Amide-based Furano-catenanes: Regioselective Template Synthesis and Crystal Structure

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The synthesis of the new octalactam catenane isomers **6** and **7** and the first X-ray structural analysis of this skeleton are reported, revealing a self-assembled, interlocked system held together by networks of inter- and intra-molecular hydrogen bonds including the amide groups and the furane oxygen atoms.†

In 1992, the one-[1] and two-step[2] template syntheses[3] of a new catenane type[4] with octalactam structure were reported. We demonstrated that the macromonocycle which is also formed as a byproduct plays a key role in the catenane formation.[5] On this basis we also synthesized an amide-linked rotaxane.[6]

In order to gain further insight into the catenane formation we were interested in the consequences for the template mechanism arising from replacement of the metaphenylene subunits by different units. For this, we carried out the synthesis **A** represented in Scheme 1 by reaction of the diamino-functionalized diamide **1**[2] with the dichloride **2** of 2,5-furandicarboxylic acid under high dilution conditions. Here no catenanes could be detected, but the macromonocycle **3** was isolated in 15% yield.

We repeated the reaction with a 'reversed pattern' (synthesis **B**) by reaction of the diamide **4** with isophthaloyl dichloride **5**. After purification by column chromatography we again obtained **3** (4% yield); however, in addition the catenane isomers **6** and **7** in 8 and 20% yield, respectively, were also produced. Whereas in both syntheses **A** and **B** the same macromonocycle **3** is formed, only in the case of **B** does the isophthaloyl dichloride **5** [*cf.* Fig. 1(*a*)] or the monoamide [*cf.* Fig. 1(*b*)] nest inside **3**,[5] followed by catenane formation. It is remarkable that the analogous nestling of 2,5-furandicarboxylic acid dichloride **2** in the course of **A** does not seem to occur to a comparable extent.

From the three possible catenane isomers **6**, **7** and **8**, resulting from the hindered circumrotation of the catenane rings,[1,5] we only observed the regioselective formation of **6** and **7**, which is in agreement with our proposed template mechanism.‡

The structures of the two isomers **6** and **7** were confirmed by FAB-MS, ^{13}C and ^{1}H NMR. Compound **6** could be crystallized from CH_2Cl_2–MeOH and its X-ray crystal structure§ was solved (Fig. 2), the first in this octaamide series.¶ In the crystal, both 34-membered and structurally identical catenane rings which are composed of rigid building blocks, have the same conformation and they are connected by numerous intra- and inter-molecular hydrogen bonds (see Table 1). Compound **6** possesses crystallographic C_2 symmetry.

Each isophthaloyl moiety is buried in the cavity of the other macromonocycle, being involved in offset π-stacking interactions with two *m*-xylylene units. One of its carbonyl groups (*trans*-diamide) is hydrogen bonded to the amide proton of the second isophthaloyl unit. The other carbonyl group takes part in

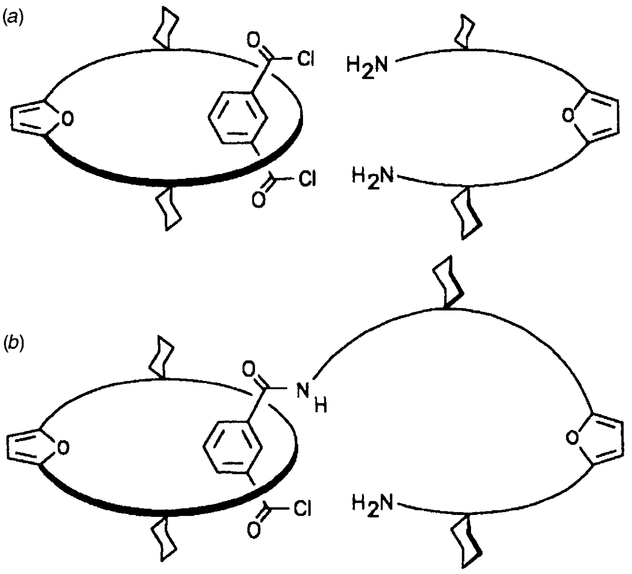
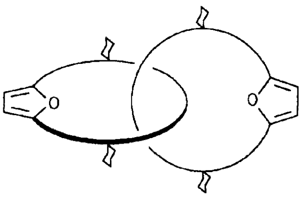
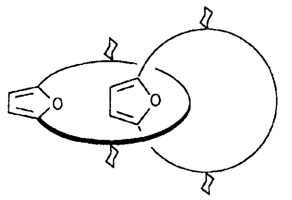


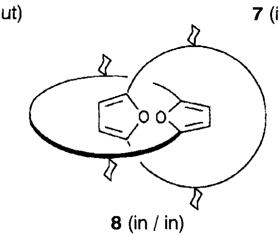
Fig. 1 Guest-nestling and threading of isophthalic acid (*a*) or isophthalic acid monochloride-monoamide (*b*) inside the macromonocycle **3**



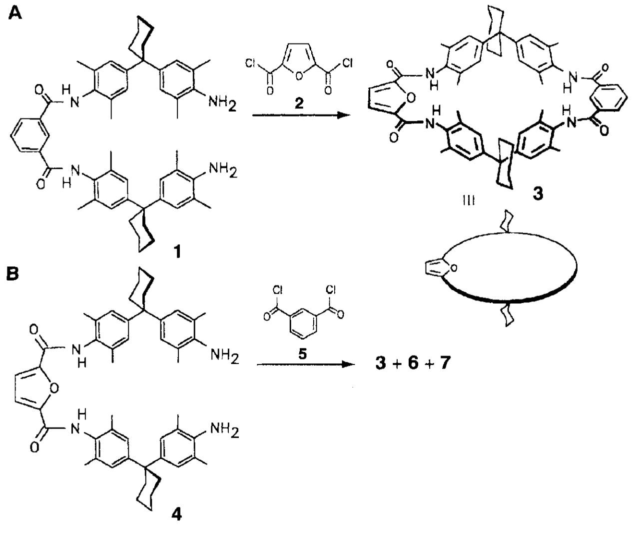
6 (out / out)



7 (in / out)



8 (in / in)



Scheme 1

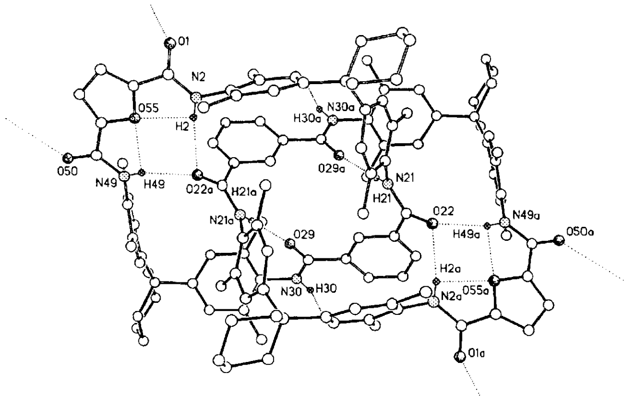


Fig. 2 X-Ray structure of **6**

Table 1 Selected distances in compound **6**

Intramolecular distances/pm		Intermolecular distances/pm	
O(55)···N(2)	269[a]	O(50)···O(MeOH)	294[a]
O(55)···N(49)	269[a]	O(1)···N(amide)	279[c]
O(29)···N(21a)	290[b]		
N(2)···O(22a)	317[b]		
N(49)···O(22a)	310[b]		

Symmetry transformations: [a] x, y, z; [b] $-x, y, 0.5 - z$; [c] $-0.5 + x, 0.5 + y, z$ (amide hydrogen of the adjacent catenane molecule).

an unusual framework of hydrogen bonds connecting the two amide protons of the neighbouring furanoyl units and the furan oxygen.||

Two types of carbonyl groups (*endo* and *exo*) can be differentiated. The *cis*-diamide furanoyl carbonyl groups (*exo*) point to the exterior and form hydrogen bonds to methanol molecules and adjacent catenane molecules. The isophthaloyl units contribute with their carbonyl groups (*endo*) to the hydrogen bonding interations between the two intertwined macromonocycles.

The conformation of **6** is in good agreement with the three-dimensional structure determined for a symmetrical octalactam-catenane in solution by ^{1}H NMR.[2]

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Footnotes

† Parts of this work have been communicated at lectures at Mainz (13.8), Tel Aviv (26.10), Rehovot (31.10) and Haifa (1.11.1994).

‡ For a detailed mechanism which explains the regioselective formation of catenane isomers like **6** and **7** see ref. 5.

§ *Crystal data* for **7**: $C_{116}H_{124}N_8O_{10}{\cdot}4MeOH{\cdot}4H_2O$, M_r = 1990.5, monoclinic, space group $C2/c$ (no. 15); a = 23.922(1), b = 16.702(1), c = 35.486(1) Å, β = 105.39(1)°, V = 13670 Å, Z = 4, μ(Cu-Kα) = 0.52 mm^{-1}, F(000) = 4272. 12238 Intensity data (4154 unique data, R_{merge} = 0.060) were collected on a Rigaku R-AXIS IIC area detector using Cu-Kα radiation produced by a Rigaku RU200HB rotating anode (50 kV, 180 mA) to a resolution of 1.1 Å (completeness of data 74%), crystal-to-detector distance 70 mm, detector 2θ angle −35°, 36 frames, 10° oscillation. The area detector data were processed using RAXIS IIC software. The structure was solved by direct methods (SHELXS-90) and refined anisotropically (full-matrix least-squares refinement on F^2, SHELXL-93) to $wR2$ = 0.415 [R_1 = 0.141 for 3467 $I > 2\sigma(I)$]. Cyclohexylidene rings were disordered. Reprocessing of area detector data using the DENZO program is still in progress. Atomic coordinates, bond lengths angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

¶ After completion of this work a successful X-ray analysis of a different octalactam catenane system came to our knowledge. We thank Dr David A. Leigh (Department of Chemistry, University of Manchester) for this information prior to publication.

|| A similar hydrogen bonding pattern has been found in a host–guest complex of benzoquinone and a tetralactam-type macromonocycle: *cf.* ref. 7.

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