ORGANIC
LETTERS

2008
Vol. 10, No. 15
3187−3190

A Reverse Donor-Acceptor Bistable [2]Catenane

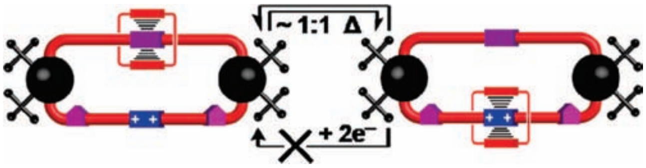
Ali Coskun,[†,‡] Sourav Saha,[†] Ivan Aprahamian,[†] and J. Fraser Stoddart*[,†,‡]

*California NanoSystems Institute and Department of Chemistry and Biochemistry,
University of California, Los Angeles, 405 Hilgard Avenue, Los Angeles, California 90095,
and Department of Chemistry, Northwestern University, 2145 Sheridan Road, Evanston,
Illinois 60208*

stoddart@northwestern.edu

Received April 22, 2008

ABSTRACT



A [2]catenane, composed of a π-electron-rich bis-1,5-dioxynaphthalene[38]crown10 (BDNP38C10) ring, mechanically interlocked with a large macrocycle containing two disubstituted tetraarylmethane “speed bumps” and two different π-electron-deficient units—namely, naphthalene dimide (NpI) and bipyridinium ($BIPY^{2+}$) units—has been synthesized from a [2]rotaxane, containing the former recognition unit, after performing two sequential Cu(I)-catalyzed azide-alkyne cycloadditions with a linker containing the latter recognition unit. The product, which exists as a single co-conformer, wherein the BDNP38C10 ring encircles the NpI unit, undergoes equilibration to give approximately equal amounts of the other co-conformer in which the BDNP38C10 ring encircles the $BIPY^{2+}$ unit.

Mechanically interlocked molecules,[1] in particular bistable [2]catenanes and [2]rotaxanes,[2] constitute some of the most intriguing candidates to serve as nanoscale switches and machines in the fields of molecular electronic devices (MEDs)[3] and nanoelectromechanical systems[4] (NEMS). The advantages of using such bistable molecules stem from their abilities to display controllable relative mechanical motions in response to external stimuli. In a bistable [2]catenane, for example, the competitive associations of one (degenerate)

[†] University of California, Los Angeles.

[‡] Northwestern University.

(1) (a) Schill, G.; *Catenenes, Rotaxanes, and Knots*; Academic Press: New York, 1971. (b) *Molecular Catenanes, Rotaxanes, and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C. O., Eds.; Wiley-VCH: Weinheim, 1999.

(2) (a) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133–137. (b) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M.; Venturi, M.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 333–337. (c) Jeppesen, J. O.; Perkins, J.; Becher, J.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2001**, *40*, 1216–1221. (d) Tseng, H.-R; Vignon, S. A.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1491–1495. (e) Tseng, H.-R.; Vignon, S. A.; Celestre, P. C.; Perkins, J.; Jeppesen, J. O.; Di Fabio, A.; Ballardini, R.; Gandolfi, M. T.; Venturi, M.; Balzani, V.; Stoddart, J. F. *Chem. Eur. J.* **2004**, *10*, 155–172. (f) Nygoard, S.; Leung, K. C.-F; Aprahamian, I.; Ikeda, T.; Saha, S.; Laursen, B. W.; Kim, S.-Y.; Hansen, S. W.; Stein, B. C.; Flood, A. H.; Stoddart, J. F.; Jeppesen, J. O. *J. Am. Chem. Soc.* **2007**, *129*, 960–970. (g) Aprahamian, I.; Yasuda, T.; Ikeda, T.; Saha, S.; Dichtel, W. R.; Isoda, K.; Kato, T.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 4675–4679.

(3) (a) Collier, C. P.; Mattersteig, G.; Wong, E. W.; Luo, Y.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. *Science* **2000**, *289*, 1172–1175. (b) Collier, C. P.; Jeppesen, J. O.; Luo, Y.; Perkins, J.; Wong, E. W.; Heath, J. R.; Stoddart, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 12632–12641. (c) Luo, Y.; Collier, C. P.; Jeppesen, J. O.; Neilsen, K. A.; DeIonno, E.; Ho, G.; Perkins, J.; Tseng, H.-R.; Yamamoto, T.; Stoddart, J. F.; Heath, J. R. *ChemPhysChem* **2002**, *3*, 519–525. (d) Diehl, M. R.; Steuerman, D. W.; Tseng, H.-R.; Vignon, S. A.; Star, A.; Celestre, P. C.; Stoddart, J. F.; Heath, J. R. *ChemPhysChem* **2003**, *4*, 1335–1339. (e) Yu, H. B.; Luo, Y.; Beverly, K.; Stoddart, J. F.; Tseng, H.-R.; Heath, J. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 5706–5711. (f) Flood, A. H.; Stoddart, J. F.; Steuerman, D. W.; Heath, J. R. *Science* **2004**, *306*, 2055–2056. (g) Choi, J. W.; Flood, A. H.; Steuerman, D. W.; Nygoard, S.; Braunsweig, A. B.; Moonen, N. N. P.; Laursen, B. W.; Luo, Y.; DeIonno, E.; Peters, A. J.; Jeppesen, J. O.; Xe, K.; Stoddart, J. F.; Heath, J. R. *Chem. Eur. J.* **2006**, *12*, 261–279. (h) DeIonne, E.; Tseng, H.-R.; Harvey, D. D.; Stoddart, J. F.; Heath, J. R. *J. Phys. Chem. B* **2006**, *110*, 7609–7612. (i) Dichtel, W. R.; Heath, J. R.; Stoddart, J. F. *Phil. Trans. R. Soc. London, Ser. A* **2007**, 1607–1625. (j) Green, J. E.; Choi, J. W; Boukai, A.; Bunimovich, Y.; Johnston-Halprin, E.; DeIonno, E.; Luo, Y.; Sheriff, B. A.; Xu, K.; Shin, Y. S.; Tseng, H.-R.; Stoddart, J. F.; Heath, J. R. *Nature* **2007**, *445*, 414–417.

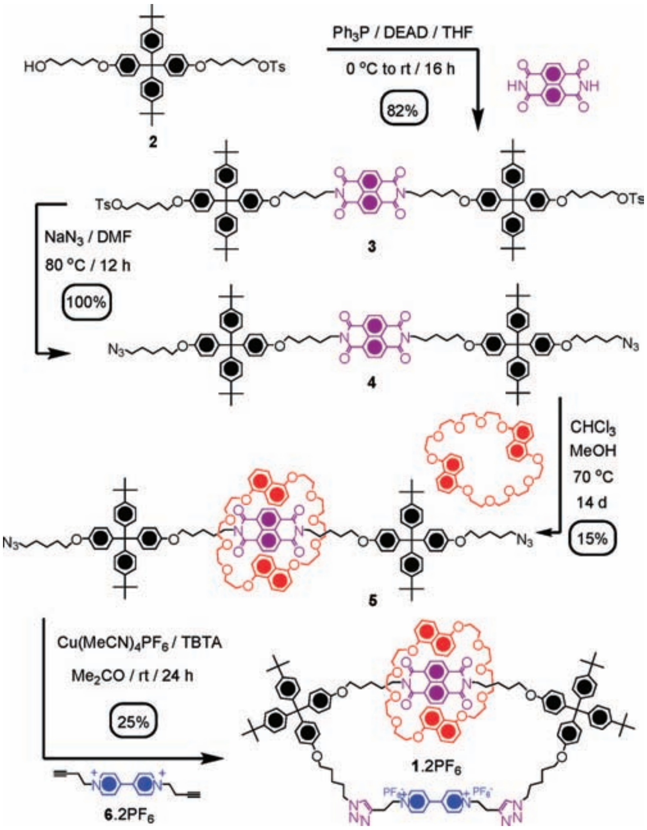
10.1021/ol800931z CCC: $40.75

ring with two recognition sites grafted into the other (nondegenerate) ring can be employed to stimulate the circumrotation of the first ring around the second one.

Thus, a large-amplitude molecular mechanical motion can be realized within a mechanically interlocked molecule—be it a [2]catenane or a [2]rotaxane—provided it exhibits bistability within the time frame of the experiment in progress. Further necessary conditions for generating highly controllable molecular actuations in a bistable [2]rotaxane, for example, are (i) an appreciable difference in the binding affinities of the ring component for the two different recognition sites on the dumbbell component and (ii) a means of altering completely the binding affinities in a wholly reversible manner. A free energy difference of greater than 1.2 kcal mol^{-1} between the two translational isomers of a bistable rotaxane ensures that, at room temperature, at least 90% of the molecules have the ring residing around one site in preference to the other one. In order to induce motion of the ring along the dumbbell component within such bistable rotaxanes, a variety of stimuli—e.g., chemical, electrochemical, and photochemical—have been employed[3,4] with considerable success. In the case of MEDs,[3] successful device performance has also been asscociated with a free energy barrier in excess of 21 kcal mol^{-1} between the translational isomers where the so-called metastable state co-conformation (MSCC) and the ground-state co-conformation (GSCC) corresponding to the ON and OFF states, respectively of the switch.

In the past, bistable donor-acceptor [2]catenanes have been sythesized by a template-directed protocol[5] in which the recognition sites in one ring act as a template for the formation of the mechanically interlocked second ring. The advent more recently[6] of the copper(I)-catalyzed azide-alkyne cycloaddition[7] (CuAAC) has made it possible to synthesize (Scheme 1) a bistable [2]catenane **1**·2PF$_6$ with a much larger free energy barrier between its MSCC and GSCC, while hopefully retaining the free energy difference between the two translational isomers. This communication describes the synthesis, employing CuAAC, of **1**·2PF$_6$ and the characterization of the bistable [2]catenane using ^{1}H NMR spectroscopy and cyclic voltammetry in (CD$_3$CN/MeCN) solution.

Scheme 1. Synthesis of the [2]Catenane **1**·2PF$_6$



The synthesis of **1**·2PF$_6$, which is composed of a π-electron rich bis-1,5-dioxynaphthalene[38]crown-10 (BDNP38C10) ring mechanically interlocked with a second macrocycle containing two π-electron-deficient recognition sites—namely, a naphthalene diimide (NpI) unit and a 4,4′-bipyridinium (BIPY^{2+}) one—which are separated by two bulky tetraarylmethane residues, designed to act as "speed bumps", is outlined in Scheme 1. The tetraarylmethane derivative **2**, carrying a tosyl group at one end and a hydroxyl group at the other, was prepared according to the literature.[8] The NpI derivative **3** was isolated in 82% yield, after carrying out a Mitsunobu reaction between NpI and **2** in the presence of

---

(4) (a) Collin, J.-P.; Dietrich-Buchecker, C.; Gavinã, P.; Jimenez-Molero, M. C.; Sauvage, J.-P. *Acc. Chem. Res.* **2001**, *34*, 477–487. (b) Kim, K.; Jeon, W. S.; Kang, J.-K.; Lee, J. W.; Jon, S. Y.; Kim, T.; Kim, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 2293–2296. (c) Lioubashevski, O.; Chegel, V. I.; Patolsky, F.; Katz, E.; Willner, I. *J. Am. Chem. Soc.* **2004**, *126*, 7133–7143. (d) Berna, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Perez, E. M.; Rudolf, P.; Teobaldi, G.; Zerbetto, F. *Nat. Mater.* **2005**, *4*, 704–710. (e) Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Vignon, S. A.; Northrop, B. H.; Tseng, H.-R.; Jeppesen, J. O.; Huang, T. J.; Brough, B.; Baller, M.; Maganov, S.; Solares, S. D.; Goddard, W. A.; Ho, C. M.; Stoddart, J. F *J. Am. Chem. Soc.* **2005**, *127*, 9745–9759. (f) Balzani, V.; Clemente-León, M.; Credi, A.; Fetter, B.; Venturi, M.; Flood, A.; Stoddart, J. F. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 1178–1183. (g) Brough, B.; Northrop, B.; Schmidt, J. J.; Tseng, H.-R.; Houk, K. N.; Stoddart, J. F.; Ho, C.-M. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8583–8588. (h) Serreli, V.; Lee, C. F.; Kay, E. R.; Leigh, D. A. *Nature* **2007**, *445*, 523–527. (i) Saha, S.; Stoddart, J. F. *Chem. Soc. Rev.* **2007**, *36*, 77–92. (j) Saha, S.; Flood, A. H.; Stoddart, J. F.; Impellizzeri, S.; Silvi, S.; Credi, A. *J. Am. Chem. Soc.* **2007**, *109*, 12159–12171. (k) Patel, K.; Angelos, S.; Dichtel, W. R.; Coskun, A.; Yang, Y.-W.; Zink, J. I.; Stoddart, J. F *J. Am. Chem. Soc.* **2008**, *130*, 2382–2383. (l) Fioravatti, G.; Haraozkiewicz, N; Kay, E. R.; Mendoza, S. M.; Bruno, C.; Marcaccio, M.; Wiering, P. G.; Paolucci, F.; Rudolf, P.; Brouwer, A. M.; Leigh, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 2593–2601.

(5) (a) *Templated Organic Synthesis*; Diederich, F., ; Stang, P. J., Eds.; Wiley-VCH, Weinheim, 2000. (b) Busch, D. H.; Stephenson, N. A. *Coord. Chem. Rev.* **1990**, *100*, 119–154. (c) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469–475. (d) Breault, G. A.; Hunter, C. A.; Mayers, D. C. *Tetrahedron* **1999**, *55*, 5265–5293. (e) Hubin, T. J.; Busch, D. H. *Coord. Chem. Rev.* **2000**, *200*, 5–52. (f) Stoddart, J. F.; Tseng, H.-R. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4797–4800. (g) Blanco, M.-J.; Chambron, J.-C.; Jimenez, M. C.; Sauvage, J.-P. *Top. Stereochem.* **2003**, *23*, 125–173. (h) Busch, D. H. *Top. Curr. Chem.* **2005**, *249*, 1–65. (i) Wu, J.; Leung, K. C.-F.; Stoddart, J. F. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 17266–17271. (j) Griffiths, K. E.; Stoddart, J. F. *Pure. Appl. Chem.* **2008**, *80*, 485–506.

(6) Miljanić, O. Š.; Dichtel, W. R.; Aprahamian, I.; Rohde, R. D.; Agnew, H. D.; Heath, J. R.; Stoddart, J. F. *QSAR 2 Comb. Sci.* **2007**, *26*, 1165–1174.

(7) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599. (b) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057–3064.

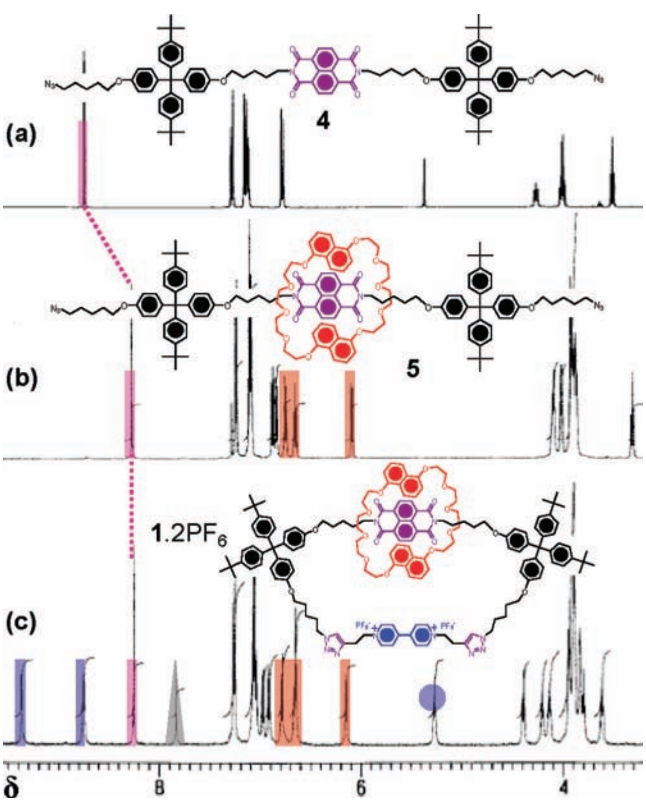


Figure 1. ^{1}H NMR spectra (500 MHz, room temperature) of (a) the NpI diazide **4** in $CDCl_3$, (b) the corresponding [2]rotaxane **5** in $CDCl_3$, and (c) the [2]catenane **1**·2PF$_6$ in $(CD_3)_2CO$. Annotations are shown in color. Blue: H_α, H_β and the methylene protons neighboring BIPY^{2+}. Purple: NpI protons. Red: Aromatic protons of BDNP38C10.

diethyl azodicarboxylate (DEAD) and PPh_3. The resulting ditosylate **3** was then converted quantitatively to the corresponding diazide **4** by treating **3** with NaN_3 at 80 °C in DMF for 12 h. The [2]rotaxane **5** was obtained in 15% yield by slippage[9] of the BDNP38C10 ring over the bulky tetraarylmethane stoppers onto the dumbbell **4** at 70 °C in $CHCl_3$/MeOH. The bistable [2]catenane was isolated in 25% yield, following reaction of **5** under CuAAC conditions with the bisalkyne **6**·2PF$_6$ obtained from bipyridine.[10]

Comparison (Figure 1) of the ^{1}H NMR spectra of the dumbbell **4**, the [2]rotaxane **5**, and the [2]catenane **1**·2PF$_6$ provides evidence for the encirclement of the NpI unit by the BDNP38C10 ring in the [2]rotaxane as well as in the [2]catenane, a situation which is evident from the upfield shifts of the signals for the four protons on the NpI unit from 8.75 ppm in **4** to 8.26 ppm in **5** and 8.22 ppm in **1**·2PF$_6$. The fact that there is a very small difference in the δ values for the four NpI protons in **5** and **1**·2PF$_6$ confirms that the BDNP38C10 ring still encircles the NpI unit in the [2]catenane at ambient temperature, establishing its structural integrity. Heating **1**·2PF$_6$ in CD_3CN at 70 °C during 60 h results in the equilibration of the two possible co-conformations—the one in which the BDNP38C10 ring still encircles the NpI unit and another in which the crown ether encircles the BIPY^{2+} unit as a consequence of its circumrotation over the bulky tetraarylmethane groups, or “speed bumps”. The equilibration of the two co-conformers was monitored at 70 °C by running ^{1}H NMR spectra (Figure 2) at suitable time intervals at room temperature. At the outset, the chemical shifts for (i) the methylene protons adjacent to the triazole rings, (ii) the triazole ring protons, (iii) the NpI protons, and the β-protons on the BIPY^{2+} units resonate at 4.96, 7.55, 8.17, and 8.20 ppm, respectively. As time passed, however, a second set of peaks emerged downfield at 5.06, 7.82, 8.51, and 8.57 ppm for (i), (ii),

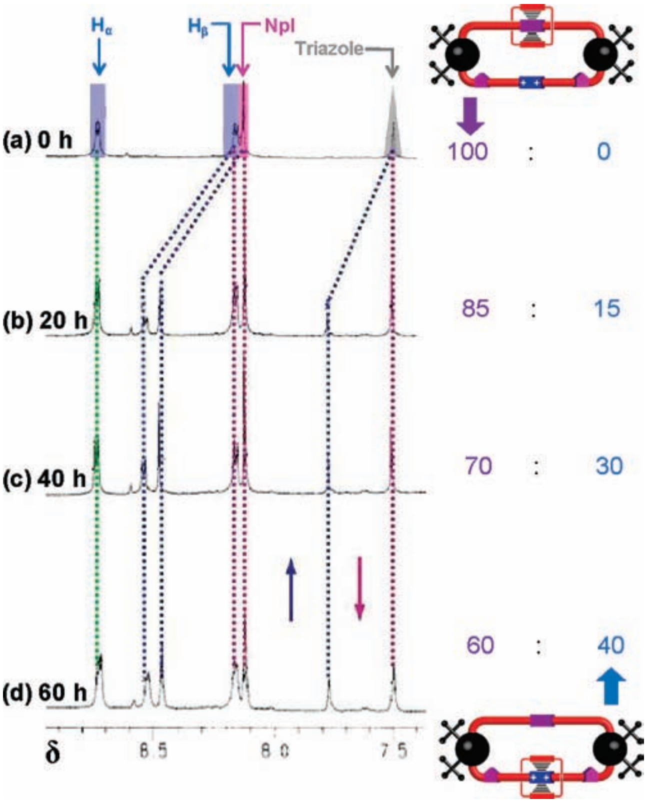


Figure 2. ^{1}H NMR spectra (500 MHz, CD_3CN, room temperature) of the [2]catenane **1**·2PF$_6$ after heating the solution at 70 °C for (a) 0 h, (b) 20 h, (c) 40 h, and (d) 60 h. The spectrum (a) recorded before heating the sample shows the presence of only one co-conformation in which BDNP38C10 ring encircles the NpI unit. The thermal activation produces the other co-conformation with the crown ether ring encircling the BIPY^{2+} unit, as observed from the emergence of the corresponding peaks in (b), (c), and (d). Annotations are shown in color. Green line: H_α of BIPY^{2+}. Blue line (indicating the co-conformation in which BIPY^{2+} is encircled by BDNP38C10): downfield shifts in H_β of BIPY^{2+}, NpI unit and triazole protons. Purple line (indicating the co-conformation in which NpI is encircled by BDNP38C10): H_β of BIPY^{2+}, NpI, and triazole protons.

---

(8) Dichtel, W. R.; Miljanić, O. Š.; Spruell, J. M.; Heath, J. R.; Stoddart, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10388–10390.

(9) (a) Kaiser, G.; Jarrosson, T.; Otto, S.; Ng, Y.-F.; Sanders, J. K. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 1959–1962. (b) Iijima, T.; Vignon, S. A.; Tseng, H.-R; Jarrosson, T.; Sanders, J. K. M.; Marchioni, F.; Venturi, M.; Apostoli, E.; Balzani, V.; Stoddart, J. F. *Chem. Eur. J.* **2004**, *10*, 6375–6392.

(10) Moon, K.; Kaifer, A. E. *Org. Lett.* **2004**, *6*, 185–188.

(iii), and (iv), respectively, assignable to the co-conformer of **1**·2PF$_6$ in which the BDNP38C10 ring encircles the BIPY^{2+} unit. After 60 h, the ratio of the two sets of peaks was 60:40 in favor of **1**·2PF$_6$. Although the energy barrier to circumrotation is calculated to be 28.5 ± 0.3 kcal mol^{-1}, the free energy difference between the two co-conformers is less than 0.3 kcal mol^{-1}. Thus, one of our objectives has been reached at the expense of the other. Although the magnitude of the energy barrier makes **1**·2PF$_6$ a suitable candidate for molecular flash memory in MEDs, the almost equal populations of the two states of the molecular switch undermines its candidature somewhat. Cyclic voltammetry (CV) of the product, after warming **1**·2PF$_6$ in MeCN at 70 °C for 60 h, in addition to the CVs of the dumbbell **4** and the bisalkyne **6**·2PF$_6$, confirm (Figure 3) the presence of both translation isomers in a roughly 1:1 ratio. The CV of the equilibrated bistable [2]catenane shows that ca. 60% of the BIPY^{2+} units are reduced to the radical cation (BIPY$^{\bullet+}$) at -0.33 V—a potential which is identical with that for the first reduction potential of a free BIPY^{2+} unit—while the other ca. 40% is reduced subsequently at more negative potentials (-0.47 to -0.55 V), suggesting that the BIPY^{2+} unit is encircled by the π-electron rich BDNP38C10 ring in this minor isomeric form of the bistable [2]catenane. The second reduction of the BIPY$^{\bullet+}$ unit to the neutral species (BIPY^{0}) and the reduction of the NpI unit are all shifted toward more negative potentials, observations that are commensurate with both BIPY^{2+} and NpI units being encircled by the BDNP38C10 ring. Neither of the isomers of the bistable [2]catenane could be switched, however, to the other one by electrochemical inputs, presumably because of relatively high energy barrier to their inconversion.

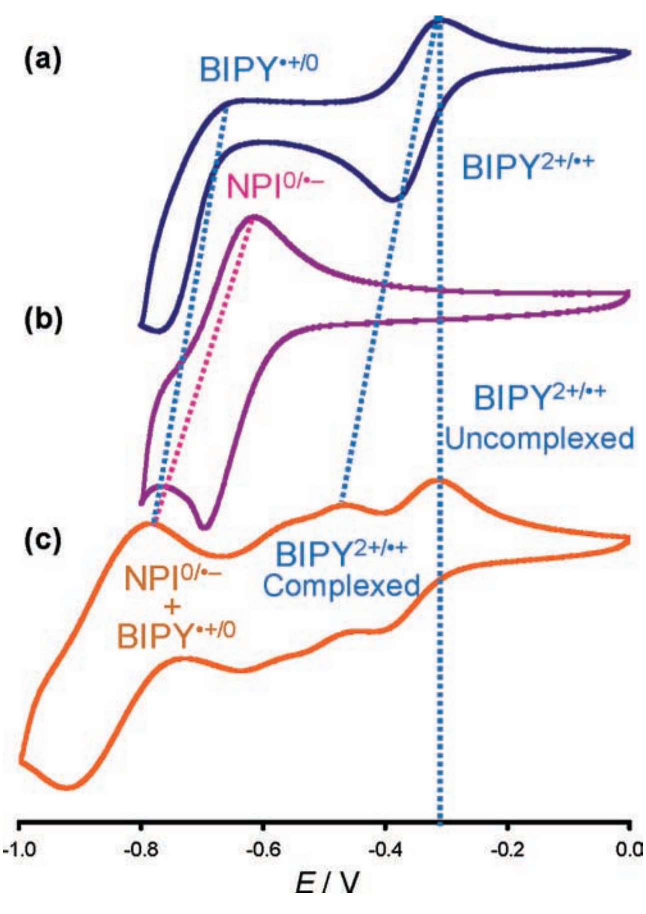


Figure 3. Cyclic voltammograms (0.1 M TB·APF$_6$/MeCN, vs SCE, 100 mVs^{-1}) of (a) the BIPY^{2+} derivative **6**·2PF$_6$ (2 mM), (b) the NpI derivative **4** (2 mM), and (c) the [2]catenane **1**·2PF$_6$ (1 mM) after heating at 70 °C for 60 h, conditions which generated a 60:40 mixture of the two co-conformations.

The synthesis of a nondegenerate bistable [2]catenane under kinetic control using Cu(I)-catalyzed azide-alkyne cycloadditions turns out to be reasonably efficient, employing an interaction which may be augmented by some templation between the diazide **5** and the bisalkyne **6**·2PF$_6$. It is not unlikely, however, that this noncovalent interaction lives on within [2]catenane afterward helping to equalize the proportion of the two translational isomers. As so often happens in science, one finds the answer to one question only to raise another two questions to be answered. It is after this fashion that our knowledge base is enhanced and progress is made.[11]

Acknowledgment. This work was supported by the Microelectronics Advanced Research Corporation (MARCO) and its focus center on Functional Engineered NanoArchitectonics (FENA) and the Center for Nanoscale Innovative Defense (CNID).

Supporting Information Available: Experimental details and spectral characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL800931Z

---

(11) In bistable catenanes and rotaxanes, with degeneracy present in the π-donating cyclophane—namely, in cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}) —and bistability present in the π-donating crown ether or the acyclic polyether component of a dumbbell, where the recognition sites are commonly tetrathiafulvalene (TTF) and 1,5-dioxynaphthalene (DNP) units, the free energy barriers associated with the cyclophane travelling from the metastable co-conformation with CBPQT^{4+} encircling DNP back to the ground state co-conformation in which CBPQT^{4+} encircles TTF are in the range 16−23 kcal mol^{-1}, depending upon the structure of the bistable molecule and the medium in which it finds itself. (Choi, J. W.; Flood, A. H.; Steuerman, D. W.; Nygaard, S.; Braunschwieg, A. B.; Moonen, N. N. P.; Laursen, B. W.; Luo, Y.; DeIonno, E.; Peters, A. J.; Jeppesen, J. O.; Xu, K.; Stoddart, J. F.; Heath, J. R. *Chem. Eur. J.* **2006**, *12*, 261–279.). When this recognition motif is reversed—as it is in the case **1**$^{2+}$—the free energy barrier is expected to be very much lower, commonly in the region of only 10 kcal mol^{-1}. (Ashton, P. R.; Belohradsky, M.; Philp, D.; Spencer, N.; Stoddart, J. F *J. Chem. Soc., Chem. Commun.* **1993**, 1274–1277.). This $\Delta G^{\ddagger}$ value is much too low for most device-oriented applications, and so it was for this reason that we incorporated speed bumps between the NpI and BIPY^{2+} units in **1**$^{2+}$. The $\Delta G^{\ddagger}$ value of 28.5 kcal mol^{-1} indicates that the speed bumps in this bistable [2]catenane are considerably higher than we would wish in relation to this compound being used in a device setting. This is the bad news. The good news is that we can, in principle, lower the $\Delta G^{\ddagger}$ value by "pruning" methyl groups off the tertiary butyl groups attached to the tetraarylmethane cores. This exercise is already underway.