A mechanical "flip-switch". Interconversion between co-conformations of a [2]rotaxane with a single recognition site

Stephen J. Loeb,* Jorge Tiburcio and Sarah J. Vella

[2]Rotaxanes utilising the 1,2-bis(pyridinium)ethane, 24-crown-8 motif can exist in two distinct co-conformations whose relative abundances are solvent dependent.

The transformation of mechanically linked molecules such as [2]rotaxanes and [2]catenanes into molecular machines requires the synthesis of systems in which two distinct molecular arrangements can be identified, quantified and ultimately controlled.[1] One of the most widely studied of these is the molecular shuttle pioneered by Stoddart.[1,2] In a molecular shuttle, two different recognition sites are present on the axle for the binding of a single macrocyclic wheel. The two states are translational isomers related by the relative positioning of the two interlocked components. Similarly in a switchable [2]catenane, the molecule can adopt different co-conformations which are positional isomers based on the relative orientations of the two interlocked rings.[1,3]

The incorporation of dibenzo-24-crown-8 ether, (**DB24C8**) as the wheel for interlocked molecules in which the axle is a 1,2-bis(pyridinium)ethane cation has been shown to be a versatile motif for the formation of [2]rotaxanes,[4] [3]rotaxanes,[5] [3]catenanes,[6] molecular shuttles,[7] branched [n]rotaxanes[8] (n = 2–4) and recently metal–organic rotaxane frameworks (MORFs).[9] Herein, we report a new set of positional isomers based on [2]rotaxanes which contain a single recognition site but have different end groups on both the bis(pyridinium) axle and crown ether wheel. The relative positioning of the two interlocked components produces two co-conformations and their re-orientation is reminiscent of a mechanical "flip switch".[10]

Perhaps the simplest example of a [2]rotaxane with the 1,2-bis(pyridinium)ethane template is [(**1**)(**DB24C8**)]$^{4+}$ formed when bulky *t*Bu-benzyl stoppers are added to 1,2-bis(4,4′-dipyridinium)-ethane axles and **DB24C8** is the wheel (Fig. 1, top).[4a] If **DB24C8** is replaced by benzo-naphtho-24-crown-8 (**BN24C8**), to give [2]rotaxane [(**1**)(**BN24C8**)]$^{4+}$ the two ends of the molecule are now different (Fig. 1, bottom). At room temperature (300 K), the ^{1}H NMR spectrum of [(**1**)(**BN24C8**)]$^{4+}$ in CD$_2$Cl$_2$ (Fig. 2, top) shows only four averaged peaks for the eight pairs of pyridyl protons due to rapid end-to-end exchanging of the crown aromatic rings. However at low temperature (213 K), these peaks split into six distinct resonances due to the two different and equally populated environments (Fig. 2, bottom). The low temperature spectrum can be rationalised based on the fact that the outer pyridyl protons (3$_B$, 3$_N$, 4$_B$, 4$_N$) experience different amounts of shielding from the presence or absence of the larger naphtho ring
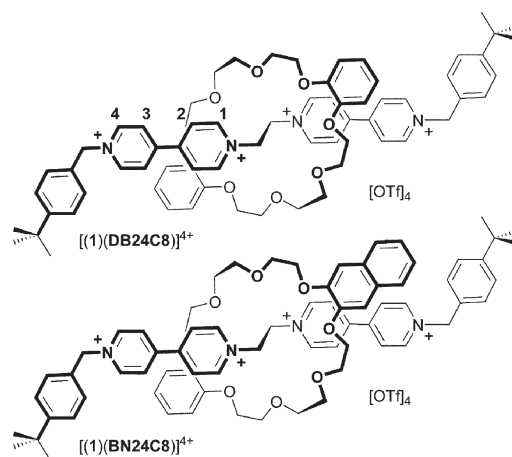
Department of Chemistry and Biochemistry, University of Windsor, Windsor, Ontario, Canada. E-mail: loeb@uwindsor.ca; Fax: 1-519-973-7098; Tel: 1-519-253-3000

Fig. 1 The [2]rotaxane [(**1**)(**DB24C8**)]$^{4+}$ (top) can be made to have different ends by simply changing the crown ether wheel from **DB24C8** to **BN24C8** to give [(**1**)(**BN24C8**)]$^{4+}$ (bottom).

while the inner pyridyl protons (1$_B$, 1$_N$, 2$_B$, 2$_N$) are consistently shielded by the inner portion of the naphtho or benzo ring. Thus, the outer pyridyl protons split into two separate resonances with a Δδ of ∼0.35 ppm. This is in the range observed previously for π-stacking in these types of rotaxanes. The rate of this end-to-end exchange or "flipping" was calculated to be 1.5 × 10^3 s^{-1} at 298 K with a barrier of 25 kJ mol^{-1}.[11]

Another important spectral feature is that the two sets of limiting chemical shifts for 3$_B$,4$_B$ and 3$_N$,4$_N$ in [(**1**)(**BN24C8**)]$^{4+}$ are
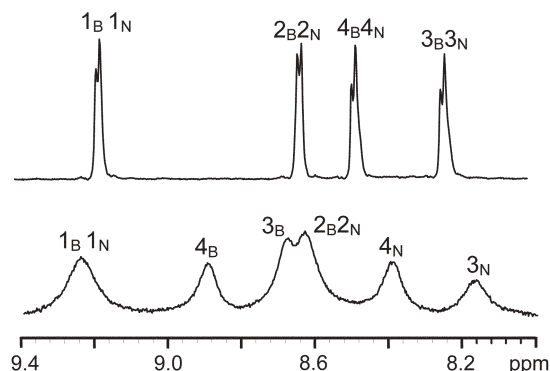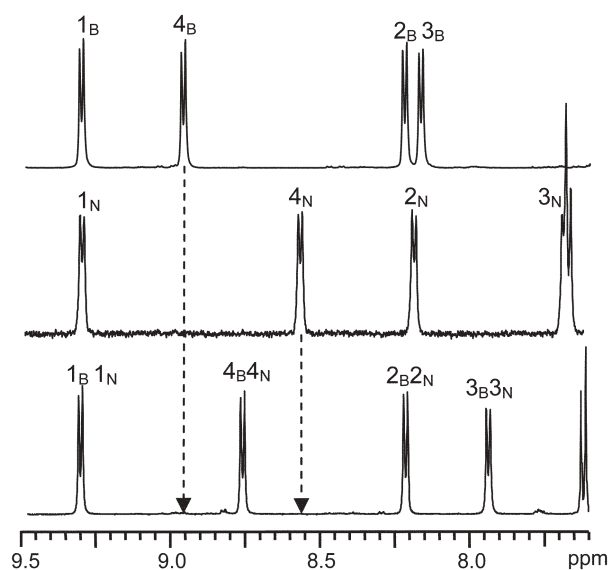

Fig. 2 Partial ^{1}H NMR spectra of [(**1**)(**BN24C8**)]$^{4+}$ in CD$_2$Cl$_2$. Top: room temperature (300 K) showing averaged peaks. Bottom: low temperature (213 K) showing the splitting of the individual pyridinium protons on the different ends of the [2]rotaxane. Subscripts B and N denote the benzo (B) and naphtho (N) ends of the molecule.

exactly the same as those observed for the same protons in the [2]rotaxanes [(1)(DB24C8)]$^{4+}$ and [(1)(DN24C8)]$^{4+}$. Consequently, at room temperature, protons $3_B,3_N$ and $4_B,4_N$ for the rotaxane [(1)(BN24C8)]$^{4+}$ resonate at chemical shifts which are the weighted average (50 : 50 by definition) of the positions observed for the same protons on the rotaxanes [(1)(DB24C8)]$^{4+}$ and [(1)(DN24C8)]$^{4+}$. Not surprisingly, the resonances for protons $1_B,1_N$ and $2_B,2_N$ are essentially independent of the crown as their environment changes very little for this series of [2]rotaxanes. These trends are shown in Fig. 3.

[(1)(BN24C8)]$^{4+}$ represents a simple [2]rotaxane containing a wheel with two different aromatic rings. However, it was of interest to make *both* the wheel and the axle different. We therefore synthesized [2]rotaxanes using the axles 2^{3+}, 3^{3+} and 4^{4+} each with crown ethers **DB24C8**, **DN24C8** and **BN24C8** (Fig. 4). In these cases, when the crown ether **BN24C8** is used, there exists the possibility of two co-conformational isomers depending on the relative orientation of the aromatic groups of the wheel and axle. These two isomers are analogous to the two translational isomers observed in molecular shuttles. It was therefore of interest to i) determine the relative populations of the two co-conformations and ii) to see if this ratio could be manipulated by some external perturbation.

Ideally, it would be possible to record the limiting low temperature ^{1}H NMR spectra and integrate the appropriate peaks for each pyridyl proton to determine the relative populations. Unfortunately, chemical exchange was still rapid at the lowest temperatures accessible (~195 K in CD$_2$Cl$_2$). Instead, the room temperature (300 K) resonances representing the weighted averages for protons 4_B and 4_N in [(2)(BN24C8)]$^{3+}$, [(3)(BN24C8)]$^{3+}$ and [(4)(BN24C8)]$^{4+}$ were compared to the limiting shifts for these protons in the analogous rotaxanes [(1)(DB24C8)]$^{4+}$ and [(1)(DN24C8)]$^{4+}$ to determine the ratio of co-conformational isomers in these compounds in MeCN-d$_3$ (Table 1). This method shows that in MeCN-d$_3$ the larger

Fig. 3 The partial ^{1}H NMR spectra (top to bottom) of [(1)(DB24C8)]$^{4+}$, [(1)(DN24C8)]$^{4+}$ and [(1)(BN24C8)]$^{4+}$ in MeCN-d$_3$. Subscripts B and N denote the benzo (B) and naphtho (N) ends of the molecule; the numbering scheme is the same as Fig. 1.
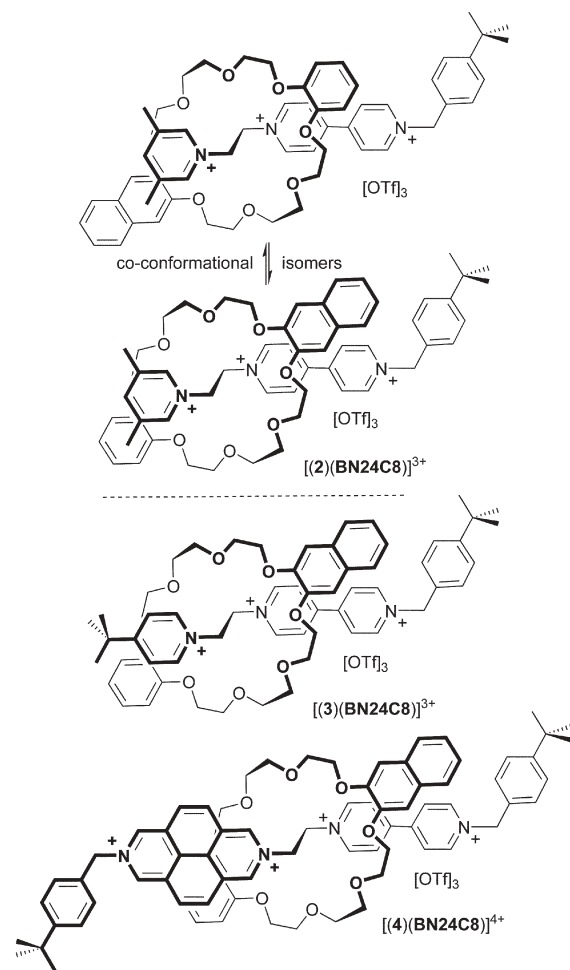
Fig. 4 The axles 2^{3+}, 3^{3+} and 4^{4+} combine with **BN24C8** to produce [2]rotaxanes with two distinct co-conformational isomers whose stability and abundance are dependent on the relative positions of the two interlocked components (only one isomer is shown for 3^{3+}, 4^{4+}).

naphtho group prefers π-stacking with the 4,4′-bipyridinium group rather than the 3,5-lutidinium (2^{3+}), 4-tBu-pyridinium (3^{3+}) or 4,7-diazapyrenium (4^{4+}) groups. For [(2)(BN24C8)]$^{3+}$ and [(3)(BN24C8)]$^{3+}$ this is probably due to increased steric interactions between the Me or tBu substituents and the larger naphtho group compared to the smaller benzo group.

Fig. 5 shows the X-ray structure of [(2)(BN24C8)]$^{3+}$ which adopts the more favourable isomer in the solid state with the benzo

Table 1 Isomer ratios determined from ^{1}H NMR data for [2]rotaxanes in MeCN-d$_3$ solution

[2]Rotaxane	Isomer ratio[a] N/DP : B/DP	Solvent system
[(1)(BN24C8)]$^{4+}$	51 : 49[b]	MeCN-d$_3$
[(2)(BN24C8)]$^{4+}$	57 : 43	MeCN-d$_3$
[(3)(BN24C8)]$^{4+}$	79 : 21	MeCN-d$_3$
[(4)(BN24C8)]$^{4+}$	60 : 40	MeCN-d$_3$

[a] N/DP indicates naphtho π-stacked with 4,4′-dipyridinium and B/DP benzo π-stacked with 4,4′-dipyridinium. Errors for ratios are estimated to be < 5%. [b] By definition the isomer ratio for [(1)(BN24C8)]$^{4+}$ is 50 : 50.
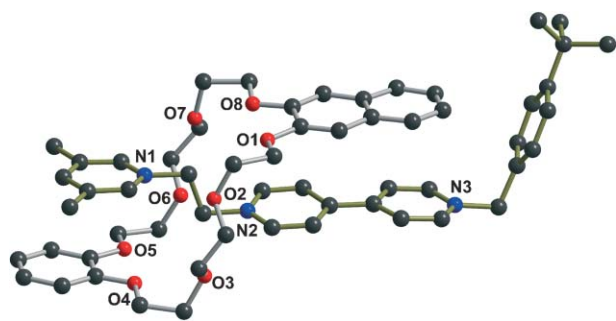
Fig. 5 A ball-and-stick representation of the X-ray structure for the cationic portion of the [2]rotaxane [(**2**)(**BN24C8**)]³⁺.

Table 2 Ratios of conformational isomers determined for [(**4**)(**BN24C8**)]⁴⁺ from ¹H NMR data in various solvents

N/DP : B/DP isomer ratio	Solvent system[a]	Z (kcal/mol)[b]
60 : 40	MeCN-d_3	71.3
58 : 42	CD_2Cl_2	64.2
65 : 35	MeOH-d_4	83.6
71 : 29	acetone-d_6	65.7
58 : 42	MeNO$_2$-d_3	[c]
82 : 18	DMSO-d_6	71.1
70 : 30	D_2O	94.6

[a] The OTf salt of the axle was used for all solvents except D_2O for which the chloride salt was used. [b] Z, solvent polarity parameters were taken from reference 14. [c] No value was available for nitromethane.

group over the 3,5-lutidinium and the naphtho group over the 4,4′-bipyridinium.† It appears that the benzo ring can fit between the two Me groups whereas a similar situation with the naphtho group might cause unfavourable steric interactions. Certainly, one could imagine that the *t*Bu group in the 4-position of [(**3**)(**BN24C8**)]³⁺ would have a much more severe steric interaction with a naphtho group and this is mirrored in the observed solution populations.

Since the populations of the two isomers seem to be dependent upon the relative degrees of π-stacking available it was of interest to try to manipulate the populations. Hunter has shown that changing solvent polarity can have a profound influence on intramolecular face-to-face π-stacking between aromatic rings[12] and others have used solvent polarity to control co-conformational changes in molecular shuttles.[13] We chose to study [(**4**)(**BN24C8**)]⁴⁺ as it contains two different planar pyridinium groups of different surface area and offers no negative steric contributions. Table 2 contains data for [(**4**)(**BN24C8**)]⁴⁺ in MeCN-d_3, CD_2Cl_2, MeOH-d_4, acetone-d_6, MeNO$_2$-d_3, DMSO-d_6 and D_2O and demonstrates that the ratio of co-conformational isomers can indeed be tuned by a simple external perturbation such as solvent polarity. The ratio of isomers shows an increase in π-stacking of the naphtho group with the 4,4′-dipyridinium group in the more polar solvents. This is consistent with observed trends and shows that the naphtho-dipyridinium combination is the more favourable interaction.

In summary, we have shown that [2]rotaxanes of the 1,2-bis(pyridinium)ethane, 24-crown-8 type with a single recognition site can be constructed to yield interlocked molecules that can adopt either of two possible co-conformations. We are currently

investigating ways to incorporate redox and photoactive components as well as functional groups that could be used to control this molecular motion.

Notes and references

1 J. W. Choi, A. H. Flood, D. W. Steuerman, S. Nygaard, A. B. Braunschweig, N. N. P. Moonen, B. W. Laursen, Y. Luo, D. DeIonno, A. J. Peters, J. O. Jeppesen, K. Xu, J. F. Stoddart and J. R. Heath, *Chem.–Eur. J.*, 2005, **12**, 261 and references therein.

2 (a) P. L. Anelli, N. Spencer and J. F. Stoddart, *J. Am. Chem. Soc.*, 1991, **113**, 5131; (b) C. M. Keaveney and D. A. Leigh, *Angew. Chem., Int. Ed.*, 2004, **43**, 1222; (c) D.-H. Qu, Q.-C. Wang, J. Ren and H. Tian, *Org. Lett.*, 2004, **6**, 2085 and references therein.

3 (a) V. Balzani, A. Credi, S. J. Langford, F. M. Raymo, J. F. Stoddart and M. Venturi, *J. Am. Chem. Soc.*, 2000, **122**, 3542; (b) W.-Q. Deng, A. H. Flood, J. F. Stoddart and W. A. Goddard, III, *J. Am. Chem. Soc.*, 2000, **122**, 3542 and references therein.

4 (a) S. J. Loeb and J. A. Wisner, *Angew. Chem., Int. Ed.*, 1998, **37**, 2838; (b) S. J. Loeb and J. A. Wisner, *Chem. Commun.*, 1998, 2757; (c) N. Georges, S. J. Loeb, J. Tiburcio and J. A. Wisner, *Org. Biomol. Chem.*, 2004, **2**, 2751; (d) G. J. E. Davidson, S. J. Loeb, N. A. Parekh and J. A. Wisner, *J. Chem. Soc., Dalton Trans.*, 2001, 3135.

5 S. J. Loeb and J. A. Wisner, *Chem. Commun.*, 2000, 845.

6 A. L. Hubbard, G. J. E. Davidson, R. H. Patel, J. A. Wisner and S. J. Loeb, *Chem. Commun.*, 2004, 138.

7 S. J. Loeb and J. A. Wisner, *Chem. Commun.*, 2000, 1939.

8 S. J. Loeb and D. A. Tramontozzi, *Org. Biomol. Chem.*, 2005, **3**, 1393.

9 (a) S. J. Loeb, *Chem. Commun.*, 2005, 1511; (b) D. J. Hoffart and S. J. Loeb, *Angew. Chem., Int. Ed.*, 2005, **44**, 901; (c) G. J. E. Davidson and S. J. Loeb, *Angew. Chem., Int. Ed.*, 2003, **42**, 74; (d) J. Tiburcio, G. J. E. Davidson and S. J. Loeb, *Chem. Commun.*, 2002, 1282.

10 The term "flip" is used to visualize the change in relative positions of the two components rather than as a statement about any mechanism of reorientation. Formally, the term "switch" should be reserved for molecules which are truly bistable. Although our molecules never exist 100% as one isomer, there is potential for bistability in this system and this is a primary goal in this work.

11 The limiting spectrum for [(**1**)(**BN24C8**)]⁴⁺ in CD_2Cl_2 (Fig. 2) was too broad to allow the direct measurement of the rate of "flip" by NMR exchange spectroscopy. The value reported herein was calculated by fitting the variable temperature data to a simulation using the program gNMR. Unfortunately, rates were unattainable for the other systems due to poor solubility at low temperature or the use of solvents with high freezing points.

12 C. A. Hunter, *Angew. Chem., Int. Ed.*, 2004, **43**, 5310.

13 (a) A. S. Lane, D. A. Leigh and A. Murphy, *J. Am. Chem. Soc.*, 1997, **119**, 11092; (b) T. Da Ros, D. M. Guldi, A. Farran Morales, D. A. Leigh, M. Prato and R. Turco, *Org. Lett.*, 2003, **5**, 689; (c) D. A. Leigh, M. A. F. Morales, E. M. Perez, 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 and F. Zerbetto, *Angew. Chem., Int. Ed.*, 2005, **44**, 3062.

14 A. J. Gordon and R. A. Ford, *The Chemist's Companion*, Wiley: New York, 1972, pp. 22–23 and references therein. Isotope effects for deuterated solvents were ignored. For more information on the origins of Z see E. M. Kosower, *J. Am. Chem. Soc.*, 1958, **80**, 3253.

15 G. M. Sheldrick, SHELXTL 5.03 Program Library, Brüker Analytical Instrument Division, Madison, Wisconsin, USA.

16 1997.DIAMOND 3.0 – Visual Crystal Structure Information System, CRYSTAL IMPACT, Postfach 1251, D-53002 Bonn.