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Translational Isomerism in a [3]Catenane and a [3]Rotaxane

Sheng-Hsien Chiu, Arkadij M. Elizarov, Peter T. Glink, and J. Fraser Stoddart*

Department of Chemistry and Biochemistry, University of California, Los Angeles, 405 Hilgard Avenue, Los Angeles, California 90095-1569

stoddart@chem.ucla.edu

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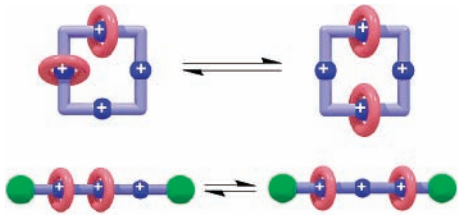
ABSTRACT



Post-assembly covalent modification using Wittig chemistry of [2]rotaxane ylides, wherein NH_2^+ centers in the dumbbell-shaped components are recognized by dibenzo[24]crown-8 (DB24C8) rings, has afforded a [3]catenane and a [3]rotaxane with a precise and synthetically prescribed shortage of DB24C8 rings. The nondegenerate pairs of translational isomers present in both of these interlocked molecular compounds provide the fundamental platform on which to construct sensory devices and nanochemomechanical systems.

Because of their ability to flip between two or more states when external stimuli induce relative movements of their noncovalently interacting components, mechanically interlocked molecules, such as catenanes[1] and rotaxanes,[2] hold considerable promise[3] for the fabrication of actuators, amplifiers, motors, sensors, and switches on the nanoscale level.[4] For this reason, there is a continual need to develop new and efficient methods to prepare catenanes and rotaxanes with multiple recognition sites and to investigate the translational isomerism involving their interactive components. Previously, we have demonstrated,[5] by employing the Wittig reaction, that benzylic triphenylphosphonium-stoppered [2]rotaxanes,[6] in which the NH_2^+ recognition sites on the dumbbell-shaped components are encircled[7] by dibenzo-[24]crown-8 (DB24C8), are convenient building blocks for the one-pot synthesis of a [4]molecular necklace[8] and a branched [4]rotaxane.[9] Here, we report how a [2]rotaxane,[6] carrying one such stopper, may be grafted onto and crafted

(1) Catenanes are molecules comprising two or more interlocked rings. For recent examples, see: (a) Chambron, J.-C.; Sauvage, J.-P.; Mislow, K.; De Cian, A.; Fischer, J. *Chem. Eur. J.* **2001**, *7*, 4085−4096. (b) Hori, A.; Kumazawa, K.; Kusukawa, T.; Chand, D. K.; Fujita, M.; Sakamoto, S.; Yamaguchi, K. *Chem. Eur. J.* **2001**, *7*, 4142−4149. (c) Park, K.-M.; Kim, S.-Y.; Heo, J.; Whang, D.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *J. Am. Chem. Soc.* **2002**, *124*, 2140−2147.

(2) Rotaxanes are molecules in which one or more rings are trapped on the rod section of a dumbbell-shaped component by bulky stoppers. For recent examples, see: (a) Bryant, W. S.; Guzei, L. A.; Rheingold, A. L.; Gibson, H. W. *Org. Lett.* **1999**, *1*, 47−50. (b) Seel, C.; Vögtle, F. *Chem. Eur. J.* **2000**, *6*, 21−24. (c) Tachibana, Y.; Kihara, N.; Ohga, Y.; Takata, T. *Chem. Lett.* **2000**, 806−807. (d) Mahoney, J. M.; Shukla, R.; Marshall, R. A.; Beatty, A. M.; Zajicek, J.; Smith, B. D. *J. Org. Chem.* **2002**, *67*, 1436−1440. (e) Asakawa, M.; Brancato, G.; Fanti, M.; Leigh, D. A.; Shimizu, T.; Slawin, A. M. Z.; Wong, J. K. Y.; Zerbetto, F.; Zhang, S. *J. Am. Chem. Soc.* **2002**, *124*, 2939−2950. (f) Chiu, S.-H.; Stoddart, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 4174−4175. (g) Andersson, M.; Linke, M.; Chambron, J.-C.; Davidsson, J.; Heitz, V.; Hammarstroem, L.; Sauvage, J.-P. *J. Am. Chem. Soc.* **2002**, *124*, 4347−4362. (h) Stanier, C. A.; Alderman, S. J.; Claridge, T. D. W.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 1769−1772.

(3) (a) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348−3391. (b) Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Venturi, M. *Acc. Chem. Res.* **2001**, *34*, 445−455.

(4) (a) Collier, C. P.; Wong, E. W.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. *Science* **1999**, *285*, 391−394. (b) 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. (c) Luo, Y.; Collier, C. P.; Jeppesen, J. O.; Nielsen, K. A.; DeIonno, E.; Ho, G.; Perkins, J.; Tseng, H.-R.; Yamamoto, T.; Stoddart, J. F.; Heath, J. R. *ChemPhysChem* **2002**, *3*, 519−525.

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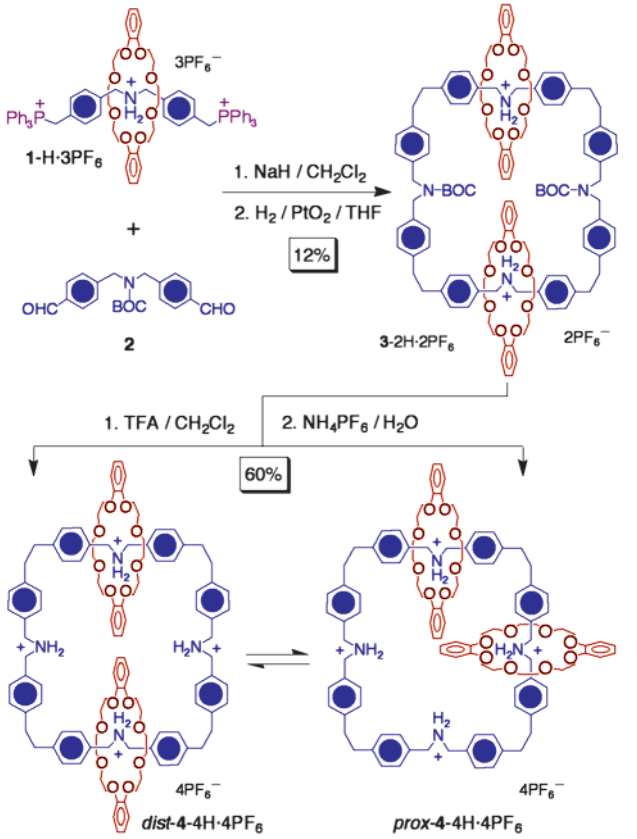
into (i) a [3]catenane and (ii) a [3]rotaxane with *four* and *three* NH_2^+ recognition sites, respectively, for *two* DB24C8 rings. Thus, while the translational isomerism exhibited in solution by the [3]catenane is reminiscent of a model circular railroad with four stations and two trains, the [3]rotaxane resembles a model straight railroad with three stations for two trains. We also demonstrate that in both the [3]catenane and [3]rotaxane the proximal (*prox*) and distal (*dist*) isomers are almost equally populated in solution, a property that could be exploited in the development of sensory devices and nanochemomechanical systems.

Previously, we have reported[8] an unsuccessful attempt to make a [3]catenane from **1**-H·3PF_6 (Scheme 1) by subjecting

Scheme 1



it to a bis-Wittig olefination with a benzyloxymethoxy-protected 2,5-dihydroxyterephthalaldehyde derivative. We suspect that our failure to isolate a [3]catenane was the result of steric overcrowding of the two DB24C8 rings, a situation that disfavors macrocyclization and possibly also encourages subsequent hydrogenolysis, rather than hydrogenation, when the crude complex mixture of olefins is treated with hydrogen in the presence of a catalyst. Consequently, we decided to use a dialdehyde with a longer spacer unit separating the two formyl groups and also to employ it to introduce additional NH_2^+ recognition sites into the [3]catenane.

(9) Chiu, S.-H.; Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.*, in press.

Dialdehyde[10] **2** not only fulfills these requirements but its Boc-protected amino function acts also as a temporary stopper to prevent the extrusion of the DB24C8 rings during the Wittig olefinations: removal of protecting groups after cyclization unmasks extra recognition sites for the crown ethers. Thus, when an equimolar mixture of **1**-H·3PF_6 and **2** was reacted (Scheme 1) in the presence of base (NaH/CH_2Cl_2) under high dilution conditions, the [3]catenane **3**-2H·2PF_6 was isolated in 12% yield, following hydrogenation (H_2/PtO_2/THF) and chromatography (SiO_2: CH_2Cl_2/MeCN, 9:1). No higher order catenanes were observed[11] by mass spectrometry, which revealed peaks at *m*/*z* 2137 and 1991 corresponding to [**3**-2H·PF_6]$^+$ and [**3**-H]$^+$, respectively. The molecular train set **4**-4H·4PF_6 was obtained in 60% yield after removal (TFA/CH_2Cl_2) of the Boc protecting groups and counterion exchange (NH_4PF_6/H_2O). We investigated the distribution in solution by NMR spectroscopy of the two translational isomers of the molecular train set—one (*prox*-**4**-4H·4PF_6) in which the two DB24C8 rings are proximal and the other (*dist*-**4**-4H·4PF_6) where they are distal. A previously reported[12] molecular train set—comprising two tetracationic cyclophanes encircling a four-station π-electron-rich macrocyclic polyether—was found by ^{1}H NMR spectroscopy to exist in solution as only the *dist* translational isomer, presumably in order to minimize electrostatic repulsions between the two tetracationic cyclophanes. In the case of **4**-4H·4PF_6, however, there is no such repulsion and so the *prox* and *dist* translational isomers are expected to be of similar energies.[13] On account of the overlapping of signals in the ^{1}H NMR spectrum, ^{13}C NMR spectroscopy was used to investigate the proportions of the two translational isomers. Because of the rapid rotation of the DB24C8 rings of **4**-4H·4PF_6 in the vicinity of their NH_2^+ recognition sites and the C_{2v} and D_{2h} symmetries of the *prox* and *dist* translational isomers, respectively, we expected to observe one set of signals in the ^{13}C NMR spectra of each of these translational isomers. The ^{13}C NMR spectrum of **4**-4H·4PF_6 in CD_2Cl_2 shows two distinct sets of signals (a, c, d, e in Figure 1) arising from the DB24C8 rings.[14] Although the signals for the tetracationic macrocycle are more complicated than those

(10) (a) Ashton, P. R.; Fyfe, M. C. T.; Glink, P. T.; Menzer, S.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 12514−12524. (b) Chiu, S.-H.; Pease, A. R.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 270−274.

(11) The only byproducts in this synthesis were compounds, possibly oligomeric rotaxanes, that could not be moved off the baseline during TLC analysis.

(12) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Parry, K. P.; Pietraszkiewicz, M.; Spencer, N.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1042−1045.

(13) The symmetry numbers of the *prox* and *dist* isomers of this compound differ by a factor of 2. Thus, a statistical mixture of the translational isomers should exist as a 2:1 ratio of the *prox* and *dist* isomers. See: Bailey, W. F.; Monahan, A. S. *J. Chem. Ed.* **1978**, *55*, 489−493.

(14) In CD_3CN, the resolution in the ^{13}C NMR spectra of these two sets of signals for the DB24C8 rings was poorer when compared with those obtained in CD_2Cl_2. Additionally, increasing the temperature reduced the signal separation and decreasing the temperature increased it. These observations suggest that the resolution of the signals is related to the rate of interconversion between the *prox* and *dist* isomers. At high temperatures or in more-polar solvents, less energy is required to break the hydrogen bonding interactions, both influences which will lower the activation free energy for the shutting process. Thus, the rate of exchange between the two translational isomers is increased and results in poorer resolution of the signals.

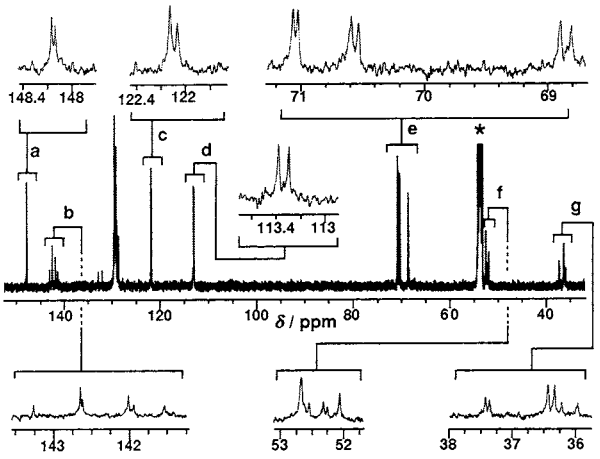
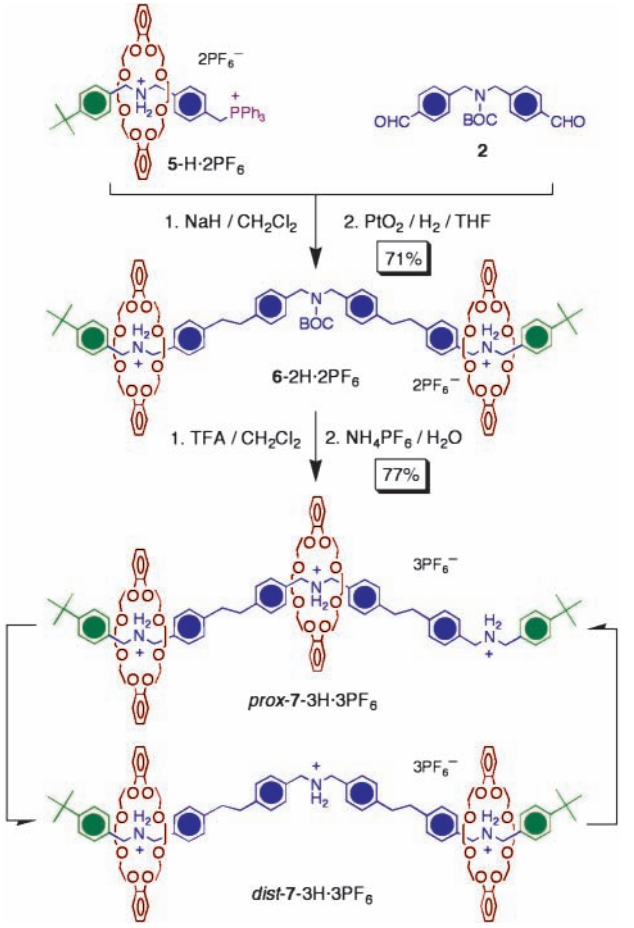


Figure 1. Partial ^{13}C NMR spectra (125 MHz, CD_2Cl_2, 298 K) of **4**-4H·4PF$_6$ displaying a ca. 1:1 mixture of *prox* and *dist* isomers interconverting slowly. Each carbon atom of the DB24C8 subunits (a, c, d, and e) appears as two signals. The signals of the $ArCH_2$-CH_2Ar units (g) and one of the aromatic carbon atoms (b) of the tetracationic macrocycle reveal the expected six different environments they each encounter (in 1:1:1:1:2:2 ratios), but only five of them are resolved (in a 3:1:1:1:2 ratio) in the case of the CH_2N^+ units (f).

for the crown ether rings, they are still consistent with the symmetries of the two translational isomers. There are two different environments for the CH_2N^+ carbon atoms in *dist*-**4**-4H·4PF$_6$ and four different environments for them in *prox*-**4**-4H·4PF$_6$. In an approximately 1:1 mixture of the two translational isomers, one would predict that a total of six different environments would result in six peaks for these carbon atoms in approximately a 1:1:1:1:2:2 ratio. This situation manifests itself in the signal (Figure 1f) observed for the CH_2N^+ carbon atoms, but not all of the six signals are resolved and a 3:1:1:1:2 ratio of them is the outcome. The signals (Figure 1g) for the methylene carbon atoms of the $ArCH_2CH_2Ar$ units and for one (Figure 1b) of the aromatic carbon atoms do, however, display all of the six signals in well-resolved 1:1:2:2:1:1 and 1:2:1:2:1:1 ratios, respectively. Because of the almost equal concentrations of the two translational isomers in solution,[13] *prox*-**4**-4H·4PF$_6$ must be disfavored by a weak steric effect. Attempts to observe coalescence of the signals in ^{13}C NMR spectra—and hence determine the activation barrier for interconversion between the two translational isomers—were thwarted by the fact that the [3]catenane **4**-4H·4PF$_6$ was found[15] to be thermally unstable.

A similar synthetic strategy was employed to make the [3]rotaxane **7**-3H·3PF$_6$ comprising a dumbbell-shaped trication in which three NH_2^+ centers are encircled by two DB24C8 rings. This [3]rotaxane was isolated (Scheme 2) after Wittig olefination of the benzylic monotriphenylphosphonium-stoppered [2]rotaxane **5**-H·2PF$_6$ with the dialdehyde

Scheme 2



2, followed by removal of the Boc protecting group on the central amino function in **6**-2H·2PF$_6$ to give the molecular train set **7**-3H·3PF$_6$ as a mixture of translational isomers. Once again, the ^{13}C NMR spectrum (125 MHz) at ambient temperature in CD_2Cl_2 of the [3]rotaxane shows two sets of signals of roughly equal intensities for the DB24C8 rings, an observation that is consistent with there being two translational isomers of **7**-3H·3PF$_6$—one (*prox*-**7**-3H·3PF$_6$) in which the two DB24C8 rings are proximal and another (*dist*-**7**-3H·3PF$_6$) in which they are distal. Since the differences in the chemical shifts between the two sets of signals are small, we were unable to extract meaningful data from the ^{13}C NMR spectra. Fortunately, however, the ^1H NMR spectra of **7**-3H·3PF$_6$ display distinctly different signals for the protons of the terminal *tert*-butyl groups in the two translational isomers. In both CD_2Cl_2 and CD_3SOCD_3, the chemical shift of the signal for a *tert*-butyl substituent on a phenyl group adjacent to an NH_2^+ center appears further upfield when that NH_2^+ center is encircled by a DB24C8 ring than when it is not, presumably because of shielding effects by the crown ether's catechol units. In *dist*-**7**-3H·3PF$_6$ both *tert*-butyl groups are homotopic and one singlet is expected in the upfield region. In *prox*-**7**-3H·3PF$_6$, however, they are heterotopic and so two singlets of equal intensities are expected—one relatively upfield and the other

(15) Although there is no obvious reason for its instability, we observed signals for free DB24C8 in the ^{13}C NMR spectrum of **4**-4H·4PF$_6$ when it was heated above 60 °C in CD_3CN.

relatively downfield—for this translational isomer. Not unexpectedly, perhaps, the more upfield of these signals for both *dist*- and *prox*-**7**-3H·3PF$_6$ overlap with each other. Thus, the relative concentrations—which are related to the equilibrium constant (K_{eq})—of the *dist*/*prox* translational isomers of **7**-3H·3PF$_6$ can be determined by taking the ratio of the integral of the more upfield signal (minus the integral of the downfield one) and double the integral of the more-downfield signal. Using this method, the value of K_{eq} was determined to be 0.53 in both CD_2Cl_2 and CD_3SOCD_3 at 298 K. Thus, *prox*- is more stable[12] than *dist*-**7**-3H·3PF$_6$, in both nonpolar and polar solvents, by ca. 0.4 kcal mol^{-1} at room temperature. To determine the enthalpic and entropic contributions to this free energy difference between these two translational isomers, we studied the equilibrium at different temperatures. The plot (Figure 2) of the free energy difference ($\Delta G°$) as a function of temperature (T) gave straight lines, from which $\Delta H°$ and $\Delta S°$ were calculated. In both solvents, *prox*-**7**-3H·3PF$_6$ is the more enthalpically stable and *dist*-**7**-3H·3PF$_6$ the more entropically stable.[16]

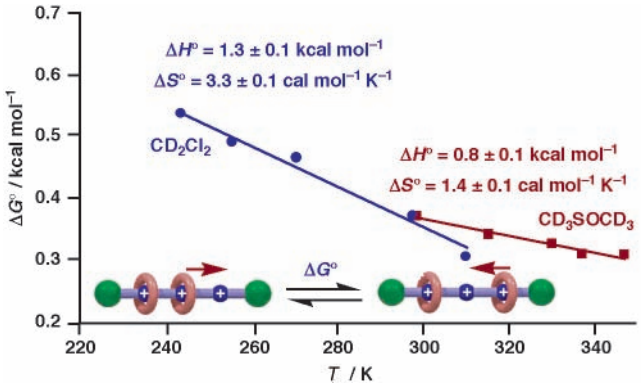


Figure 2. Plot of $\Delta G°$ vs T for the equilibrium between *prox*-**7**-3H·3PF$_6$ and *dist*-**7**-3H·3PF$_6$ in CD_2Cl_2 (blue circle) and CD_3SOCD_3 (red box) determined by 500 MHz ^{1}H NMR spectroscopy. The slope and intercept of each line of best fit give the values of $\Delta S°$ and $\Delta H°$, respectively, from the equation $\Delta G° = \Delta H° - T\Delta S°$.

To obtain a value for the activation energy required to shuttle a DB24C8 ring between NH_2^+ stations in **7**-3H·3PF$_6$, we investigated the coalescence of the signals of the *tert*-butyl groups by variable-temperature ^{1}H NMR spectroscopy. In CD_3SOCD_3, the signals for the *tert*-butyl groups coalesced at 400 K (Figure 3). Although varying the temperature does affect the equilibrium between the two translational isomers, their ratio remains close to 1:1 over the range 380−420 K. As such, we can employ[17] the approximate rate expression ($k_c = \pi\Delta\nu/\sqrt{2}$) to calculate the rate (k_c) of shuttling at the

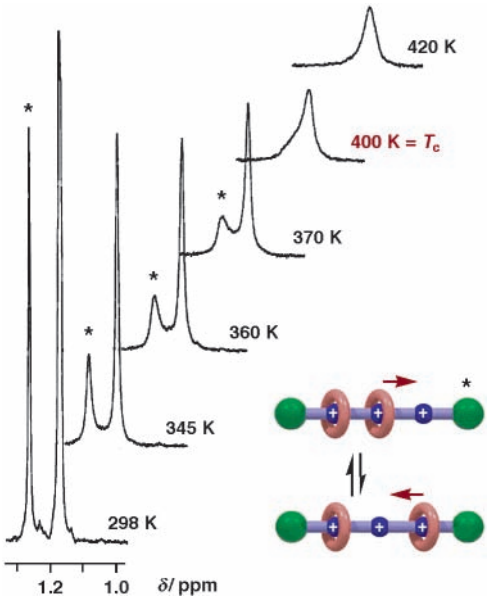


Figure 3. Partial variable-temperature 500 MHz ^{1}H NMR spectra displaying the coalescence of the *tert*-butyl signals of the [3]rotaxane **7**-3H·3PF$_6$ in CD_3SOCD_3. The signal marked with the asterisk corresponds to the resonance of the *tert*-butyl protons adjacent to an unoccupied NH_2^+ center.

coalescence temperature to be ca. 105 s^{-1}, a value of k_c that corresponds to an energy barrier ($\Delta G_c^‡$) of ca. 20 kcal mol^{-1}. These values are very similar to those determined (k_{424K} = 98 s^{-1}, $\Delta G^‡_{424K}$ = 21.3 kcal mol^{-1}) for a simple two-station [2]rotaxane[18] comprised of a DB24C8 ring and a dumbbell-shaped dication in which the NH_2^+ centers are separated by a *p*-xylyl unit.

We have established that Wittig chemistry can be employed to advantage to convert appropriately functionalized [2]rotaxanes into a [3]catenane and a [3]rotaxane, both of which can exist as two slowly interconverting translational isomers on the NMR time scale. These nondegenerate interlocked molecules complement the dual-mode co-conformational switching in catenanes[19] incorporating bipyridinium and dialkylammonium sites and avail us of yet another opportunity to develop molecular-level machines.[3]

Acknowledgment. We thank the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support. This material is based upon work supported by the National Science Foundation under equipment grant no. CHE-9974928.

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

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(16) Statistically (ref 13), the *dist*/*prox* ratio is expected to be 0.5, suggesting—from consideration of the "trivial" entropy of the system—that the *prox* isomer should be the more entropically stable (by ca. 1.4 cal mol^{-1} K^{-1}). The observation that the *dist* isomer is the more entropically stable suggests that symmetry factors alone do not explain the observed *dist*/*prox* ratio of 0.53.

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(18) Cao, J.; Fyfe, M. C. T.; Stoddart, J. F.; Cousins, G. R. L.; Glink, P. T. *J. Org. Chem.* **2000**, *65*, 1937−1946.

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