

Using Host–Guest Complexation to Fold a Flexible Linear Organic String: Kinetically Controlled Syntheses of [3]Catenanes and a Five-Membered Molecular Necklace**

Chia-Fong Chang, Chun-Ju Chuang, Chien-Chen Lai, Yi-Hung Liu, Shie-Ming Peng, and Sheng-Hsien Chiu*

Unlike rotaxanes, which have attracted much attention as relevant materials in diverse research fields (e.g., sensing,^[1] drug delivery,^[2] gelation,^[3] fluid transportation^[4]), catenanes have been less applicable as functional interlocked materials, possibly because of their synthetic complexity (i.e., the requirement for efficient macrocyclization). For small-ring systems, the introduction of heteroatoms or *gem*-dialkyl groups^[5] into alkyl chains can minimize their preference for forming linear zigzag conformations, thereby facilitating their cyclization; both effects have much lower influence on the closing of large rings.^[6] Therefore, minimizing the concentrations of the reacting species (high dilution) or decreasing the substrate entropy through conformational control are frequently used strategies for efficient macrocyclizations.^[7] Two commonly employed approaches toward facilitating macrocyclizations are 1) positioning a nonlinear organic junction (e.g., C=O group or disubstituted ring system) within a linear molecule to form a “turn” in its structure^[8] and 2) introducing noncovalent templates to “fold” the linear molecule (e.g., metal ions in the synthesis of crown ethers).^[9] The use of an organic template to mediate the macrocyclization of a linear flexible organic molecule remains a challenge, because the components must interact with sufficient binding affinity and in a suitable complexation geometry; these features must be programmed in the molecular design.^[10] In the synthesis of catenanes, however, the host molecule can theoretically act as a template to “fold” its threaded linear guest into a preprogrammed conformation (geometry, Figure 1), in a similar way to metal ions that bridge the organic ligands of molecular containers and metal–organic frameworks (MOFs).^[11] Thus this synthetic approach allows the selective construction, at a normal concentration, of an interlocked molecule of a particular size. Moreover, the

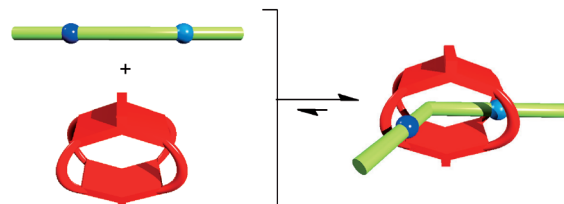


Figure 1. Cartoon representation of the precise folding of a linear guest within a cage-like host.

macrocyclizations of organic threadlike molecules folded in such a manner should allow the covalent construction of complicated, but robust, organic interlocked structures directly through irreversible (kinetically controlled) organic reactions—that is, without the need for the self-correction processes found in reversible (thermodynamically controlled) reactions.^[12] Herein, we report the development of host–guest complexes in which threaded flexible linear guests are folded at approximately right angles (ca. 90°); we have applied these complexes to macrocyclizations, producing up to 60- and 92-membered rings as centerpieces of unique [3]catenanes and a five-membered molecular necklace ([5]MN), respectively.

Previously, we found that the catechol- and dibenzo[24]-crown-8 (DB24C8)-like motifs of the molecular cage **1** (Scheme 1) interact selectively with pyridinium and dialkylammonium ions, respectively.^[13] We suspected that if pyridinium and dialkylammonium units were to be connected through a suitable linker in a linear threadlike guest, then we could obtain a system in which the dialkylammonium unit would prefer to be located within the cavity of the DB24C8-like opening of **1**, while the pyridinium unit would stack with the catechol-like aromatic rings. To obtain additional $^+N\cdots C-H\cdots O$ stabilization energy through hydrogen bonding of the H_α atoms of the pyridinium unit and adjacent ethylene glycol motifs, we would expect the main axis of the pyridinium unit to pass through one of the 34-membered rings of the molecular cage (Scheme 1). Thus, a suitably functionalized linear thread would be folded at a right angle (90°); this conformation would be stabilized as a result of penetration of its two recognition sites through adjacent openings of the molecular cage **1**.

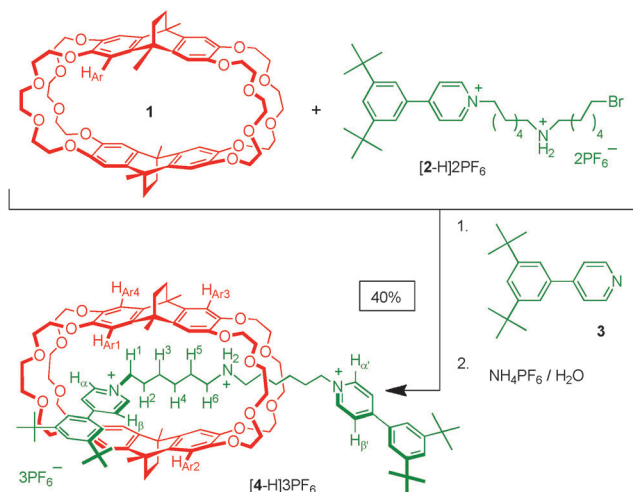
To realize this concept, we synthesized the threadlike salt [2-H]2PF₆, containing both dialkylammonium and alkylpyridinium units, in two steps from 4-(3,5-di-*tert*-butylphenyl)-pyridine **3**^[14] and *N,N*-bis(6-bromohexyl)-*p*-toluenesulfonamide^[15] (Scheme 1). The ¹H NMR spectrum of an equimolar

[*] C.-F. Chang, C.-J. Chuang, Y.-H. Liu, Prof. S.-M. Peng, Prof. S.-H. Chiu
Department of Chemistry, National Taiwan University
No. 1, Sec. 4, Roosevelt Road, Taipei, Taiwan, 10617 (R.O.C.)
E-mail: shchiu@ntu.edu.tw

Prof. C.-C. Lai
Institute of Molecular Biology, National Chung Hsing University
and Graduate Institute of Chinese Medical Science
China Medical University, Taichung, Taiwan (R.O.C.)

[**] We thank the National Science Council (Taiwan) (NSC-100-2119-M-002-026 and NSC-101-2628-M-002-010) and National Taiwan University (NTU-101-R890913) for financial support.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ange.201205498>.



Scheme 1. Synthesis of the [2]rotaxane [4-H]3PF₆.

(2 mM) mixture of the molecular cage **1** and the threadlike salt [2-H]2PF₆ in CDCl₃/CD₃CN (3:7) at room temperature reveals (Figure 2) that the rates of complexation and decomplexation were slow under these conditions; we observe three sets of signals: one for the free molecular cage **1**, one for the free threadlike salt [2-H]2PF₆, and one for their complex formed with 1:1 binding stoichiometry. By using a single-point method,^[16] we determined the association constant (K_a) for the complex formed between the molecular cage **1** and the threadlike salt [2-H]2PF₆ to be 2000 M⁻¹. The splitting of the originally symmetric signal for the aromatic units of the molecular cage **1** into four different sets of signals of equal intensity suggested the nonsymmetrical passage of the threadlike guest 2-H²⁺ through adjacent openings of the molecular

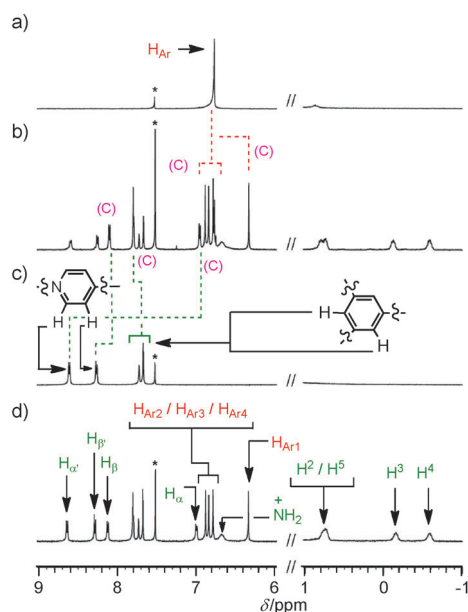


Figure 2. Partial ¹H NMR spectra (400 MHz, CDCl₃/CD₃CN (3:7), 298 K) of a) the molecular cage **1**, b) an equimolar mixture of **1** and the threadlike salt [2-H]2PF₆ (2 mM), c) [2-H]2PF₆, and d) the [2]rotaxane [4-H]3PF₆. In the spectrum in (b) the signals of protons in the complex are indicated by (C).

cage **1** to form the unique [2]pseudorotaxane [1⊃2-H]²⁺ (Figure 1). To confirm our suspicions, we added the bulky pyridine derivative **3** to a mixture of the molecular cage **1** (13 mM) and the threadlike salt [2-H]2PF₆ (26 mM) in CH₃NO₂, and obtained the expected [2]rotaxane [4-H]3PF₆ in 40% yield after chromatography and ion-exchange processes (Scheme 1).

We grew single crystals suitable for X-ray crystallography through liquid diffusion of *i*Pr₂O into a MeCN solution of the [2]rotaxane [4-H]3PF₆. The solid-state structure (Figure 3) of [4-H]3PF₆ reveals^[17,18] that the NH₂⁺ center is positioned

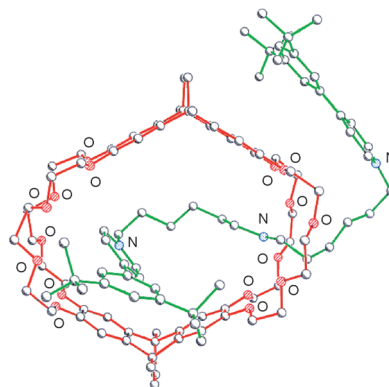
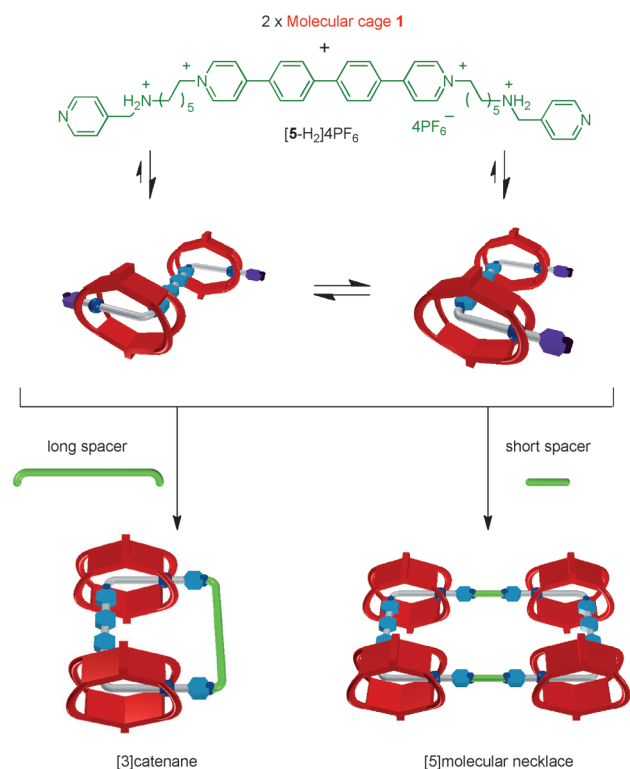


Figure 3. Ball-and-stick representation of the solid-state structure of the [2]rotaxane [4-H]³⁺.

within the cavity of one of the 24-membered rings of the cage, with one of the pyridinium units involved in π stacking and hydrogen-bonding interactions with the molecular cage component in such a manner that its axis passes through the 34-membered ring opening. The significant upfield shifts of the signals of the protons of the “inside” hexyl group and of the “inside” pyridinium unit (H_α and H_β, Figure 2), relative to those of the “outside” pyridinium unit (H_{α'} and H_{β'}), in the ¹H NMR spectrum suggest that the molecular conformation of the [2]rotaxane [4-H]3PF₆ in solution is similar to that observed in the solid state; that is, one of the pyridinium units and one of the hexyl chains reside within the cavity of the molecular cage moiety.

After finding that the molecular cage **1** could contort the threadlike salt [2-H]2PF₆ into an approximately 90° bend, we wished to extend this concept to the folding of a linear organic structure with two right angles, with the anticipation of using such a complex to synthesize a corresponding [3]catenane and/or [5]MN^[19] through irreversible covalent macrocyclization with spacers of appropriate lengths (Scheme 2). Thus, we synthesized the threadlike salt [5-H₂]4PF₆ and investigated its complexation with two units of the molecular cage **1** (see the Supporting Information).

As we had observed for the complex [1⊃2-H]²⁺, the ¹H NMR spectrum of a mixture of the molecular cage **1** (6 mM) and the linear threadlike salt [5-H₂]4PF₆ (2 mM) in CD₃CN/CDCl₃ (1:1; Figure 4) displayed four singlets of equal intensity representing the aromatic protons of the complexed molecular cage **1**. Furthermore, only one symmetrical set of aromatic protons appeared for the threadlike component in



Scheme 2. Cartoon representation of the synthetic approach toward the [3]catenane and the [5]MN.

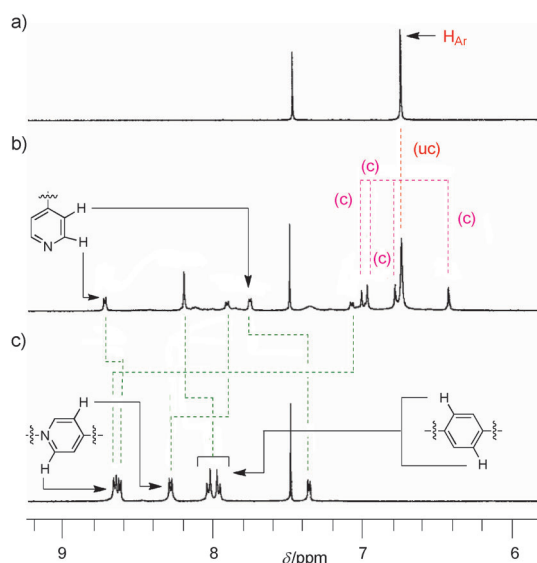
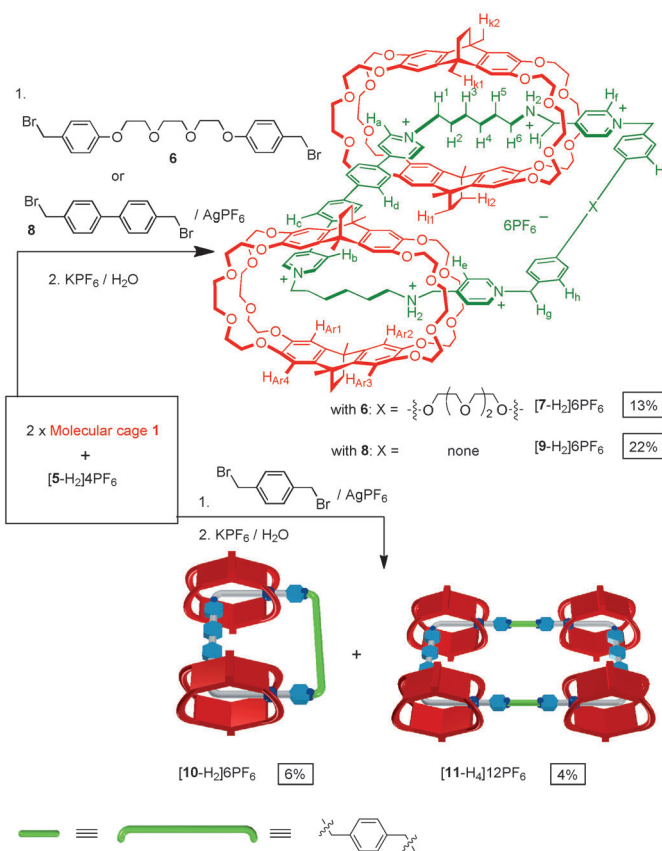


Figure 4. Partial ^1H NMR spectra (400 MHz, $\text{CD}_3\text{CN}/\text{CDCl}_3$ (1:1), 298 K) of a) the molecular cage **1**, b) a mixture of **1** (6 mM) and the threadlike salt $[\mathbf{5}\text{-H}_2]\text{4PF}_6$ (2 mM), and c) $[\mathbf{5}\text{-H}_2]\text{4PF}_6$. In the spectrum in (b) the signals of protons in the complex are indicated by (c); (uc) stands for those of the uncomplexed molecule.

the complex, thus suggesting that a 2:1 (host–guest) complex had formed, with the threadlike guest having been folded twice at right angles. We confirmed the binding stoichiometry using isothermal titration calorimetry (ITC) and obtained binding constants K_1 and K_2 of 1.5×10^5 and $3 \times 10^4 \text{ M}^{-1}$, respectively. Because the value of K_1/K_2 is close to 4, the two

complexation events in the binding of the threadlike salt $[\mathbf{5}\text{-H}_2]\text{4PF}_6$ to the molecular cage **1** are relatively independent. In the complex $[\mathbf{1}_2 \supset \mathbf{5}\text{-H}_2]^{4+}$, the conformation of the threadlike unit, presumably featuring two 90° bends, would position the two pyridyl termini in a favorable arrangement for linking through a relatively long linear spacer, to obtain a corresponding [3]catenane. Indeed, after stirring a mixture of **1** (8 mM), $[\mathbf{5}\text{-H}_2]\text{4PF}_6$ (2 mM), and the dibromide **6** (2 mM) in $\text{MeCN}/\text{CHCl}_3$ (1:1) at 318 K for three days, and subsequent purification by ion exchange ($\text{KPF}_6/\text{H}_2\text{O}$) and chromatography (SiO_2), we isolated the [3]catenane $[\mathbf{7}\text{-H}_2]\text{6PF}_6$ in 13% yield (Scheme 3). Notably, the formation of this [3]catenane required the macrocyclization of a 60-membered ring from a linear flexible organic string—a challenging task in most cases.



Scheme 3. Syntheses of three [3]catenanes and a [5]MN.

In comparison, when we reacted an equimolar mixture of $[\mathbf{5}\text{-H}_2]\text{4PF}_6$ and the dibromide **6** under the same conditions, but in the absence of **1**, we obtained a complicated mixture with no notable signals corresponding to the [1+1] macrocycle (^1H NMR spectroscopy, ESI-MS). Thus, the folding and conformational freezing of the flexible threadlike salt $[\mathbf{5}\text{-H}_2]\text{4PF}_6$ that results from its complexation with the molecular cage **1** increased the efficiency of the irreversible macrocyclization significantly. 2D COSY and NOESY experiments allowed us to identify most of the signals in the ^1H NMR spectrum of the [3]catenane $[\mathbf{7}\text{-H}_2]\text{6PF}_6$ in CD_3CN at 298 K (Figure 5). The presence of four (two) signals of equal

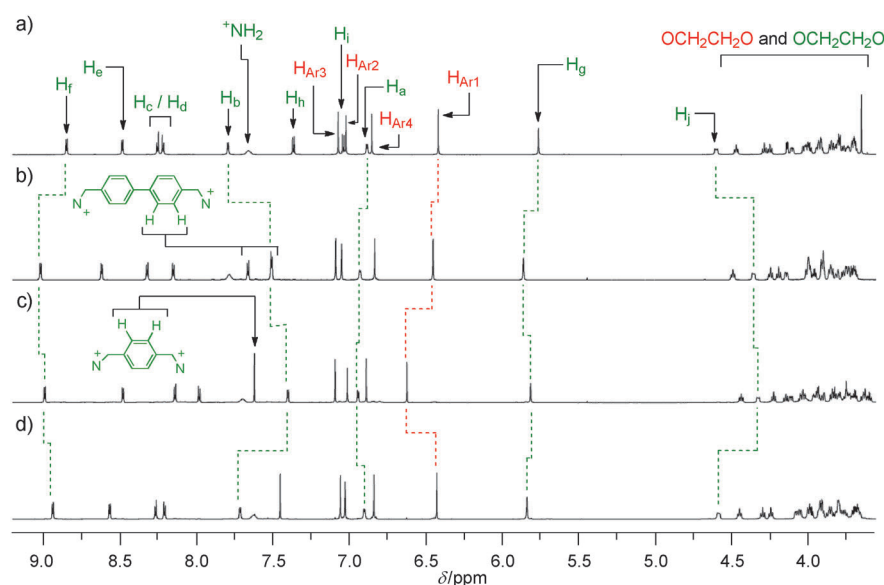


Figure 5. Partial ^1H NMR spectrum (800 MHz, CD_3CN , 298 K) of the [3]catenanes a) $[7\text{-H}_2]6\text{PF}_6$, b) $[9\text{-H}_2]6\text{PF}_6$, c) $[10\text{-H}_2]6\text{PF}_6$, and d) the [5]MN $[11\text{-H}_4]12\text{PF}_6$.

intensity for the aromatic (methyl) protons of the molecular cage units, together with the symmetry of the signals of the 60-membered-ring macrocycle, supported our proposed molecular structure for the catenane $[7\text{-H}_2]6\text{PF}_6^{4+}$, in which the 60-membered ring was interlocked with the molecular cage units by its threading through adjacent 24- and 34-membered rings.

The expectation that a more-rigid spacer might link the two pyridyl termini of the complex $[1_2\text{5-H}_2]^{4+}$ more efficiently was realized by reacting 4,4'-bis(bromomethyl)biphenyl (**8**)^[20] with a mixture of **1** (8 mm), $[5\text{-H}_2]4\text{PF}_6$ (2 mm), and AgPF_6 (4 mm) under conditions similar to those we had used for the synthesis of $[7\text{-H}_2]6\text{PF}_6$, and we obtained the corresponding [3]catenane $[9\text{-H}_2]6\text{PF}_6$ in 22% yield (Scheme 3).^[21] Encouraged by this result, we performed a similar reaction using a mixture of **1** (12 mm), $[5\text{-H}_2]4\text{PF}_6$ (2 mm), and α,α' -dibromo-*p*-xylene with the anticipation that this shorter spacer would be less effective at linking the two relatively distant pyridyl termini in $[1_2\text{5-H}_2]^{4+}$, thereby potentially favoring the formation and isolation of a [5]MN, which would require the assembly of eight molecular components through four irreversible chemical reactions.

As expected, we isolated the [5]MN $[11\text{-H}_4]12\text{PF}_6$, with a 92-membered ring as its centerpiece, in 4% yield after ion exchange and column chromatography, together with the corresponding [3]catenane $[10\text{-H}_2]6\text{PF}_6$ (6%). The electrospray ionization (ESI) mass spectrum of $[11\text{-H}_4]12\text{PF}_6$ revealed intense peaks at m/z 2370.6 and 1741.7, corresponding to the ions $\{[11\text{-H}_4]9\text{PF}_6\}^{3+}$ and $\{[11\text{-H}_4]8\text{PF}_6\}^{4+}$, respectively (Figure 6). The good matches between the observed and calculated isotope patterns (Figure 6) for these ions support the successful synthesis of the [5]MN $[11\text{-H}_4]12\text{PF}_6$. We identified the signals in the ^1H NMR spectra of the [3]catenanes $[9\text{-H}_2]6\text{PF}_6$ and $[10\text{-H}_2]6\text{PF}_6$ in CD_3CN at 298 K through 2D COSY, NOESY, or ROESY experiments. Upon decreasing the length of the spacer in the [3]catenane $[7\text{-H}_2]6\text{PF}_6$ to that in $[10\text{-H}_2]6\text{PF}_6$, the two signals of the

pyridinium protons (H_a and H_b) moved downfield and upfield, respectively (Figure 5), thus suggesting that a shorter spacer resulted in a change of the stacking position between the pyridinium ring and the aromatic “roof” of the molecular cage unit. The appearance of characteristic broad signals at $\delta = 7.60\text{--}7.80$ ppm for the NH_2^+ centers of all of these catenanes suggested that $\text{N}\cdots\text{H}\cdots\text{O}$ hydrogen bonding was the primary noncovalent interaction between the host and guest components. The signals for the external methylene protons adjacent to the NH_2^+ center (H_i) were, however, more downfield for the [3]catenane $[7\text{-H}_2]6\text{PF}_6$ and the [5]MN $[11\text{-H}_4]12\text{PF}_6$ than for those of $[9\text{-H}_2]6\text{PF}_6$ and $[10\text{-H}_2]6\text{PF}_6$, thereby implying that $^+\text{N}\cdots\text{C}\cdots\text{H}\cdots\text{O}$ hydrogen bonding to the oxygen atoms of the crown ether was

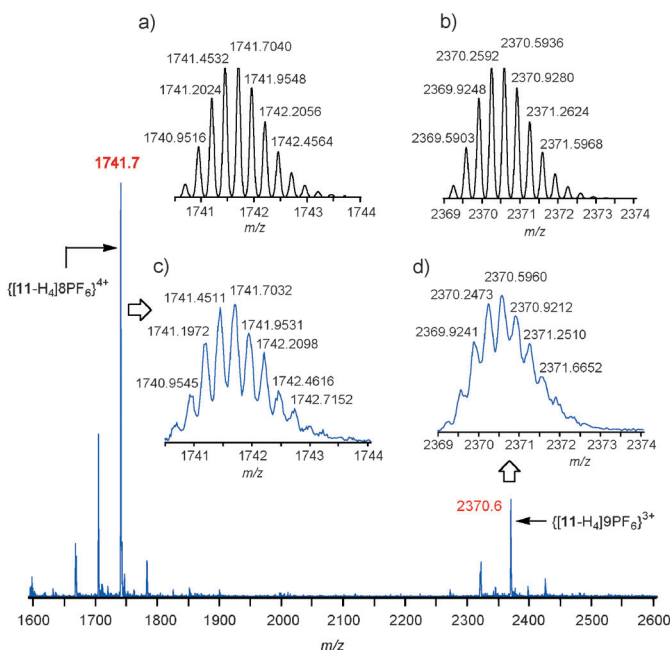


Figure 6. ESI mass spectrum of the [5]MN $[11\text{-H}_4]12\text{PF}_6$ exhibiting peaks corresponding to the molecular ions $\{[11\text{-H}_4]8\text{PF}_6\}^{4+}$ and $\{[11\text{-H}_4]9\text{PF}_6\}^{3+}$ and their calculated (a, b) and observed (c, d) isotopic distributions.

weakened through structural distortion of the latter two compounds.

We have demonstrated that host–guest complexation can be used to bend a flexible linear organic molecule into a particular shape for the successful synthesis of [3]catenanes and a [5]MN, with up to 60- and 92-membered rings as their centerpieces, respectively, through host-templated macrocyclizations.

Received: July 12, 2012
Published online: September 11, 2012

Keywords: catenanes · macrocyclizations · molecular necklaces · molecular recognition · template synthesis

- [1] a) P. H. Kwan, M. J. MacLachlan, T. M. Swager, *J. Am. Chem. Soc.* **2004**, *126*, 8638–8639; b) N.-C. Chen, P.-Y. Huang, C.-C. Lai, Y.-H. Liu, Y. Wang, S.-M. Peng, S.-H. Chiu, *Chem. Commun.* **2007**, 4122–4124; c) O. Hayashida, M. Uchiyama, *Org. Biomol. Chem.* **2008**, *6*, 3166–3170; d) J. J. Gassensmith, S. Matthys, J.-J. Lee, A. Wojcik, P. V. Kamat, B. D. Smith, *Chem. Eur. J.* **2010**, *16*, 2916–2921; e) M. J. Chmielewski, J. J. Davis, P. D. Beer, *Org. Biomol. Chem.* **2009**, *7*, 415–424; f) D. J. Mercer, S. J. Loeb, *Chem. Soc. Rev.* **2010**, *39*, 3612–3620; g) N. H. Evans, C. J. Serpell, P. D. Beer, *Chem. Commun.* **2011**, 47, 8775–8777.
- [2] a) J. W. Lee, K. Kim, *Top. Curr. Chem.* **2003**, *228*, 111–140; b) X. Wang, X. Bao, M. McFarland-Mancini, I. Isaacsohn, A. F. Drew, D. B. Smithrud, *J. Am. Chem. Soc.* **2007**, *129*, 7284–7293; c) A. Fernandes, A. Viterisi, F. Coutrot, S. Potok, D. A. Leigh, V. Aucagne, S. Papot, *Angew. Chem.* **2009**, *121*, 6565–6569; *Angew. Chem. Int. Ed.* **2009**, *48*, 6443–6447; d) M. W. Ambrogio, T. A. Pecorelli, K. Patel, N. M. Khashab, A. Trabolsi, H. A. Khatib, Y. Y. Botros, J. I. Zink, J. F. Stoddart, *Org. Lett.* **2010**, *12*, 3304–3307; e) J. M. Baumes, J. J. Gassensmith, J. Giblin, J.-J. Lee, A. G. White, W. J. Culligan, W. M. Leevy, M. Kuno, B. D. Smith, *Nat. Chem.* **2010**, *2*, 1025–1030; f) M. Adeli, R. S. Sarabi, R. Y. Farsi, M. Mahmoudi, M. Kalantari, *J. Mater. Chem.* **2011**, *21*, 18686–18695; g) Y. Yamada, T. Nomura, H. Harashima, A. Yamashita, N. Yui, *Biomaterials* **2012**, *33*, 3952–3958.
- [3] a) Y.-L. Zhao, I. Aprahamian, A. Trabolsi, N. Erina, J. F. Stoddart, *J. Am. Chem. Soc.* **2008**, *130*, 6348–6350; b) S.-Y. Hsueh, C.-T. Kuo, T.-W. Lu, C.-C. Lai, Y.-H. Liu, H.-F. Hsu, S.-M. Peng, C.-h. Chen, S.-H. Chiu, *Angew. Chem.* **2010**, *122*, 9356–9359; *Angew. Chem. Int. Ed.* **2010**, *49*, 9170–9173; c) Y. Kohsaka, K. Nakazono, Y. Koyama, S. Asai, T. Takata, *Angew. Chem.* **2011**, *123*, 4974–4977; *Angew. Chem. Int. Ed.* **2011**, *50*, 4872–4875.
- [4] J. Berná, D. A. Leigh, M. Lubomska, S. M. Mendoza, E. M. Pérez, P. Rudolf, G. Teobaldi, F. Zerbetto, *Nat. Mater.* **2005**, *4*, 704–710.
- [5] a) M. E. Jung, J. Gervay, *J. Am. Chem. Soc.* **1991**, *113*, 224–232; b) J. B. Sperry, D. L. Wright, *J. Am. Chem. Soc.* **2005**, *127*, 8034–8035.
- [6] a) C. Galli, G. Giovannelli, G. Illuminati, L. Mandolini, *J. Org. Chem.* **1979**, *44*, 1258–1261; b) G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, *14*, 95–102.
- [7] E. Weber, F. Vogtle, *Top. Curr. Chem.* **1992**, *161*, 1–36.
- [8] a) B. A. Mayes, L. Simon, D. J. Watkin, C. W. G. Ansell, G. W. J. Fleet, *Tetrahedron Lett.* **2004**, *45*, 157–162; b) M. Gupta, S. Kang, M. F. Mayer, *Tetrahedron Lett.* **2008**, *49*, 2946–2950; c) A. I. Prikhod'ko, J.-P. Sauvage, *J. Am. Chem. Soc.* **2009**, *131*, 6794–6807; d) Y. Liu, J. Rawlston, A. T. Swann, T. Takatani, C. D. Sherrill, P. J. Ludovice, M. Weck, *Chem. Sci.* **2011**, *2*, 429–438.
- [9] a) G. W. Gokel, *Crown Ethers and Cryptands*, Royal Society of Chemistry, London, **1992**; b) J. W. Steed, J. L. Atwood, *Supramolecular Chemistry*, 2nd ed., Wiley, Chichester, **2009**.
- [10] Using 1,5-dihydroxynaphthalene and ferrocene derivatives as templates allows cyclobis(paraquat-*p*-phenylene) and cyclobis-(paraquat-4,4'-biphenylene), 28- and 36-membered ring macrocycles, respectively, to be synthesized from their corresponding linear pyridinium salts; see: a) C. L. Brown, D. Philip, J. F. Stoddart, *Synlett* **1991**, 462–464; b) P. R. Ashton, S. Menzer, F. M. Raymo, G. K. H. Shimizu, J. F. Stoddart, D. J. Williams, *Chem. Commun.* **1996**, 487–490.
- [11] For reviews, see: a) S. J. Loeb, *Chem. Soc. Rev.* **2007**, *36*, 226–235; b) M. D. Pluth, R. G. Bergman, K. N. Raymond, *Acc. Chem. Res.* **2009**, *42*, 1650–1659; c) D. J. Tranchemontagne, J. L. Mendoza-Cortes, M. O'Keeffe, O. M. Yaghi, *Chem. Soc. Rev.* **2009**, *38*, 1257–1283; d) T. Hügler, M. Hartl, D. Lentz, *Chem. Eur. J.* **2011**, *17*, 10184–10207; e) R. Chakrabarty, P. S. Mukherjee, P. J. Stang, *Chem. Rev.* **2011**, *111*, 6810–6918.
- [12] a) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem.* **2002**, *114*, 896–952; *Angew. Chem. Int. Ed.* **2002**, *41*, 899–952; b) P. T. Corbett, J. Leclaire, L. Vial, K. R. West, J.-L. Wietor, J. K. M. Sanders, S. Otto, *Chem. Rev.* **2006**, *106*, 3652–3711; c) S. R. Beeren, M. Pittelkow, J. K. M. Sanders, *Chem. Commun.* **2011**, 47, 7359–7361.
- [13] a) C.-F. Lin, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2007**, *13*, 4350–4355; b) C.-J. Chuang, W.-S. Li, C.-C. Lai, Y.-H. Liu, S.-M. Peng, I. Chao, S.-H. Chiu, *Org. Lett.* **2009**, *11*, 385–388.
- [14] a) N.-C. Chen, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Chem. Eur. J.* **2008**, *14*, 2904–2908; b) Y.-L. Huang, C.-F. Lin, P.-N. Cheng, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Tetrahedron Lett.* **2008**, *49*, 1665–1669.
- [15] K. E. Krakowiak, G. Yi, J. S. Bradshaw, *J. Heterocycl. Chem.* **1996**, *33*, 2013–2017.
- [16] For a description of the single-point method, see: a) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, N. Spencer, J. F. Stoddart, P. A. Tasker, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 709–728; b) P. R. Ashton, M. C. T. Fyfe, S. K. Hickingbottom, J. F. Stoddart, A. J. P. White, D. J. Williams, *J. Chem. Soc. Perkin Trans. 2* **1998**, 2117–2124.
- [17] CCDC 889574 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [18] Crystal data for [4-H]3PF₆: [C₁₁₀H₁₅₂O₁₆N₃]3PF₆·4CH₃CN; *M*_r = 2377.39; monoclinic; space group *C2/c*; *a* = 57.243(3); *b* = 13.7391(4); *c* = 36.6570(11) Å; *V* = 26459.6(19) Å³; *ρ*_{calcd} = 1.194 g cm^{−3}; *μ*(Cu_{Kα}) = 1.134 mm^{−1}; *T* = 200(2) K; yellow prism; 23 750 independent measured reflections; *R*² refinement; *R*₁ = 0.1191; *wR*₂ = 0.3287.
- [19] Molecular necklaces have been defined as cyclic oligorotaxanes comprising a few small rings threaded onto a large macrocycle; see: a) S.-G. Roh, K.-M. Park, G.-J. Park, S. Sakamoto, K. Yamaguchi, K. Kim, *Angew. Chem.* **1999**, *111*, 671–675; *Angew. Chem. Int. Ed.* **1999**, *38*, 637–641; b) K. Kim, *Chem. Soc. Rev.* **2002**, *31*, 96–107; c) S.-H. Chiu, S. J. Rowan, S. J. Cantrill, L. Ridvan, P. R. Ashton, R. L. Garrell, J. F. Stoddart, *Tetrahedron* **2002**, *58*, 807–814; d) S. Dasgupta, J. Wu, *Org. Biomol. Chem.* **2011**, *9*, 3504–3515. Molecular necklaces and catenanes are topological isomers. A few high-order catenanes have been synthesized using the “clipping” approach; see: e) D. B. Amabilino, P. R. Ashton, S. E. Boyd, J. Y. Lee, S. Menzer, J. F. Stoddart, D. J. Williams, *Angew. Chem.* **1997**, *109*, 2160–2162; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2070–2072; f) D. B. Amabilino, P. R. Ashton, V. Balzani, S. E. Boyd, A. Credi, J. Y. Lee, S. Menzer, J. F. Stoddart, M. Venturi, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 4295–4307; g) L. Fang, M. A. Olson, D. Benitez, E. Tkatchouk, W. A. Goddard III, J. F. Stoddart, *Chem. Soc. Rev.* **2010**, *39*, 17–29.
- [20] A. Conejo-García, L. Pisani, M. C. Núñez, M. Catto, O. Nicolotti, F. Leonetti, J. M. Campos, M. A. Gallo, A. Espinosa, A. Carotti, *J. Med. Chem.* **2011**, *54*, 2627–2645.
- [21] The reaction proceeded much slower in the absence of AgPF₆. Addition of this salt did not improve the reaction efficiency, however, in the synthesis of the [3]catenane [7-H₂]6PF₆.