Enantiomeric Resolution of Cycloenantiomeric Rotaxane, Topologically Chiral Catenane, and Pretzel-Shaped Molecules: Observation of Pronounced Circular Dichroism

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In the course of our template synthesis[1] of amide-connected rotaxanes[2,3] by threading a dumbbell part through a prepared wheel, we successfully synthesized the [2]rotaxane **1** (cf. Figure 1) and the [1]rotaxane **2** (cf. Figure 2).[4] These mechanically bonded molecules are the first examples for rotaxane cycloenantiomers,[5] consisting of a dumbbell and a wheel which are not chiral themselves. The object and its mirror image in this case result from different sequences of the sulfonamide group and the three amide groups on the wheel in rotaxanes **1** and **2**, bearing an unsymmetrical dumbbell. The dumbbells in **1** and **2** are unsymmetrical because of the amide group and the sulfonamide group (cf. Figure 1). The wheels differ in the sequence of their connectivities. One enantiomer has a clockwise direction with respect to the unsymmetrical dumbbell, whereas the other enantiomer shows the opposite arrangement (Figure 1).

The high conformational flexibility of the molecular parts of rotaxane **1**, which leads to decreased structural dissymmetry of the enantiomers compared to more rigid molecules, opens the question whether such racemates can be separated into the enantiomers by the use of usual HPLC and chiral column materials.[6] Surprisingly enantioseparation of the cycloenantiomeric rotaxane **1** was now found to be possible by HPLC on "Chiralpak AD".[7] The separation factor α was found to be 1.48, and almost complete resolution was obtained.[8] In this separation the (+)-enantiomer was eluted first.

The HPLC chromatogram of the enantioseparation of rotaxane **2** (on "Chiralcel OD"[7]) shows a clear baseline separation with

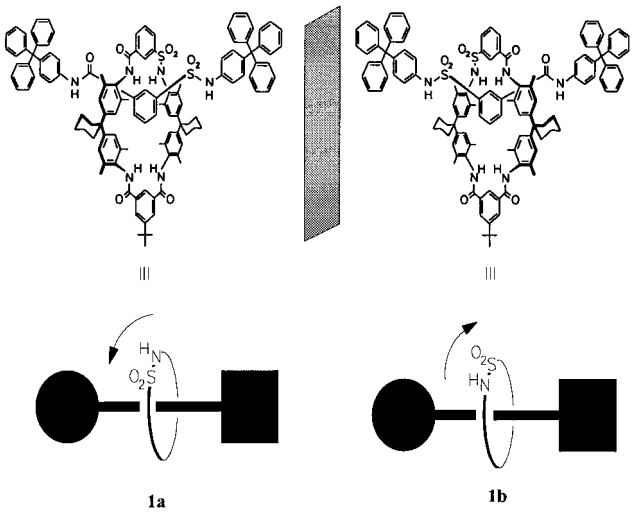

Figure 1. Cycloenantiomeric [2]rotaxane **1** (mirror plane gray shaded, arrows indicate the sequence of the atoms).

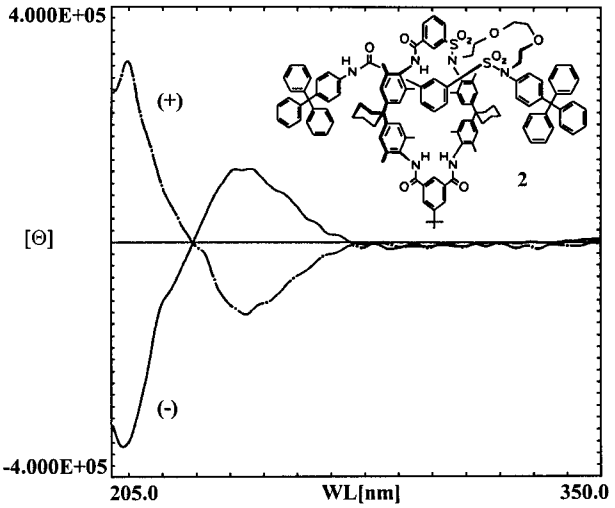

Figure 2. Circular dichrogram of the cycloenantiomeric [1]rotaxane **2** in trifluoroethanol (TFE); *c*[(−)-**2**], 1.5 × 10^{-4} M; *c*[(+)-**2**], 1.1 × 10^{-4} M.

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(4) For an explanation of the term [1]rotaxane, see: Jäger, R.; Händel, M.; Harren, J.; Rissanen, K.; Vögtle, F. *Liebigs Ann.* **1996**, 1201. A molecule with the same topology was described as a "prerotaxane" in Schill's book (ref 5b, pp 151−152).

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(8) Conditions: column, Chiralpak AD (25 × 0.46 cm i.d.) (amylose tris[3,5-(dimethylphenyl)carbamate], eluent, hexane/2-propanol (82/18); flow rate, 1.0 mL/min; detector, UV (JASCO MD-910); polarimeter (JASCO OR-990); sample, 15 mL (5 mg/mL, CH_2Cl_2/methanol (8/1)).

(9) Conditions: column, Chiralcel OD (25 × 0.46 cm i.d.) [cellulose tris[3,5-(dimethylphenyl)carbamate]; eluent, hexane/ethanol (85/15); flow rate, 1.0 mL/min; detector, UV (JASCO MD-910); polarimeter (JASCO OR-990); sample, 5 mL (5 mg/mL, CH_2Cl_2/methanol (8/1)).

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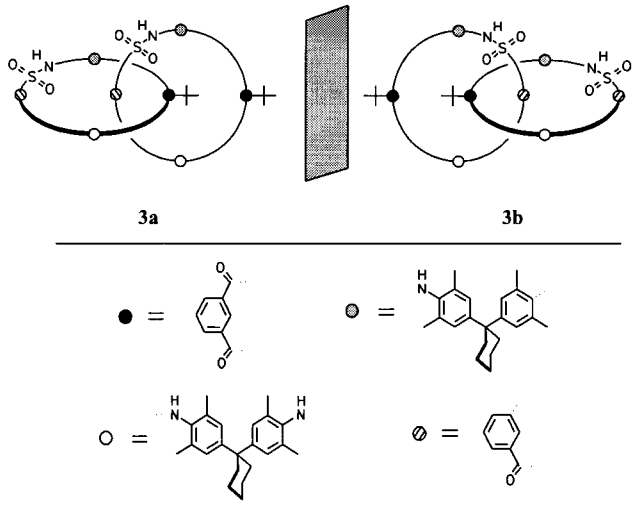

Figure 3. Topologically chiral sulfonamide catenane **3** (mirror plane gray shaded).

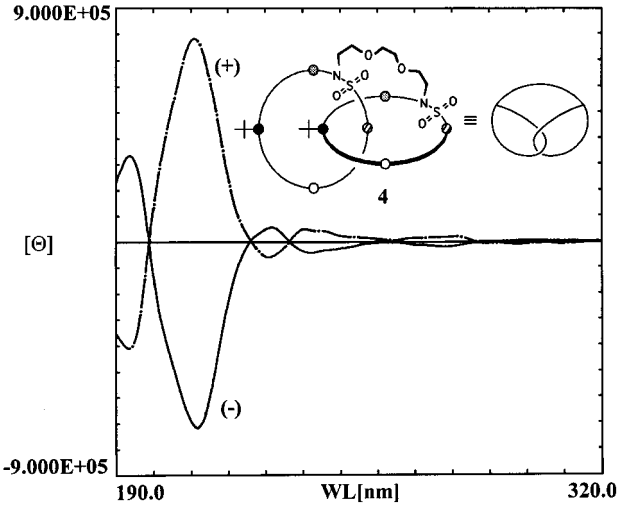

Figure 4. Circular dichrogram of the pretzel-shaped molecule **4** in TFE (for the meaning of the symbols see Figure 3): *c*[(−)-**4**], 2.2 × 10^{-4} M; *c*[(+)-**4**], 1.4 × 10^{-4} M.

$\alpha = 1.69$, and the (−)-enantiomer was eluted first in this case.[9] Figure 2 shows the circular dichrogram of the enantiomers of **2**.

In 1988, Sauvage *et al.* published the first synthesis of a topologically chiral[5,10] catenane,[11,12] and five years later, the same group achieved the partial separation into the enantiomers in cooperation with Okamoto *et al.*[13] In 1996, we reported the synthesis of a topologically chiral sulfonamide catenane **3**.[4,14] To introduce this type of chirality into a catenane, the rings must have a sequence information. Depending on the orientation of the sulfonamide groups, catenane **3** possesses two stereoisomers **3a**,**b** (Figure 3).

The successful enantioseparation of the cycloenantiomeric rotaxane **2** encouraged us to separate the corresponding catenane[15] racemate **3** under similar conditions.[16] Again a baseline separation of this topologically chiral species was accomplished with the (+)-enantiomer being eluted first. A very large separation factor $\alpha = 6.95$ value was measured.

Intramolecular bridging of the two sulfonamide units in catenane **3** leads to molecule **4** (cf. Figure 4) with a molecular graph equaling that of a pretzel.[17] Enantioseparation of this topologically chiral compound also was accomplished in the form of a baseline separation (the (−)-enantiomer eluted first) again with a large separation factor α (5.20).[18] The circular dichrogram of **4** (Figure 4) shows pronounced Cotton effects in the aromatic chromophore region.

The optical rotation values were determined by using Tröger Base ($[\alpha]_D = 281°$) as a standard. The chromatographic analysis was performed under the same conditions as for compounds **1**−**4**. Using this calibration value the $[\alpha]_D$ values are 20° for **1**, 84° for **2**, and 168° for **3** and **4**.[19] These optical rotation values are smaller than those, e.g., from a Tröger base, but nevertheless appreciable. Such pronounced values have not been observed previously.

In conclusion, cycloenantiomerism of rotaxanes has been observed for the first time. The corresponding racemates **2** were baseline separated. A topologically chiral sulfonamide catenane **3** and a pretzel-shaped molecule **4** have been completely separated into the pure enantiomers, too. These findings allow a more general and more quantitative understanding of mechanically bonded chiral molecules, whose chirality depends on atom sequence information.

Introduction of additional chromophores in the future will give more pronounced Cotton effects and will possibly permit determination of absolute configurations. Furthermore, the chirality ought to be increased by affixing substituents at the sulfonamide groups that render the molecule less symmetrical. Second, the circumrotation or translation of the wheel could be influenced by the size of the attached substituents.[20] If this is achieved, it may be possible to steer or even switch chirality, e.g. depending on temperature or light.[21]

Supporting Information Available: A listing of the HPLC chromatograms and the CD spectra (6 pages). See any current masthead page for ordering and Internet access instructions.

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(16) Conditions: column, Chiralcel OD (25 × 0.46 cm i.d.); eluent, hexane/2-propanol (60/40); flow rate, 1.0 mL/min; detector: UV (JASCO MD-910); polarimeter (JASCO DIP-181C); sample, 5 mL (6 mg/mL, CH_2Cl_2/methanol (8/1)).

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(19) Solvents for specific optical rotations $[\alpha]_D$ [(deg·cm^2)/10 g]: **1** in hexane/2-PrOH (82/18), **2** in hexane/EtOH (85/15), **3** in hexane/2-PrOH (60/40), **4** in hexane/EtOH (75/25).

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