Tandem Hetero-Catenation: Templating and Self-Assembly in the Mutual Closure of Two Different Interlocking Rings

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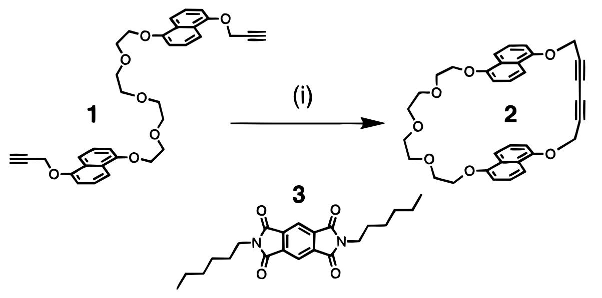
We report here the templated synthesis and solid-state structure of an unusual [2]catenane (**5**) containing three hexadiyne linkers, all of which may be formed in a single reaction. The molecule may also be prepared by traditional catenation of a preformed dinaphtho macrocycle. Remarkably, the one-pot reaction, utilizing the corresponding acyclic precursors to close the two different interlocking rings in tandem, proceeds with *equal efficiency*.

Crowns containing two or more electron-rich aromatic components have formed the basis of the series of polycationic catenanes prepared by the Stoddart group.[1] In the solid-state structures of these systems, where 4,4′-bipyridinium units are used as the electron-deficient components, hydrogen-bonding interactions between "acidic" bipyridinium protons and oxygen atoms in the crown polyether chains augment donor−acceptor stacking interactions in organizing their crystal structures.[2] We have recently demonstrated that neutral π-associated [2]catenanes may be assembled from the oxidative coupling of electron-deficient, acetylenic aromatic diimides (e.g., **4**) in the presence of a dinaphtho crown macrocycle.[3] Since hydrogen-bonding interactions do not appear to be dominant structural features of these molecules,[4] we sought to examine their importance to the assembly process by replacing one of the crown polyether chains with a spacer of comparable length. An obvious choice was the hexadiyne linker which is both geometrically and chemically compatible with catenane assembly.

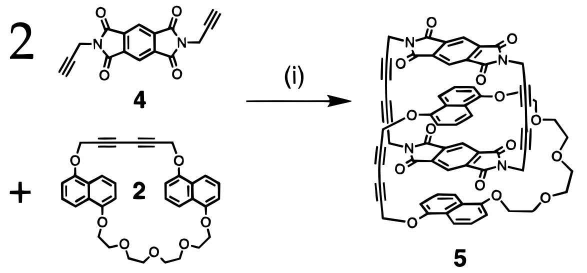
At 5 mM concentration in CH_2Cl_2, acyclic precursor **1**[5] can be cyclized[6] to macrocycle **2** in 36−41% yield (Scheme 1);[7] a small amount (1−2%) of the dimeric analogue of **2** can also be isolated.

Scheme 1[a]



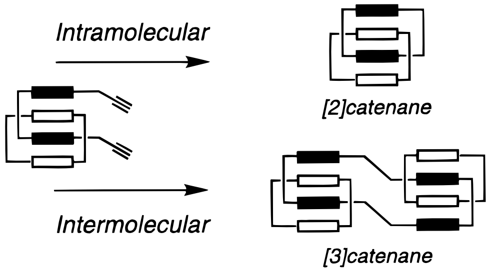
[a] Key: (i) CuCl, TMEDA, DCM, Air, rt.

Scheme 2[a]



[a] Key: (i) CuCl, $CuCl_2$, DMF, Air, rt.

Scheme 3



Under identical cyclization conditions, the presence of a 5-fold excess of the diimide template **3** raises the isolated yield of **2** to 68−74%.[8] This 2-fold increase in efficiency is ascribed to the wrapping of the acyclic precursor around the template, raising the probability of the reactive terminal acetylene functions finding themselves in close proximity.

Catenation of hybrid macrocycle **2** was achieved by treatment of a 1:2 molar ratio of **2** and **4** in dry DMF with anhydrous CuCl and $CuCl_2$: the [2]catenane **5** was obtained as a yellow-orange solid in 13−16% yield (Scheme 2). Additionally, a small amount (<1%) of the corresponding [3]catenane could also be isolated;[9] this is the product of *intermolecular* rather than *intramolecular* ring closure of the catenane precursor (Scheme 3). This observation and the rather low yield of [2]catenane suggest that the

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(1) (a) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828. (b) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1155−1196.

(2) These interactions have also been found to be of great importance in templating the assembly of certain systems: Ashton, P. R.; Menzer, S.; Raymo, F. M.; Shimizu, G. K. H.; Stoddart, J. F.; Williams, D. J. *Chem. Commun.* **1996**, 487−488.

(3) Hamilton, D. G.; Sanders, J. K. M.; Davies, J. E.; Clegg, W.; Teat, S. J. *Chem. Commun.* **1997**, 897−898.

(4) Hamilton, D. G.; Davies, J. E.; Prodi, L.; Sanders, J. K. M. *Chem. Eur. J.* In press.

(5) Prepared from the monoalkylation of 1,5-dihydroxynaphthalene with propargyl bromide (K_2CO_3/acetone) and subsequent bridging of the remaining hydroxyls with $Ts(OCH_2CH_2)_4OTs$ (K_2CO_3/acetone).

(6) Cyclization is effected by the addition of anhydrous CuCl and TMEDA under conditions developed for the synthesis of cyclic porphyrin oligomers: Anderson, H. L.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2223−2229.

(7) For all of the described reactions, the quoted yield ranges represent the results of at least three independent runs.

(8) Attempts to prepare the free diimide macrocyclic component of [2]-catenane **5** by macrocyclization of **4** in the presence of a π-electron-rich naphthalene diether template have proved unsuccessful, perhaps due to the extremely low solubility of **4** in organic solvents. Accordingly, we prepared a more soluble diimide derivative bearing ethyl groups at the junction between the diimide framework and the acetylene link. However, macrocyclization (CuCl, TMEDA, DCM, air) of this derivative yields only trimer as an isolable cyclic oligomer; the yield is low (<10%) and appears unaffected by the presence of a complementary template. It seems likely that a successful template for cyclodimerization of these derivatives would need to be macrocyclic in nature and possess a cleavable (e.g., ester) link to allow subsequent release of the desired macrocycle, see: Asakawa, M.; Ashton, P. R.; Menzer, S.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 877−893.

(9) Characterised by mass spectrometry (M_r = 2264).

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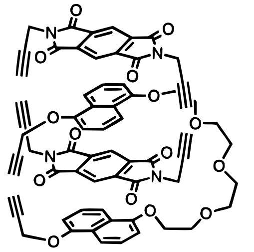

Figure 1. Self-assembled array of acyclic components leading to [2]-catenane **5**.

macrocyclic cavity of **2** is rather constrained and does not provide a particularly efficient template for catenation.

The significant increase in the macrocyclization efficiency of **1** provided by the presence of the dihexyl template molecule **3** prompted speculation that the bisacetylene diimide **4** might also act as a positive template[10] for this cyclization. Inevitably, since **1** bears the same reactive functionality as **4**, material will be consumed in an unprofitable fashion through any direct coupling of **1** to **4**. However, a proportion of the mixture should self-assemble, via the establishment of favorable donor−acceptor interactions, to afford precyclization arrays favoring the formation of the [2]catenane **5** (Figure 1). Indeed, when exposed to the standard coupling conditions, a 1:2 molar ratio of **1** to **4** in DMF affords isolated yields of **5** in the range of 12−15%. It is clear that this tandem ring closure process is of comparable efficiency to that which begins with one of the rings preformed. This is a remarkable result, given the expectation of losing material in unproductive couplings.

An explanation of the similarity in yield for the one-pot process versus the traditional sequential approach is to assign a significant templating role to diimide **4**. This view is supported by order of magnitude association constant (K_a) estimates for the binding of template **3** by the naphthalene diether derivatives in CH_2Cl_2.[11] For the interaction of **3** with a *single* 1,5-naphthalene diether, fluorescence measurements yield an upper limit for K_a of around 20 M^{-1}. This value increases to 80 M^{-1} for the complex of *acyclic* bisnaphthalene compound **1** with **3** and to around 400 M^{-1} for the association of the corresponding *macrocycle* **2** with template **3**. If the bulk of acyclic **1** is converted to macrocycle **2**, by the templating action of **4**, then it is logical to expect the yield of [2]catenane **5** to be similar to that obtained from the sequential reaction.[12] Additionally, we would expect to observe a substantial amount of free macrocycle **2** in this reaction since we know catenation of *preformed* **2** to be rather inefficient. Significantly, **2** is the major product isolated from the tandem ring closure reactions.

The solid-state structure of **5**, obtained from a single microcrystal by synchrotron X-ray diffraction, reveals an unusually asymmetric arrangement of donor and acceptor subunits (Figure 2).[13] The unique orthogonality of the two electron-rich naphthalene residues comprising the recognition elements of macrocycle **2** is somewhat surprising since parallel naphthalene residues have been found in all previous catenanes incorporating dinaphtho crown rings.[1] Closing one side of macrocycle **2** with a geometrically restrictive hexadiyne linker will inevitably reduce overall conformational flexibility, but "open" conformations where the long axes of the two naphthalene units are disposed in both parallel and perpendicular arrangements appear perfectly possible. The solid-state packing of **5** is also surprising; individual catenanes do not stack one upon another to form the extended donor−acceptor arrays that characterize systems involving these building blocks.[14] Rather, slipped stacks of interlocked molecules are revealed in the packing of **5**, an unusual observation in the solid-state structure of a donor−acceptor catenane.[15]

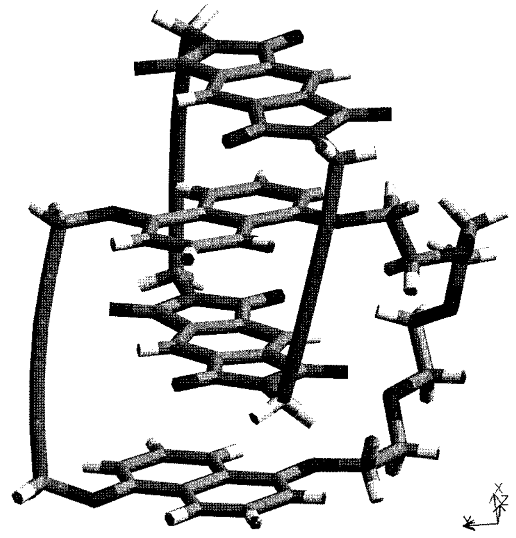

Figure 2. Solid-state structure of **5** (displayed using Cerius Molecular Simulations software).

The closure of two identical rings, tandem homo-catenation, is pivotal to the syntheses of [2]catenanes involving amide-hydrogen bonding or cation chelation templating mechanisms.[16] The assembly of **5** from acyclic precursors represents a unique use of donor−acceptor templating interactions and the *only* catenane synthesis to date where two different rings are formed in a single reaction. The effect of introducing a reversible coupling step, to allow the proof reading of unprofitable couplings, is currently under investigation.

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Supporting Information Available: X-ray structural data for **5** (12 pages). An X-ray crystallographic file, in CIF format, is available through the Web only. See any current masthead page for ordering information and Web access instructions.

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[10] Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res* **1993**, *26*, 469−475.

[11] There are rather large errors associated with these determinations: for the **1·3** complex, $K_a = 80 \pm 50$ M^{-1}; for the **2·3** complex, $K_a = 400 \pm 500$ M^{-1}. These errors are the unavoidable consequence of measuring a weak binding process in the presence of complex quenching phenomena. In particular, internal fluorescence quenching processes in macrocycle **2** hamper accurate determination of the latter value. However, there is no doubt that the relative order of binding strengths is **2·3** > **1·3**.

[12] The one-pot process also generates a small amount of [3]catenane, paralleling the situation found with the sequential reaction.

[13] Crystal data for **5**·(Me_2SO-d_6): $C_{66}H_{44}N_4O_{15}\cdot C_2D_6SO$, $M_r = 1217.24$, $T = 160(2)$ K, $\lambda = 0.6879$ Å, monoclinic, $a = 13.599(3)$, $b = 36.902(7)$, and $c = 12.546(3)$ Å, $\beta = 113.11(3)°$, $V = 5791(2)$ Å^3, space group $P2_1/c$, orange crystal (0.09 × 0.04 × 0.03 mm), $Z = 4$, $\rho_{calcd} = 1.389$ g cm^{-3}. The crystal contains one disordered Me_2SO-d_6 molecule per catenane and presents two distinct conformations for the central -CH_2OCH_2- atomic triad of the polyether chain. The final R_1 value was 5.6% ($S = 0.915$). Data collected at the Daresbury Synchrotron Radiation Source (U.K.).

[14] For examples of donor−acceptor stacks formed by aromatic diimides and aromatic diethers, see: (a) Lokey, R. S.; Iverson, B. L. *Nature* **1995**, *375*, 303−306. (b) Hamilton, D. G.; Lynch, D. E.; Byriel, K. A.; Kennard, C. H. L. *Aust. J. Chem.* **1997**, *50*, 439−445. (c) Houghton, M. A.; Bilyk, A.; Harding, M. M.; Turner, P.; Hambley, T. W. *J. Chem. Soc., Dalton Trans.* **1997**, 2725−2733.

[15] This unusual packing mode has previously been noted in the solid-state structure of a bipyridinium-derived catenane which, significantly, also contains one unusually constrained macrocycle: Amabilino, D. B.; Ashton, P. R.; Tolley, M. S.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1297−1301.

[16] (a) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; Kintzinger, J. P. *Tetrahedron Lett.* **1983**, *24*, 5095−5098. (b) Hunter, C. A. *J. Am. Chem. Soc.* **1992**, *114*, 5303−5311. (c) Vögtle, F.; Meier, S.; Hoss, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1619−1622. (d) Johnston, A. G.; Leigh, D. A.; Pritchard, R. J.; Deegan, M. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1209−1212.