DOI: 10.1002/anie.201000807

Catenanes

A Water Soluble Donor–Acceptor [2]Catenane that Can Switch between a Coplanar and a Gemini-Sign Conformation**

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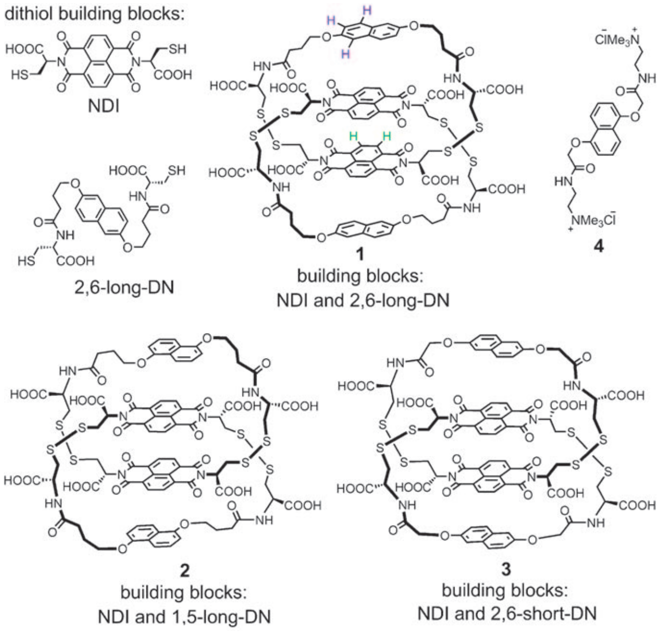
We describe herein the discovery of a conformationally switchable donor–acceptor (D–A) [2]catenane **1**, which was obtained from an aqueous dynamic combinatorial library (DCL; Scheme 1). One of the two observed conformations of catenane **1** is an unprecedented arrangement of the π surfaces, which form the shape of ♊, the astrological Gemini sign. Switching between the conformers of this catenane can be achieved by changing the temperature or solvent polarity, or by introducing an appropriate guest.



Scheme 1. Structures of the two building blocks NDI and DN, catenanes **1**–**3**, and template **4**. **1** is presented in conformation I. 1,5-long-DN and 2-6-short-DN refer to changes in the substitution and carbon chain lengths, respectively (see text).

Supramolecular assemblies based on π donors and π acceptors are often designed with an alternating arrangement of the D–A units,[1] in which the flat π cores are vertically stacked in parallel with each other. The T-shape geometry, although favorable for two interacting π systems, has, to the best of our knowledge, not previously been observed in D–A interlocked systems.[2] Previously, we reported the discovery of D–A catenanes **2** and **3** that contain two interlocked rings each formed from a naphthalenediimide (NDI; acceptor) and a dioxynaphthalene (DN; donor).[3] As a result, the D–A units cannot stack in the conventional alternating fashion but adopt a D–A–A–D stacking geometry, which is one of the three possible coplanar structures (conformer I, Figure 1). We also showed that a [3]pseudorotaxane is formed from **2** and DN **4**, in which the guest is located in the center to create a fully alternating D–A–D–A–D sequence. The new catenane **1** was formed in approximately 30% yield in a high-salt-concentration ($1\,\text{M}$ $NaNO_3$) aqueous disulfide DCL of the corresponding building blocks.[4] The interlocked nature of **1** was shown by mass spectrometry (Figure 2): the molecular ion of **1** has a mass that corresponds to two of each of the building blocks, and the largest daughter ion is derived from the D–A dimer. No homodimeric fragments were observed, thus indicating that **1** is a [2]catenane formed from two interlocked D–A dimers, analogous to **2** and **3**. The difference between **1** and **2** lies in the substitution pattern of the DN core (2,6- instead of 1,5-substitution), while **1** is different from **3** because the DN core is linked with the cysteine through four rather than two carbon atoms.

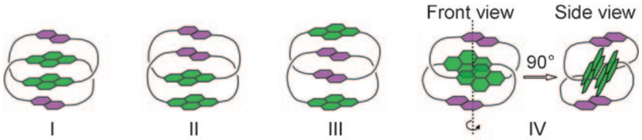


Figure 1. Possible conformers of **1**. The NDI and DN cores are represented by the green and purple shapes.

In contrast to **2** and **3**, the ^{1}H NMR spectrum of **1** contains two sets of NDI and DN signals. Variable-temperature (VT) ^{1}H NMR spectroscopy showed that these two sets of signals arise from two separate species (designated here as **1a** and **1b**) that are in slow exchange; the relative ratio of these peaks varies as a function of temperature (Figure 3).[5] A ΔH value of $-17\,\mathrm{kJ\,mol^{-1}}$ and a ΔS value of $-65\,\mathrm{J\,mol^{-1}\,K^{-1}}$ for the equilibrium between **1a** and **1b** were obtained from the VT NMR data. The presence of two exchanging species is further supported by exchange cross-peaks in the NOESY spectrum. The associated NDI and DN units are assigned from their integration. The variation in the **1a**/**1b** ratio excludes the

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[**] We thank the Croucher Foundation, Pembroke College, and EPSRC for financial support, and Dr. Ana Belenguer for maintaining the HPLC laboratory.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201000807.

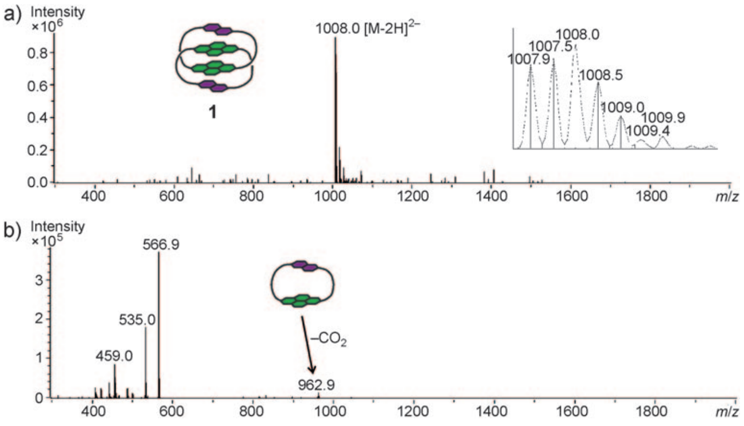

Figure 2. a) ESI-MS and b) MS–MS spectra of **1**.

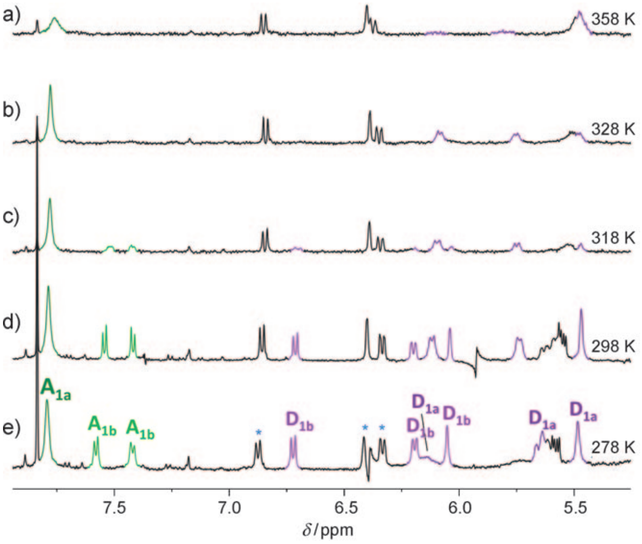

Figure 3. Partial ^{1}H NMR spectra (500 MHz, D_2O) of **1**. NDI and DN signals are labeled as A (green) and D (purple). Peaks corresponding to a small amount of the D–A dimer are labeled with a blue star.[6]

presence of the unsymmetrical conformation II. HPLC analysis of the sample showed that it was pure and contained only one compound, thus confirming the notion of two interconverting conformers on the HPLC timescale.

The NMR data showed that **1** does not adopt exclusively conformation I, which is expected to be the most favorable. While it is tempting to assign **1a** and **1b** respectively as conformers III (A–D–D–A) and I (D–A–A–D) on the basis of chemical shifts, this assignment is not consistent with the observed spectral changes of **1** upon binding with **4** and the chemical shift values of the equivalent protons for the structurally similar **2** and **3**.

In a ^{1}H NMR titration experiment, addition of **4** resulted in a decrease in the concentration of **1b** relative to that of **1a** (Figure 4). Conversion of **1b** to **1a** was completed after addition of more than two equivalents of **4**. Upfield shifts were observed for the NDI and DN resonances of **1a** as the amount of **4** increased, thus indicating fast exchange between bound and unbound states on the chemical-shift time scale. In the NOESY spectrum of the host–guest complex, correlations between the NDI and DN of **1a**, and the NDI of **1a** and the DN of **4** indicate the formation of a [3]pseudorotaxane with **4** located in the center of the catenane (see the Supporting Information). When less than two equivalents of **4** were present, no change in chemical shifts of **1b** was observed, thus indicating that **1b** does not bind to **4**.

The binding behavior of **1a** to **4** is similar to that of **2** to **4**, with the NDI and DN signals of both catenanes being shifted upfield upon addition of **4**. This result suggests that the binding of **4** to **1a** or **2** involves the same mechanism.[3a] The chemical shifts of the NDI unit in **1a**, **2**, and **3** also suggest that these NDIs are in a similar chemical environment, which is different from that of **1b** (Table 1). The DN signals follow the same trend, thus indicating an analogy between the structures of **1a**, **2**, and **3**. The NDI protons of the homologues **1a** and **3** both appear as a singlet, which shows that both sets of protons experience the same local symmetry. All these observations indicate that **1a**, **2**, and **3** are all in conformation I (D–A–A–D π stack).

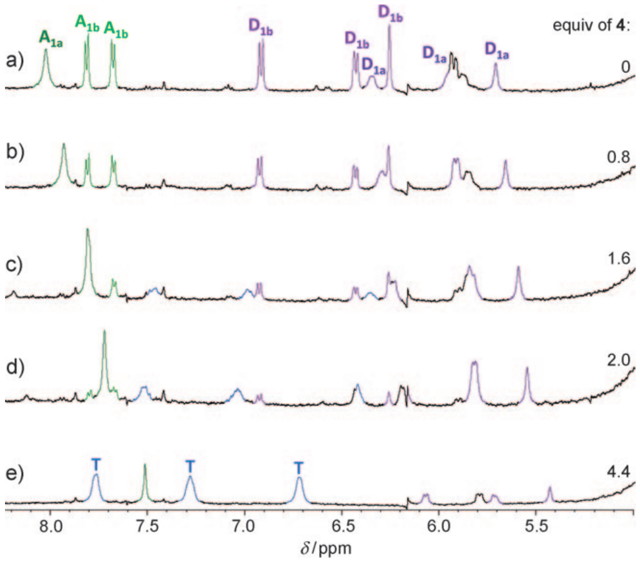

Figure 4. Partial ^{1}H NMR spectra (500 MHz, D_2O, 300 K) of **1** in the presence of varying amounts of **4**. Signals from **4** are labeled as T (blue).[6]

Table 1: Chemical shifts comparison of catenanes **1**, **2**, and **3**.

Catenane	δ NDI [ppm]	δ DN [ppm]
1a	8.02 (s)[a]	6.35, 5.97, 5.71 (d, br, br)
1b	7.80, 7.67 (d, d) average = 7.74	6.93, 6.44, 6.27 (d, d, s)
2	8.09, 7.79 (d, d) average = 7.94	6.46, 6.11, 5.50 (d, t, d)
3	7.98 (s)	6.32, 6.12, 5.83 (d, br, br)

[a] Letters in parentheses represent multiplicity; br: broad, d: doublet, s: singlet, t: triplet.

The observed spectral changes of **1a** during the titration experiment are also consistent with this assignment. The upfield shifts of both the NDI and DN resonances of **1a** upon binding the guest can be explained by a fast threading–dethreading process. When threaded with the guest, the catenane is tightened and the π units are closer. Therefore, both the NDI and DN units experience a stronger shielding effect and are shifted upfield. These changes cannot be accounted for by the formation of conformer III. Since the NOESY experiment showed that the final catenane complex has an alternate D–A stack with **4** located in the center, the binding of **4** to **1** in conformer III implies a binding mechanism that is accompanied by a conformational change of the host. Although this change is consistent with the upfield shifts of the NDI as they move from the outermost to the inner part of the stack, it contradicts the upfield shifts observed for the DN. By moving from the inner to the outermost position, the DNs are influenced by fewer neighboring aromatic units, and should be less shielded by ring currents and therefore downfield-shifted.[7]

While all the available experimental evidence supports the assignment of **1a** as conformer I (D–A–A–D π stack), the conformation of **1b** is enigmatic: conformer II has been eliminated as it requires the presence of two sets of NDI and DN signals in a 1:1 ratio, while conformation III cannot explain the relative chemical shift values of **1b**. In conformer III (A–D–D–A π-stack), the NDI and DN would be on the outermost and inner positions, respectively, of the parallel stack. Therefore, the corresponding signals should show larger downfield and upfield shifts, respectively, compared with those of conformer I. However, when compared to **1a**, which is assigned as conformer I, the NDI and DN signals of **1b** show larger upfield and downfield shifts, which are contrary to the expected behavior (see above).

Therefore, a fourth conformation where the four π units do not stack in parallel is required in order to explain these observations. In conformation IV, the two NDI cores are parallel to each other, perhaps offset, and this NDI stack is placed in between the DN moieties in an arrangement that is best represented as ♊, the astrological Gemini sign. In this conformation, the chemical shifts of the NDI protons will be shifted upfield relative to conformer I as they are deeper in the shielding region of the DNs; on the other hand, the DN signals will be shifted downfield as the DNs are in the deshielding region of the NDIs. These observations are consistent with a T-shape type of interaction that occurs between the NDI and the DN cores of catenane **1b**, and operates in tandem with face-to-face NDI contacts.

Compared to conformers I–III, conformer IV has a larger exposed hydrophobic surface area, which implies that conformer IV will be the dominant species in a solvent of lower ionic strength.[8] Indeed, in a ^{1}H NMR experiment, the ratio of **1a**/**1b** decreased as the acetone content was increased and no significant amount of **1a** was observed above approximately 40% (v/v) of acetone (Figure 5). In agreement with our hypothesis, the ratio of **1a**/**1b** increased as the ionic strength was increased, and no significant amount of **1b** was observed in the presence of 0.5 M $NaNO_3$ (see the Supporting Information). Although the stability of conformers I–III is dependent on the D–A stacking order, the overall area of exposed hydrophobic surfaces is almost identical for each conformer, so the hydrophobic effect should not have a significant influence on the relative stability and ratio of **1a**/**1b** if conformers I–III were the only possibilities. The existence of a fourth conformer is therefore essential. Further support for the structural differences of **1a** and **1b** comes from the NOESY spectrum, in which NOE cross-peaks between the NDI and DN protons were observed for a sample in which **1b** was the dominant conformer (D_2O with ca. 40% acetone). This result shows that the NDI and DN are in proximity in **1b**, and is consistent with the tilted NDI arrangement that brings the NDI and DN protons closer. On the other hand, no NOE cross-peaks were observed in the NOESY spectrum of a sample in which **1a** was the main conformer in solution (0.5 M $NaNO_3$, see the Supporting Information). Despite the lack of detailed structural parameters, the presence of a nonparallel conformation is necessary based on all these observations.

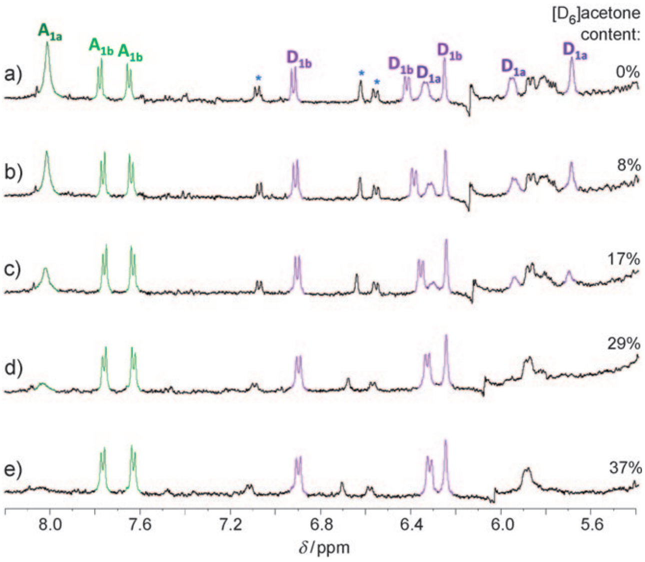

Figure 5. Partial ^{1}H NMR spectra (500 MHz, D_2O/[D_6]acetone, 300 K) of **1** with varying [D_6]acetone content.[6]

In summary, we have shown that a new flexible D–A [2]catenane **1**, which was synthesized from a dynamic combinatorial library, can adopt different conformations in solution. NMR studies showed that one of the observed conformers of **1** has a conformation, which we believe to be previously unknown, where the electronically complementary π units do not stack in parallel. In addition, we can manipulate the conformational equilibrium by thermal, solvophobic, or chemical stimuli, in contrast to the more common electrochemical methods.[9] The discovery of **1** also highlights the use of DCC in uncovering new unexpected structures with features that could not have been designed or predicted.

Received: February 9, 2010
Revised: April 16, 2010

Keywords: catenanes · host–guest systems · hydrophobic effect · π interactions · self-assembly

[1] For recent examples of [2]catenanes with alternating D–A units, see: a) D. Cao, M. Amelia, L. M. Klivansky, G. Koshkakaryan, S. I. Khan, M. Semeraro, S. Silvi, M. Venturi, A. Credi, Y. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 1110 – 1122; b) S. Ramos, E. Alcalde, J. F. Stoddart, A. J. P. White, D. J. Williams, L. Pérez-García, *New J. Chem.* **2009**, *33*, 300 – 317; c) G. Koshkakaryan, K. Parimal, J. He, X. Zhang, Z. Abliz, A. H. Flood, Y. Liu, *Chem. Eur. J.* **2008**, *14*, 10211 – 10218; d) Y. Liu, A. Bruneau, J. He, Z. Abliz, *Org. Lett.* **2008**, *10*, 765 – 768; e) A. Coskun, S. Saha, I. Aprahamian, J. F. Stoddart, *Org. Lett.* **2008**, *10*, 3187 – 3190.

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[4] H. Y. Au-Yeung, P. Pengo, G. D. Pantoş, S. Otto, J. K. M. Sanders, *Chem. Commun.* **2009**, 419 – 421.

[5] No significant difference was observed in the UV/Vis spectra of **1** at different temperatures.

[6] The ratio between **1a** and **1b** varies with the amount of polar solvent impurities (mainly MeOH) present in the samples obtained from different preparative HPLC runs. The peak at 6.17 ppm in Figure 5 and 6 is an artefact that arises from the zg30 pulse program used in data acquisition.

[7] Other π guests were also tested, and binding of **1** to **4** was found to be specific. The use of an NDI-derived guest resulted in catenated species in a conformation other than I and IV, whilst other aromatic guests did not interact with **1**. See the Supporting Information for details.

[8] For examples of conformational changes of rotaxanes induced by solvophobic effect, see: D. A. Leigh, M. Á. F. Morales, E. M. Pérez, J. K. Y. Wong, C. G. Saiz, A. M. Z. Slawin, A. J. Carmichael, D. M. Haddleton, A. M. Brouwer, W. J. Buma, G. W. H. Wurpel, S. Leon, F. Zerbetto, *Angew. Chem.* **2005**, *117*, 3122 – 3127; *Angew. Chem. Int. Ed.* **2005**, *44*, 3062 – 3067.

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