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Synthesis of a Doubly Interlocked [2]-Catenane

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Although catenanes and knots have fascinated chemists for decades,[1,2] it is only recently that they have stopped being considered as exotic chemical species. This is mostly due to the relatively recent development of templated synthetic strategies[3,4] allowing one to prepare these compounds on a truly macroscopic scale and thus to characterize them in a totally convincing way.

The prototype of interlocking ring systems is the [2]-catenane (I) depicted in Scheme I. Its molecular graph is obviously nonplanar since two crossings have to be introduced in order to represent it in a plane.[5] It is easy to imagine that topologically more complex objects can be made by multiply interlocking two rings. The second most simple [2]-catenane is the four-crossing system (II) of Scheme I. It is noteworthy that the simple [2]-catenane (I) is topologically achiral, except if both constituent rings are directed,[6] whereas the doubly interlocked [2]-catenane (II) is topologically chiral with no need to orient the cycles. In this respect the doubly interlocked [2]-catenane and all the knots with an odd number of crossings display the same kind of unconditional topological chirality, as explained in Figure 1.

We now report the synthesis of the first doubly interlocked [2]-catenane, based on the three-dimensional template effect of copper(I) which we have previously exploited for making various catenanes and trefoil knots.[3,7,8] The strategy is depicted in Figure 2. As earlier suggested,[7] double-stranded multimetallic helicoidal complexes[9] are potential precursors to multiply wound [2]-catenanes or simple knots. In particular, helices containing an odd number (*n*) of metals lead, in principle, to (*n* + 1)-crossing [2]-catenanes.

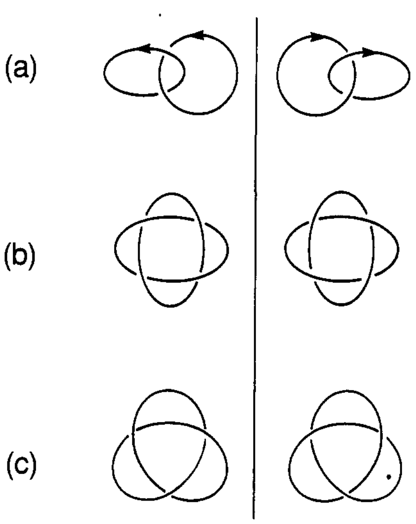


Figure 1. (a) A two-crossing [2]-catenane can be made chiral by orienting the rings (giving them directional character), whereas (b) the doubly interlocked [2]-catenane and (c) the trefoil knot are always chiral.

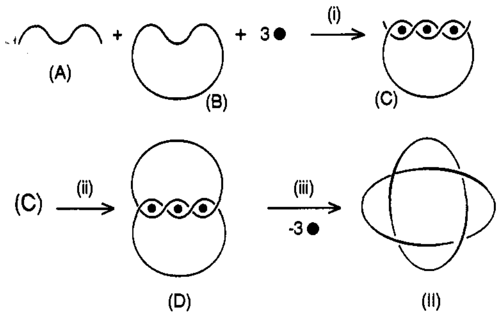
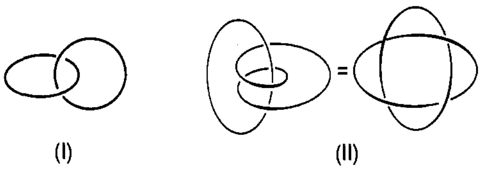


Figure 2. A and B contain three-chelate molecular fragments, A being a simple string and B having its complexing subunit included in a cycle. (i) In the presence of three metal centers (black circles), A and B can form a double-stranded double helix. (ii) By cyclization of the strand originating from A, the doubly wound catenate is obtained as a trinuclear complex. (iii) Demetalation affords the free doubly interlocked [2]-catenane (II). Of course, both right- and left-handed double-stranded helices should be formed, leading to D and subsequently II as racemates.

Scheme I



The strategy of Figure 2 has been applied with the compounds represented in Figure 3. **1** is the three-chelate fragment (A) of Figure 2, and **2** is the cyclic precursor (B).[10] It is assumed that, by mixing **1**, **2**, and $Cu(CH_3CN)_4^+ \cdot PF_6^-$ in a 1:1:3 proportion, a significant amount of the precursor $\mathbf{3}^{3+}$ is formed. Since several other copper(I) complexes were also formed (TLC, NMR), leading to an inseparable mixture of compounds, the cyclization reaction supposed to lead to $\mathbf{4}^{3+}$ was attempted on the crude mixture of products. The cyclization reaction (i) of Figure 3 was carried out in DMF with Cs_2CO_3 as base and the diiodo derivative of heptaethylene glycol as link. After workup and column chromatography, a fraction containing an interesting mixture of copper(I) complexes was isolated. Due to the relatively poor stability of the complexes, the purification procedure was continued on a demetalated mixture. As shown in Figure 4, the free ligands were obtained by treatment of the copper(I) complexes with $(CH_3CH_2)_4N^+ \cdot CN^-$. Several chromatographic separations were further carried out, affording large amounts of **2** and small quantities of **5** (2% yield; 18 mg starting from 0.405 g of **1**, 0.538 g of **2**, and 0.51 g of $Cu(CH_3CN)_4 \cdot PF_6$) and **6** (1% yield; 11.8 mg). Formation of **6** can be understood relatively easily if the precursor $\mathbf{3}^{3+}$ of Figure 3 is less wound than expected and if, among the various copper(I) complexes subjected to cyclization, simple threaded precursors are present. Isolation of *both* **5** and

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(4) Philp, D.; Stoddart, J. F. *Synlett* **1991**, 445.

(5) For a detailed discussion of chemical topology with an introduction to molecular graphs, see: Walba, D. M. *Tetrahedron* **1985**, *41*, 3161.

(6) Chambron, J. C.; Mitchell, D. K.; Sauvage, J. P. *J. Am. Chem. Soc.* **1992**, *114*, 4625. Chambron, J. C.; Dietrich-Buchecker, C. O.; Sauvage, J. P. *Topics in Current Chemistry, Vol. 165*; Springer: Berlin, 1993; p 131.

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(9) Several examples of di- or polynuclear double-stranded helicoidal complexes have recently been described. See, for instance: Struckmeir, G.; Thewalt, U.; Fuhrhop, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 278. Van Stein, G. C.; Van der Poel, H.; Van Koten, G.; Spek, A. L.; Duisenberg, A. J. M.; Pregosin, P. S. *J. Chem. Soc., Chem. Commun.* **1980**, 1016. Lehn, J. M.; Rigault, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1095. Constable, E. C.; Chotalia, R. *J. Chem. Soc., Chem. Commun.* **1992**, 64.

(10) The dimethyl ether of **1** has already been briefly described: Chambron, J. C.; Dietrich-Buchecker, C. O.; Nierengarten, J. F.; Sauvage, J. P. *J. Chem. Soc., Chem. Commun.* **1993**, 801. It was demethylated in pyridine–HCl at 210 °C to afford **1** in 94% yield. **1** and $ICH_2(CH_2OCH_2)_6CH_2I$ were reacted in DMF with Cs_2CO_3 at 60 °C under argon. **2** was isolated in 38% yield as a pale yellow, glassy product after chromatography. It was fully characterized (FAB-MS, NMR, and elemental analysis).

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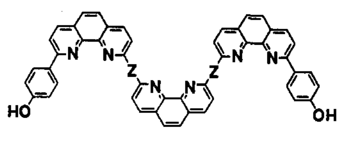
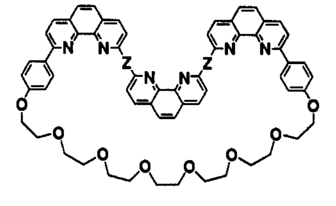


1

Z = $(CH_2)_6$



2

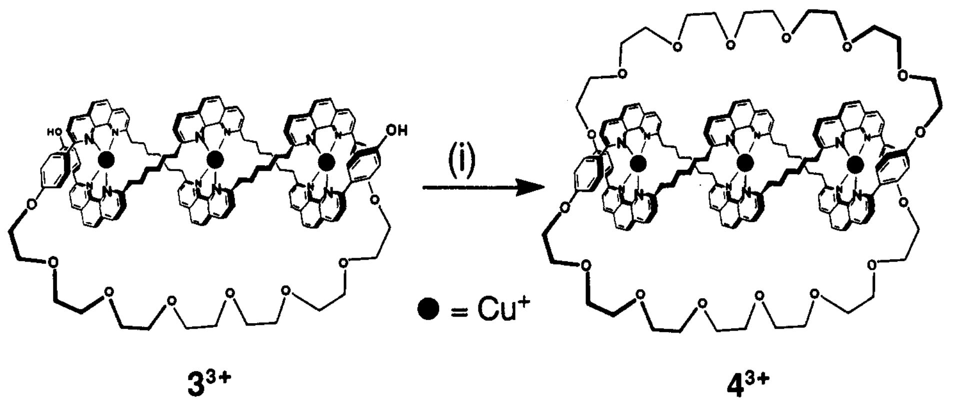


Figure 3. (i) $ICH_2(CH_2OCH_2)_6CH_2I/Cs_2CO_3/DMF/60–62$ °C.

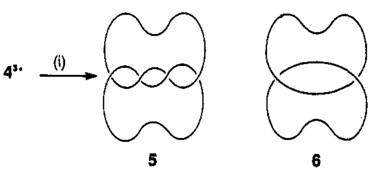


Figure 4. (i) $(CH_3CH_2)_4N^+·CN^-/CH_2Cl_2/H_2O$. Each constituent ring of ligands 5 and 6 corresponds to the macrocycle 2.

6 greatly facilitated their structural identification. Both compounds have different R_fs in TLC (alumina; eluent: CH_2Cl_2/2.5% MeOH; 0.35 for 5 and 0.8 for 6), but their electrospray mass spectra (ES-MS) are identical. *Both compounds are catenanes* as evidenced by the following experiments. At a 30-V extraction cone voltage (V_c) a single peak appears at 1179.9 for 5 and 1179.4 for 6; they correspond respectively to $M/2$ expected for $(5·H_2)^{2+}$ or $(6·H_2)^{2+}$ (calcd for $M/2$: 1179.5). Furthermore, in each case, by increasing V_c from 30 to 120 V the only intense peak appears again at 1179 but is here singly charged and thus corresponds to the constituent protonated ring $(2·H)^+$ resulting from the fragmentation of both catenanes $(5·H_2)^{2+}$ and $(6·H_2)^{2+}$.[11] The ^{1}H-NMR spectrum of 6 is normal in the sense that it is very similar to that of 2. By contrast, 5 has a broad spectrum indicating that slow conformational equilibria are taking place. The variable temperature ^{1}H-NMR study of 5 in d_6-DMSO shows a perfectly reversible narrowing of all the peaks with obtention of a fully assigned sharp spectrum at 390 K. Clearly, the doubly interlocked topology of 5 leads to a tight structure, each cycle undergoing slow gliding motions analogous to the reptation process already observed for a trefoil knot.[12]

Acknowledgment. We thank the CNRS for financial support and the French Ministry of Research and Space for a fellowship (J.F.N.). We also thank Miss E. Leize and A. Van Dorsellaer for ES-MS measurements.

Supplementary Material Available: ^{1}H NMR spectra of 2, 5, and 6 (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(11) FAB-MS measurements performed on the free ligands 5 and 6 fully confirm their topology. Both spectra show the highly characteristic fragmentation pattern expected for a catenane: molecular ion peak at 2358.9 for 5 and 2359.1 for 6 (calcd for MH⁺: 2359.0); no fragmentation occurs until the molecular peak of the monomeric ring 2 (1179.4 and 1179.8 for 5 and 6; calcd for $2·H^+$: 1179.5) is reached. Vetter, W.; Logemann, E.; Schill, G. *Org. Mass Spectrom.* **1977**, *12*, 351. Dietrich-Buchecker, C. O.; Sauvage, J. P. *Chem. Rev.* **1987**, *87*, 795.

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