Quantifying the working stroke of tetrathiafulvalene-based electrochemically-driven linear motor-molecules†

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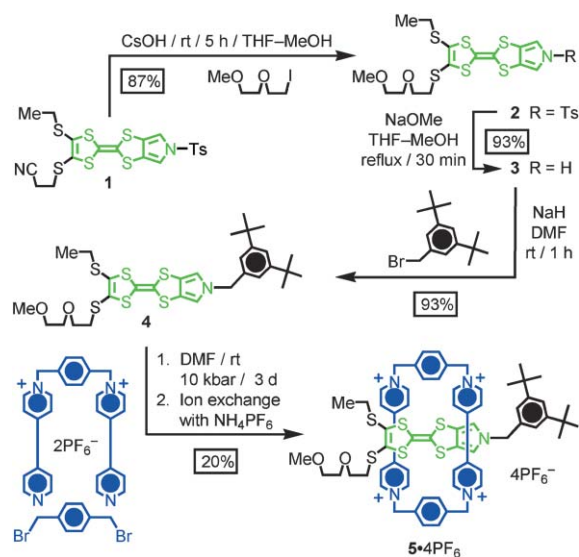
A highly constrained [2]rotaxane, constructed in such a way that the tetracationic cyclobis(paraquat-*p*-phenylene) ring is restricted to reside on a monopyrrolotetrathiafulvalene unit, has been synthesised and characterised. This design allows the deslipping free energy barrier for the tetracationic ring in all three redox states of the rotaxane to be determined.

Of all the π-electron rich guests that form 1 : 1 complexes with the π-electron poor cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) host,[1] tetrathiafulvalene (TTF) is one of the most efficient.§¶ Together with the fact that TTF can be oxidized reversibly[2]—at +321 mV (MeCN, *vs.* SCE) to the $TTF^{•+}$ radical cation, and then subsequently at +714 mV (MeCN, *vs.* SCE) to its TTF^{2+} dication—rendering its complexation with $CBPQT^{4+}$ null and void, its propensity to be encircled by a $CBPQT^{4+}$ ring has made it a prime candidate for the construction of molecular switches in the form of bistable [2]catenanes[3,4] and [2]rotaxanes.[4,5] Furthermore, in bistable [2]rotaxanes,[6] and in a doubly bistable palindromic [3]rotaxane,[7] the ability to induce mechanical movement(s) of the $CBPQT^{4+}$ ring component(s) along the rod sections of the rotaxanes' dumbbell components to another much less π-electron rich site—for example, a 1,5-dioxy-naphthalene one, by changing the redox states of the TTF unit either chemically or electrochemically—has become the basis for the construction of artificial linear motor-molecules.[8] The linear movements in such bistable, mechanically interlocked molecules, which are undoubtedly activated by the electrostatic repulsion between the oxidized and positively-charged TTF unit and the tetracationic $CBPQT^{4+}$ ring, become the basis for what can be likened to a working stroke in a linear motor.

In this communication, we report on the synthesis and thermodynamic evaluation of a highly constrained [2]rotaxane, 5^{4+}, constructed (Scheme 1) in such a way that the location of the $CBPQT^{4+}$ ring is restricted to reside on a

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monopyrrolotetrathiafulvalene (MPTTF) unit by the close proximity of the two stoppers attached to each end of the MPTTF unit. A conventional large di-*t*-butylbenzylic stopper[9] and a smaller more unconventional one, in the form of a combination of a thioethyl (SEt) group and diethyleneglycol substituent,[5b] were chosen, thereby forcing any deslipping of the $CBPQT^{4+}$ ring to take place in the direction of the latter and smaller of the two stoppers. During oxidation, the MPTTF unit acquires one and subsequently two positive charges in a stepwise fashion, effectively destabilizing the mechanically interlocked molecule and hence lowering the effective barrier to deslipping of the $CBPQT^{4+}$ ring. The design of highly constrained 5^{4+} allows us to determine the deslipping free energy barrier for the tetracationic ring in all three redox states of the rotaxane, *i.e.*, when the MPTTF unit is (i) neutral, (ii) singly and (iii) doubly oxidised. The thermodynamic parameters associated with the deslipping barriers allow the magnitude of the electrostatically-driven working stroke produced in MPTTF/$CBPQT^{4+}$-based molecular machines to be determined.

The [2]rotaxane $5·4PF_6$ was synthesised as outlined in Scheme 1. (Methoxyethoxy)ethyl iodide was coupled with MPTTF building block 1, following its *in situ* deprotection with $CsOH·H_2O$, to give 2 in 87% yield. The tosyl protecting group on the MPTTF unit was removed in good yield (93%) using NaOMe in a THF–MeOH mixture. The resultant pyrrole nitrogen in 3 was alkylated (NaH/DMF) with 3,5-di-*t*-butyl-bromomethylbenzene, affording the dumbbell compound 4 in 93% yield. Self-assembly of $5·4PF_6$

Scheme 1 Synthesis of the highly constrained [2]rotaxane $5·4PF_6$.

was carried out from its precursor dumbbell **4** by employing a standard high pressure clipping procedure, in which **4** acts as a template for the reaction between 1,1″-[1,4-phenylenebis(methylene)]bis(4,4′-bipyridin-1-ium) bis(hexafluorophosphate)[1] and 1,4-bis(bromomethyl) benzene, followed by counterion exchange, yielding the product in 20% yield overall. It was characterised† fully by mass spectrometry and NMR spectroscopy.

The deslipping of **5**[4+] was carried out in PhCN at sufficiently high temperatures to promote the CBPQT[4+] ring to overcome the steric barrier imposed by the SEt stopper. Deslipping was monitored by absorption spectroscopy at room temperature using the decrease in the intensity of the characteristic charge transfer (CT) band at 844 nm (PhCN), originating from the CT interaction between the MPTTF unit and the CBPQT[4+] ring, as a probe for the extent of deslipping. The rate constants for deslipping were evaluated† at 405, 409, 413, 429 and 447 K by first order kinetics, giving deslipping barriers ($\Delta G^{\ddagger}$) of 32.3, 32.4, 32.5, 33.1 and 33.5 kcal mol^{-1}, respectively, in PhCN. A ^{1}H NMR spectrum† recorded of the reaction mixture remaining after a similar deslipping process in CD_3SOCD_3 revealed that it contained free dumbbell **4** and the free CBPQT[4+] ring, with only minor amounts of decomposition products being observed.

Addition of 1.0 equiv. of $Fe(ClO_4)_3$ to **5**[4+] in MeCN resulted in the mono-oxidation of the MPTTF unit, giving **5**[5+]. Deslipping of the CBPQT[4+] ring from **5**[5+] was monitored by absorption spectroscopy, utilising the distinctive 465 nm absorption band (Fig. 1) originating from the mono-oxidised MPTTF$^+$ unit formally located inside the cavity of the CBPQT[4+] ring as a probe. The intensity of this band diminishes as a function of time, giving rise to a broad absorption band centred at 625 nm. This absorption is characteristic† of the uncomplexed doubly-oxidised MPTTF^{2+} unit of the free dumbbell **4**[2+]. These spectroscopic observations suggest that a dismutation (Scheme 2) follows the initial deslipping. The oxidation potentials|| for **4**[2+/+] and **5**[5+/4+] also agree well with this model. The spectroscopic deslipping data were obtained at 313, 318, 323, 329 and 335 K and follow first order kinetics. An analysis† based on the dismutation model gave deslipping barriers ($\Delta G^{\ddagger}$) of 24.6, 24.6, 24.8, 25.1 and 25.1 kcal mol^{-1}, respectively, in MeCN.

Formation of the doubly-oxidised [2]rotaxane **5**[6+] was accomplished by adding an excess of $Fe(ClO_4)_3$ in MeCN. The thermodynamics of the deslipping of **5**[6+] were established by
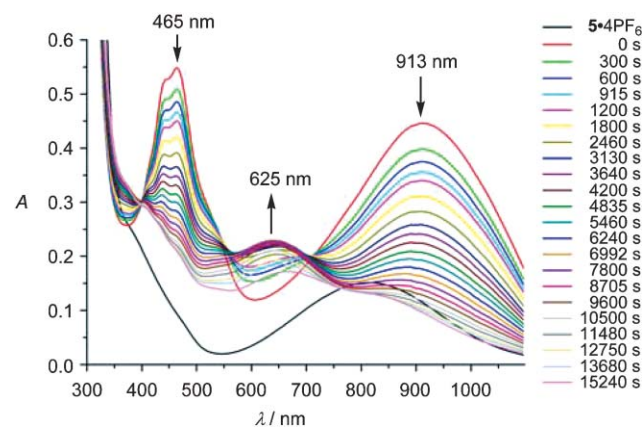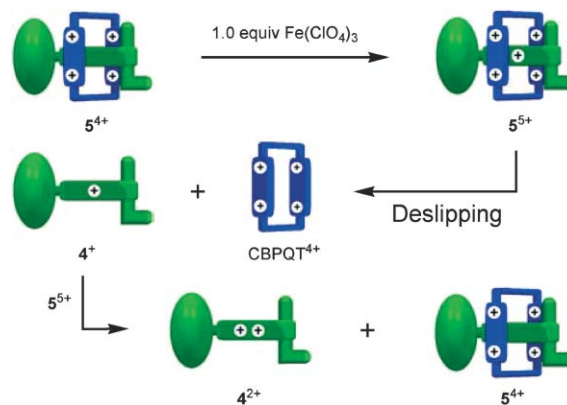

Fig. 1 Time lapse absorption spectra of **5**·4PF$_6$ recorded in MeCN at 323 K after addition of 1.0 equiv. of $Fe(ClO_4)_3$.

Scheme 2 A cartoon representation illustrating the effect of adding 1.0 equiv. of $Fe(ClO_4)_3$ to the rotaxane **5**[4+]. Firstly, the mono-oxidised rotaxane **5**[5+] is formed. Secondly, thermally-activated deslipping of **5**[5+] generates the free ring component and the dumbbell as a radical cation **4**$^+$, which then is further oxidised by a second equiv. of **5**[5+] to generate the non-oxidised rotaxane **5**[4+] and the doubly-oxidised dumbbell **4**[2+].

following the disappearance of the characteristic 750 nm band, originating from the doubly-oxidised MPTTF^{2+} unit located inside the CBPQT[4+] ring's cavity. Assuming the operation of first order kinetics, $\Delta G^{\ddagger}$ values of 19.8, 20.0, 20.0, 20.1 and 20.2 kcal mol^{-1} in MeCN at 276, 280, 283, 288 and 291 K, respectively, were obtained.†

Since the $\Delta G^{\ddagger}$ values have been determined at different temperatures, the enthalpic ($\Delta H^{\ddagger}$) and entropic ($\Delta S^{\ddagger}$) contributions to the deslipping processes can be calculated from plots† of $\Delta G^{\ddagger}$ against T. The kinetic parameters obtained from these plots are summarised in Table 1, together with the extrapolated $\Delta G^{\ddagger}$ values at 300 K.

Providing that the deslipping transition state is not affected to any significant degree by the oxidation state of the MPTTF unit, a potential energy diagram for the deslipping of the highly constrained [2]rotaxane **5**[4+] in its three oxidation states can be constructed (Fig. 2). Thus, based on the thermodynamic data obtained (Table 1) for the different deslipping processes occurring in **5**[4+], **5**[5+] and **5**[6+], the potential energy that this linear motor acquires as it is driven into the first and second oxidation state can be quantified as 4.9 and 8.7 kcal mol^{-1}, respectively. It is evident that the oxidation of the MPTTF unit reduces the energy barrier that the CBPQT[4+] ring has to overcome in order for deslipping to occur by raising the energy levels of the potential wells in the **5**[5+] and **5**[6+] oxidation states compared to the ground state **5**[4+] such that they become net repulsive to the dicationic MPTTF^{2+} unit, i.e., $\Delta G_{300} > 0$ in Fig. 2. Progressive lowering of the energy barrier

Table 1 Kinetic parameters^a for the deslipping of the CBPQT[4+] ring in **5**[4+], **5**[5+] and **5**[6+]

	Solvent	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal mol^{-1} K^{-1})	$\Delta G^{\ddagger}$ (300 K) (kcal mol^{-1})
5[4+]	PhCN	19.9	−30.6	29.1
5[5+]	MeCN	15.5	−28.8	24.2
5[6+]	MeCN	12.6	−26.2	20.4

^{a} The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values were obtained from the intercept and gradient of the straight line plots of $\Delta G^{\ddagger}$ against T using the relationship $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$, where T is the absolute temperature; the estimated errors are $\pm 5\%$ for $\Delta H^{\ddagger}$ and $\pm 10\%$ for $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$.
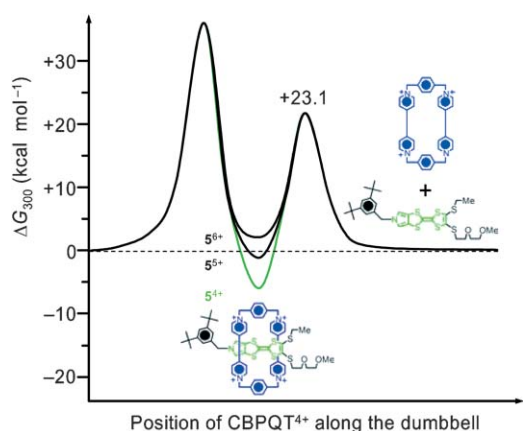
Fig. 2 Scaled schematic representation of the potential energy surface of **5**$^{4+}$, in its three oxidation states **5**$^{4+}$, **5**$^{5+}$ and **5**$^{6+}$ as a function of the reaction coordinate. The bottom of the well for **5**$^{4+}$ is approximated†† by the binding energy -6 kcal mol^{-1} between free MPTTF and the CBPQT^{4+} ring.

is mainly a result of the electrostatic repulsion** between MPTTF$^+$ or MPTTF^{2+} units and the tetracationic CBPQT^{4+} ring. Thus, a linear motor built from the same components has upwards of *ca.* 9 kcal mol^{-1} to use from the powered movement of the CBPQT^{4+} ring following two-electron oxidation of the MPTTF unit. On account of the electrostatic nature of this working stroke, it should be noted that higher as well as lower values are to be expected in other environments, depending on the local dielectric and specific ion pairing.

Notes and references

§ One of us, and later Bryce, investigated the green 1 : 1 complex formed between CBPQT^{4+} and TTF. Originally, in a communication,[10] a K_a value of 51 M^{-1} for the 1 : 1 complex in MeCN at 300 K was reported. Subsequently, it was found that this K_a value was in error. After numerous experiments had been carried out by both the Stoddart group[11] and Bryce,[12] a consistent conclusion was reached—that is, that the K_a value is *ca.* 10000 M^{-1} in MeCN at 298 K, while in Me$_2$CO at 298 K it is *ca.* 2600 M^{-1}. Later, the ability of CBPQT^{4+} to host polyether-linked TTF derivatives was investigated,[3a,13] and it was found that the ethyleneoxy substituents are of paramount importance in assisting the complexation process by virtue of their entering into [C–H⋯O] interactions with some of the α-CH hydrogen atoms in the bipyridinium units of CBPQT^{4+}. Finally, the 1 : 1 complex formation between CBPQT^{4+} and structurally modified TTF derivatives has been investigated,[14] and it has been concluded[15] that the strength of the binding between TTF derivatives and CBPQT^{4+} is strongly dependent on the π-electron donating ability of the TTF derivatives.
¶ Beside CBPQT^{4+} being able to host TTF and its derivatives, it has very recently been demonstrated[16] that TTF can be used as an efficient template for the synthesis of CBPQT^{4+}.
‖ Based on the half-wave potentials, there is a 16 mV driving force for this reaction.†
** The nature of the potential energy surface in the vicinity of the interaction of the CBPQT^{4+} ring with the MPTTF$^+$ radical cation or MPTTF^{2+} dication is expected to be transition state-like in character. Consequently, we associate the lowest energy states with highly distorted co-conformations.
†† Several studies[5b,11–16] have shown that the complexation of CBPQT^{4+} with different TTF derivatives is around four times stronger in MeCN

than in Me$_2$CO. K_a values for the complexation of CBPQT^{4+} with MPTTF derivatives have been reported[5d] in the range 1300–4000 M^{-1} in Me$_2$CO at room temperature. Consequently K_a values at room temperature in the range 5000–16000 M^{-1}, corresponding to ΔG° values in the range of -5––6 kcal mol^{-1}, in MeCN/PhCN are expected.

1 J. F. Stoddart and H.-R. Tseng, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 4797.
2 (*a*) J. L. Segura and N. Martín, *Angew. Chem., Int. Ed.*, 2001, **40**, 1372; (*b*) G. Schukat and E. Fanghänel, *Sulfur Rep.*, 2003, **24**, 1; (*c*) J. O. Jeppesen, M. B. Nielsen and J. Becher, *Chem. Rev.*, 2004, **104**, 5115.
3 (*a*) V. Balzani, A. Credi, G. Mattersteig, O. A. Matthews, F. M. Raymo, J. F. Stoddart, M. Venturi, A. J. P. White and D. J. Williams, *J. Org. Chem.*, 2000, **65**, 1924; (*b*) C. P. Collier, G. Mattersteig, E. W. Wong, Y. Luo, K. Beverly, J. Sampaio, F. M. Raymo, J. F. Stoddart and J. R. Heath, *Science*, 2000, **289**, 1172; (*c*) M. R. Diehl, D. W. Steuerman, H.-R. Tseng, S. A. Vignon, A. Star, P. C. Celestre, J. F. Stoddart and J. R. Heath, *ChemPhysChem*, 2003, **4**, 1335; (*d*) Y.-H. Kim, S. S. Jang, Y. H. Jang and W. A. Goddard, III, *Phys. Lett. Rev.*, 2005, **94**, 156801.
4 (*a*) A. H. Flood, A. J. Peters, S. A. Vignon, D. W. Steuerman, H.-R. Tseng, S. Kang, J. R. Heath and J. F. Stoddart, *Chem.-Eur. J.*, 2004, **10**, 6558; (*b*) A. H. Flood, J. F. Stoddart, D. W. Steuerman and J. R. Heath, *Science*, 2004, **306**, 2055; (*c*) P. M. Mendes, A. H. Flood and J. F. Stoddart, *Appl. Phys. A: Solid Surf.*, 2005, **80**, 1197.
5 (*a*) Y. Luo, C. P. Collier, J. O. Jeppesen, K. A. Nielsen, E. DeIonno, G. Ho, J. Perkins, H.-R. Tseng, T. Yamamoto, J. F. Stoddart and J. R. Heath, *ChemPhysChem*, 2002, **3**, 519; (*b*) J. O. Jeppesen, K. A. Nielsen, J. Perkins, S. A. Vignon, A. DiFabio, R. Ballardini, M. T. Gandolfi, M. Venturi, V. Balzani, J. Becher and J. F. Stoddart, *Chem.-Eur. J.*, 2003, **9**, 2982; (*c*) S. Kang, S. A. Vignon, H.-R. Tseng and J. F. Stoddart, *Chem.-Eur. J.*, 2004, **10**, 2555; (*d*) J. O. Jeppesen, S. Nygaard, S. A. Vignon and J. F. Stoddart, *Eur. J. Org. Chem.*, 2005, 196; For recent examples of bistable rotaxanes based on metal–ligand bonding, see; (*e*) J.-P. Sauvage, *Chem. Commun.*, 2005, 1507; and on hydrogen-bonding, see; (*f*) A. Alteri, F. G. Gatti, E. R. Kay, D. A. Leigh, D. Martel, F. Paolucci, A. M. Z. Slawin and J. K. Y. Wong, *J. Am. Chem. Soc.*, 2003, **125**, 8644.
6 (*a*) H.-R. Tseng, D. Wu, N. X. Fang, X. Zhang and J. F. Stoddart, *ChemPhysChem*, 2004, **5**, 111; (*b*) D. W. Steuerman, H.-R. Tseng, A. J. Peters, A. H. Flood, J. O. Jeppesen, K. A. Nielsen, J. F. Stoddart and J. R. Heath, *Angew. Chem., Int. Ed.*, 2004, **43**, 6486; (*c*) T. D. Nguyen, H.-R. Tseng, P. C. Celestre, A. H. Flood, Y. Liu, J. F. Stoddart and J. I. Zink, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 10029.
7 T. J. Huang, B. Brough, C.-M. Ho, Y. Liu, A. H. Flood, P. A. Bonvallet, H.-R. Tseng, J. F. Stoddart, M. Baller and S. Magonov, *Appl. Phys. Lett.*, 2004, **85**, 5391.
8 (*a*) V. Balzani, A. Credi and M. Venturi, *Molecular Devices and Machines: A Journey into the Nanoworld*, Wiley-VCH, Weinheim, 2003; (*b*) Towards rotary molecular motors, see: R. A. van Delden, T. Mecca, C. Rosini and B. L. Feringa, *Chem.-Eur. J.*, 2004, **10**, 61; (*c*) J. V. Hernandez, E. R. Kay and D. A. Leigh, *Science*, 2004, **306**, 1532; (*d*) S. Hiraoka, K. Hirata and M. Shionoya, *Angew. Chem., Int. Ed.*, 2004, **43**, 3814; (*e*) For the kinetics of movement in surface-bound [2]rotaxanes, see: E. Katz, O. Lioubashevsky and I. Willner, *J. Am. Chem. Soc.*, 2004, **126**, 15520; (*f*) For a recent review on biological and artifical molecular machines, see: K. Kinbara and T. Aida, *Chem. Rev.*, 2005, **105**, 1377.
9 M. J. Plater, A. Aiken and G. Bourhill, *Tetrahedron*, 2002, **58**, 2405.
10 D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1991, 1584.
11 P.-L. Anelli, M. Asakawa, P. R. Ashton, R. A. Bissell, G. Clavier, R. Górski, A. E. Kaifer, S. J. Langford, G. Mattersteig, S. Menzer, D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, M. S. Tolley and D. J. Williams, *Chem.-Eur. J.*, 1997, **3**, 1113.
12 W. Devonport, M. A. Blower, M. R. Bryce and L. M. Goldenberg, *J. Org. Chem.*, 1997, **62**, 885.
13 M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, G. Mattersteig, O. Matthews, N. Montalti, N. Spencer, J. F. Stoddart and M. Venturi, *Chem.-Eur. J.*, 1997, **3**, 1992.
14 (*a*) J. Lau, M. B. Nielsen, N. Thorup, M. P. Cava and J. Becher, *Eur. J. Org. Chem.*, 1999, 3335; (*b*) M. R. Bryce, G. Cooke, F. M. A. Duclairoir and V. M. Rotello, *Tetrahedron Lett.*, 2001, **42**, 1143.
15 M. B. Nielsen, J. O. Jeppesen, J. Lau, C. Lomholt, D. Damgaard, J. P. Jacobsen, J. Becher and J. F. Stoddart, *J. Org. Chem.*, 2001, **66**, 3559.
16 G. Doddi, G. Ercolani, P. Mencarelli and A. Piermattei, *J. Org. Chem.*, 2005, **70**, 3761.