

Communications to the Editor

A Chemically Achiral Molecule with No Rigidly Achiral Presentations

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Some time ago it was recognized that certain chemically achiral molecules¹ possess the curious property of being composed *entirely* of asymmetric conformations and that conformational enantiomerization must therefore take place *exclusively* by chiral pathways.^{2a} The following year saw the actualization of the first molecule of this type, with the synthesis of (1*R*)-menthyl (1*S*)-menthyl 2,2',6,6'-tetranitro-4,4'-diphenate (**1**).^{2b} Since that time, other examples of this type have been reported, including asymmetric molecular propellers, whose enantiomerization by the two-ring flip mechanism involves an exclusively chiral pathway,³ and certain bis(9-triptycyl)methane derivatives, in which the two triptycyl groups behave as highly mobile and tightly meshed bevel gears.⁴ We now report the first example of a molecule, the [2]catenane **2** depicted in Figure 1, that not only shares the stereochemical characteristics of **1** but whose molecular graph, unlike that of **1** and other molecules of this type, is rigidly (geometrically) chiral in every possible presentation.⁵ The ring containing the *p*-tolyl-substituted 1,10-phenanthroline is oriented, thanks to the asymmetric positioning of the substituent. The ring containing the 1,5-dioxynaphthalene, however, is not oriented because it can attain a conformation with C_2 symmetry. Catenation of the oriented with the nonoriented ring destroys the C_2 axis in the latter. All

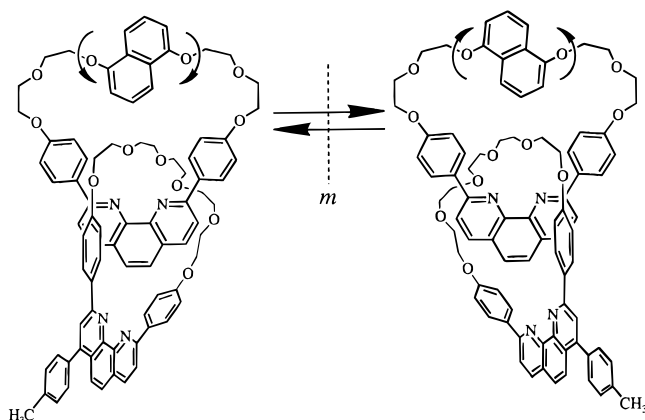


Figure 1. Enantiomorphous conformations of [2]catenane **2**. Unmarked vertices represent C, CH, or CH₂ groups. The enantiomorphs are related by the mirror plane (*m*) and are interconverted by rotation of the 1,5-dioxynaphthalene moiety about the C–O bonds (arrows).

achiral presentations available to each of the component rings in isolation have C_s symmetry, but the σ planes of the two components cannot become coplanar in the catenated state. It follows that every conceivable presentation of the [2]catenane is asymmetric. As shown in Figure 1, the mirror image of an asymmetric conformation is obtained by rotation of the 1,5-dioxynaphthalene plane by 180°. All chemically accessible conformations encountered along this or any other enantiomerization pathway, as well as all topologically accessible presentations, are asymmetric. The time-averaged symmetry of **2** is C_s , which expresses the chemical achirality of the molecule, even though no individual conformation or presentation of the molecule can possibly belong to this point group.⁶

The [2]catenane is properly characterized as a molecular “topological rubber glove”.⁷ Seeman’s figure-eight knot made from single-stranded DNA,⁸ which has been similarly characterized,⁹ is incapable of attaining chemical achirality.¹⁰ Therefore, from a stereochemical perspective, **2** has no precedent and is in a class of its own. Furthermore, while it has long been recognized that certain knots and graphs are topologically achiral but not rigidly achiral,¹¹ **2** represents the first example of a link in this class.

The synthesis of **2** is summarized in the scheme of Figure 2. Reaction of macrocycle **3**¹² with [Cu(MeCN)₄]PF₆, followed by threading of diiodide **4**¹³ at room temperature under argon, afforded precatenane [(**3,4**)Cu]PF₆ in quantitative yield. This complex was mixed with 1,5-dihydroxynaphthalene (**5**),

(1) A molecule is chemically achiral if each momentary conformational geometry can be superposed on its mirror image by a combination of the rotations, translations, and intramolecular motions that can occur under the given conditions of observation. See: Dugundji, J.; Showell, J.; Kopp, R.; Marquarding, D.; Ugi, I. *Isr. J. Chem.* **1980**, *20*, 20. Ugi, I.; Dugundji, J.; Kopp, R.; Marquarding, D. *Perspectives in Theoretical Stereochemistry (Lect. Notes Chem.* **1984**, *36*); Springer Verlag: Berlin, 1984.

(2) (a) Mislow, K. *Science* **1954**, *120*, 232. (b) Mislow, K.; Bolstad, R. *J. Am. Chem. Soc.* **1955**, *77*, 6712. See also: Mislow, K. *Trans. N.Y. Acad. Sci.* **1957**, *19*, 298. Mislow, K. *Introduction to Stereochemistry*; Benjamin: New York, 1965; pp 91–93.

(3) (a) Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 1535. (b) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26. (c) Glaser, R.; Blount J. F.; Mislow, K. *J. Am. Chem. Soc.* **1980**, *102*, 2777.

(4) (a) Hounshell, W. D.; Johnson, C. A.; Guenzi, A.; Cozzi, F.; Mislow, K. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 6961. (b) Guenzi, A.; Johnson, C. A.; Cozzi, F.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1438. (c) Iwamura, H.; Mislow, K. *Acc. Chem. Res.* **1988**, *21*, 175.

(5) The topological model of a molecule is its molecular graph, in which differently labeled vertices represent different kinds of atoms and differently labeled edges represent different types of chemical bonds. As a topological object, a molecular graph is deformable into infinitely many images called presentations. Metrics and energetics play no role in these deformations; the single constraint is that the vertices must remain connected in the same way and that no edges must be broken and reformed or passed through one another. With the notable exceptions of knots and links, the graphs of most geometrically chiral or achiral molecules can be embedded in the plane without crossing of any edges—like the constitutional formulas (line diagrams) that chemists write on blackboards—and can thus be deformed into rigidly achiral presentations. This includes the molecular graph of **1**. For a recent commentary on the topological chirality and achirality of molecules, see: Mislow, K. *Croat. Chem. Acta* **1996**, *69*, 485.

(6) Time-averaged symmetries of **1** are C_s , C_i , or S_4 .

(7) A topological rubber glove is defined as an object that is topologically achiral but rigidly chiral in every possible presentation. See: Walba, D. M. In *Graph Theory and Topology in Chemistry*; King, R. B., Rouvray, D. H., Eds.; Elsevier Science Publishers: Amsterdam, 1987; pp 23–42. Walba, D. M. In *New Developments in Molecular Chirality*; Mezey, P. G., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1991; pp 119–129. Walba, D. M.; Homan, T. C.; Richards, R. M.; Haltiwanger, R. C. *New J. Chem.* **1993**, *17*, 661.

(8) Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc.* **1992**, *114*, 9652.

(9) Flapan, E.; Seeman, N. C. *J. Chem. Soc., Chem. Commun.* **1995**, 2249.

(10) In order to convert the DNA strand to its enantiomorph, it is necessary to flatten the sugars so that they are planar, like the purine and pyrimidine bases.⁹ There is, of course, no way in which this topological transformation can be achieved by any feasible chemical operation.

(11) Flapan, E. *Pac. J. Math.* **1987**, *129*, 57.

(12) Chambron, J.-C.; Mitchell, D. K.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1992**, *114*, 4625.

(13) Amabilino, D. B.; Sauvage, J.-P. *Chem. Commun.* **1996**, 2441.

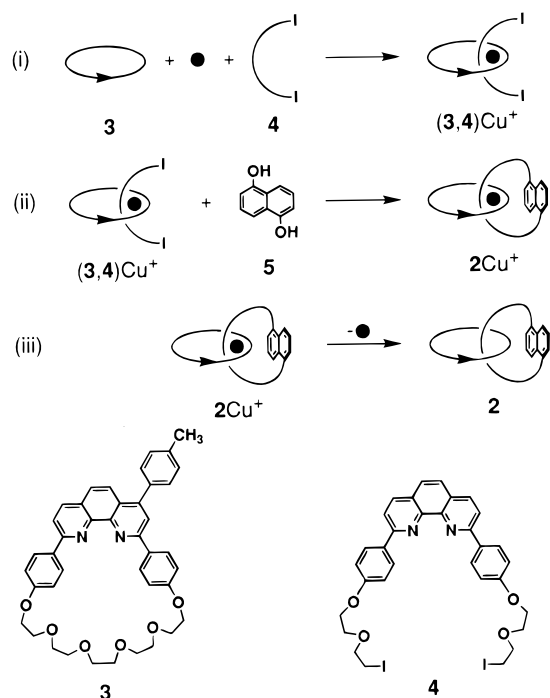


Figure 2. Reaction scheme for the synthesis of [2]catenane **2**. The black dot symbolizes Cu^+ ion. (i) Threading of diiodide **4** into oriented macrocycle **3**. (ii) Closing of the interlocked, nonoriented macrocycle by reaction with **5**. (iii) Removal of the metal template.

and the resulting solution was added slowly to a suspension of cesium carbonate in DMF at $60\text{ }^\circ\text{C}$ under argon.¹⁴ After counterion exchange and chromatography, catenane $[\text{2Cu}]\text{PF}_6$ was obtained in 35% yield. Demetallation to the catenane **2** was achieved by treatment of an acetonitrile solution of $[\text{2Cu}]$ -

(14) Dietrich-Buchecker, C.; Sauvage, J.-P. *Tetrahedron* **1990**, *46*, 503.

PF_6 with an aqueous KCN solution. After workup and chromatography, **2** was obtained in 84% yield. All compounds were characterized by proton NMR spectroscopy and by fast atom bombardment (FAB) and electrospray (ES-MS) mass spectrometries.

The ES-MS mass spectrum of $[\text{2Cu}]\text{PF}_6$ shows a major peak at 1385.1 for the molecular ion and a peak corresponding to a dicharged species at 692.5. The FAB mass spectrum of **2** shows the molecular ion peak at 1321.5 and two peaks corresponding to the constitutive macrocycles. Remarkably, no fragmentation occurs until the molecular peaks of these macrocycles. As first reported by Schill and co-workers,¹⁵ such a pattern is characteristic of a catenane structure.

The proton NMR spectra of **2** and $[\text{2Cu}]\text{PF}_6$ were fully assigned by 2D ROESY experiments.¹⁶ Despite the fact that the naphthalene-containing ring has lost its 2-fold symmetry when interlocked with macrocycle **3**, only one set of signals was observed for the former. Lowering the temperature to $-90\text{ }^\circ\text{C}$ produced only peak broadening. This clearly indicates that the naphthalene group is rotating rapidly on the NMR time scale, with concomitant interconversion of the conformational enantiomers of **2**.

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Supporting Information Available: Spectroscopic data, experimental details for the preparation of $[\text{2Cu}]\text{PF}_6$ and **2**, and VT proton NMR spectra of **2** (12 pages). See any current masthead page for ordering and Internet access instructions.

JA971598M

(15) Vetter, W.; Logemann, E.; Schill, G. *Org. Mass Spectrom.* **1977**, *12*, 351 and references cited therein.

(16) See the Supporting Information.