus used directly for the cyclisation step. In a three-necked round-bottomed flask, the crude mixture (PF_6^- salts; 0.45 mmoles) and the diiodo-derivative **14** (1 mmole) were dissolved in DMF (0.4 l). The solution was carefully degassed and brought to 60°C A suspension of dry Cs_2CO_3 (4.6 mmoles) in DMF (0.1 l) was added to the vigorously stirred reaction mixture over a period of 24 hours. The colour of the medium remained deep red throughout addition of the base, contrary to what is observed by inverting the addition procedure (Cs_2CO_3 in the flask and copper(I) complexes plus **14** or **15** in the dropping funnel). After work-up, anion exchange (PF_6^-) and careful column chromatography (silica; CH_2Cl_2-CH_3OH as eluent), the dicopper(I) knot **19** (PF_6^- salt) was obtained as a highly crystalline dark red solid in 8% yield (i.e.: 75 mg). The other knots



8, **9** or **10** + $Cu(CH_3CN)_4^+.BF_4^-$

11 : Z = $(CH_2)_2$

12 : Z = $(CH_2)_4$

13 : Z = $(CH_2)_6$

$ICH_2(CH_2OCH_2)_nCH_2I$

14 : n = 4

15 : n = 5

16 : Z = $(CH_2)_2$, X = $CH_2(CH_2OCH_2)_5CH_2$

17 : Z = $(CH_2)_4$, X = $CH_2(CH_2OCH_2)_4CH_2$

18 : Z = $(CH_2)_4$, X = $CH_2(CH_2OCH_2)_5CH_2$

19 : Z = $(CH_2)_6$, X = $CH_2(CH_2OCH_2)_4CH_2$

20 : Z = $(CH_2)_6$, X = $CH_2(CH_2OCH_2)_5CH_2$

Figure 2

16-18 and **20** were prepared using the inverted addition procedure (Fig 2). The preparative data are collected in Table 1.

Table 1.

knot prepared	linker Z	diiodo-derivative used (n)	overall knotted ring size = number of atoms	yield
16	$-(CH_2)_2-$	**15** (5)	82	0.5%
17	$-(CH_2)_4-$	**14** (4)	80	0.75%
18	$-(CH_2)_4-$	**15** (5)	86	3%
19	$-(CH_2)_6-$	**14** (4)	84	8%
20	$-(CH_2)_6-$	**15** (5)	90	2.5%

Although the yield of 8% for **19** is substantially higher than the one for **18**, probably due to a larger proportion of helix in the former case, the synthesis of knots at a really preparative scale is still a challenge.

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