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An Acid−Base Switchable [2]Rotaxane

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A chemically addressable, bistable [2]rotaxane, which incorporates a dumbbell-shaped component containing both secondary dialkylammonium and 1,2-bis(pyridinium)ethane recognition sites for its ring component, dibenzo[24]crown-8 (DB24C8), has been assembled. ^{1}H NMR spectroscopy has demonstrated that deprotonation (and reprotonation) of the secondary dialkylammonium (dialkylamine) recognition site induces the DB24C8 ring to move away from this site to the 1,2-bis(pyridinium)ethane one (and back again) in a discrete manner, particularly when the experiment is performed in $CDCl_3$ solution.

Introduction

The relentless quest for molecular machines[1] and electronic devices[2] has turned the spotlight increasingly on rotaxanes[3] and catenanes[4] as readily available sources of actuators and switches. There is a rapidly growing need to design and construct mechanically interlocked molecules that can be switched reversibly, using chemical reagents, between two different states. The discovery[5] and development[6] of molecular shuttles has shown how a [2]rotaxane, which possesses two (or possibly more) equivalent recognition sites, becomes a prototype for the design and construction of controllable molecular switches.

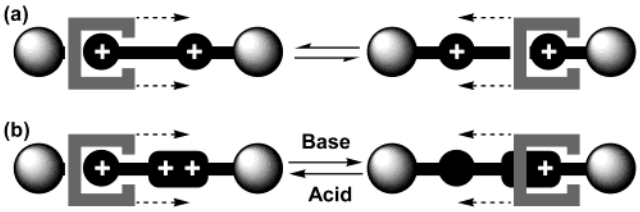

FIGURE 1. Rotaxane-based degenerate molecular shuttles (a) and switches (b). The ring trapped on the dumbbell by bulky stoppers either shuttles freely between degenerate sites or moves from site to site in a controlled manner in response to altering one of the sites by some chemical stimulus—such as treatment with either acid or base.

In degenerate molecular shuttles, it is often possible[5,6] to determine the rate of shuttling of the ring component back and forth along the dumbbell-shaped component between the two equivalent recognition sites (Figure 1a) by dynamic NMR spectroscopy. Once this kinetic information is at hand, the next obvious and logical step is to design and construct nondegenerate molecular shuttles,[7] wherein the two recognition sites are no longer equivalent. In the best case scenario, one of the two recognition sites should provide a very much better match between the ring and the dumbbell-shaped components than the other one. This is the first requirement for the development of a controllable molecular switch. The second

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requirement is having the ability to switch off the noncovalent bonding at the first (and efficient) recognition site, so that the ring will be induced to move along the rod section of the dumbbell-shaped component to the second (and much less efficient) recognition site (Figure 1b). Provided the noncovalent bonding at the first site can be reinstated easily, we have all the ingredients for the design of a simple bistable molecular switch based on a controllable molecular shuttle. The first attempts[8] at the synthesis of such a shuttle were only partially successful, insofar as shifting the thermodynamic equilibrium wholly in favor of one recognition site to give an "all-or-nothing" switch proved to be quite demanding in the beginning. For a time, the situation could be likened to being able to dim the lights in a dark room without being able to turn them off completely. Finally, however, different [2]rotaxanes have been assembled[9] in which the extent of the translational isomerism lies entirely in the direction of one of the two isomers. This is the metric that one seeks in a switch that is going to be introduced into nanomachines and electronic devices. Although proof of principle has been established, there is still an overwhelming need to research different ways and means of creating controllable molecular shuttles.

Investigations on the molecular recognition, expressed between a crown ether of at least the [24]crown-8 constitution and an NH_2^+ center on a threaded dialkylammonium ion,[10] have led to the realization that it could serve as a basis for pH-controllable molecular shuttles in situations involving competitive dual, or even multiple recognition sites. Indeed, such an "all-or-nothing" molecular switch was described[11] in the literature in 1997. It involves dibenzo[24]crown-8 (DB24C8) as the ring component and a 4,4′-bipyridinium unit as the competing recognition site in a dumbbell-shaped component, also containing an NH_2^+ center for the binding of the crown ethers.

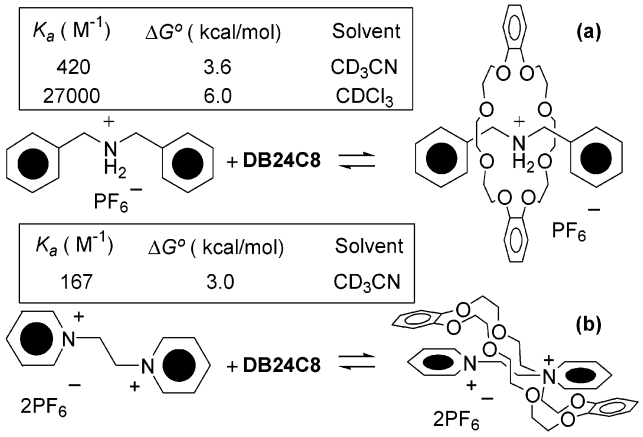

FIGURE 2. Binding studies of DB24C8 with (a) dibenzylammonium hexafluorophosphate and (b) 1,2-bis(pyridinium)-ethane.

In more recent times, however, Loeb and co-workers[12] have demonstrated that a 1,2-bis(pyridinium)ethane dication can also serve as a binding site for DB24C8, although to nothing like the same extent as does the dibenzylammonium ion. The respective binding constants[10b,12a] in CD_3CN for the two 1:1 complexes formed by the hexafluorophosphate salts and DB24C8 are 167 and 420 M^{-1}, i.e., they are different enough to warrant investigation of the competition that results when they are incorporated into the same dumbbell-shaped component of a [2]rotaxane containing a DB24C8 ring component.

In this paper, we report the template-directed synthesis of a [2]rotaxane **1**-H·3PF_6 incorporating within its dumbbell-shaped component both a dialkylammonium monocationic recognition site and a 1,2-bis(pyridinium)-ethane one for the DB24C8 ring component. Because of the modest differences in the strengths of the noncovalent bonding interactions associated with the recognition sites, the switching behavior within the [2]rotaxane might be expected to be highly sensitive to the environment, e.g., solvent and temperature. Nonetheless, in certain circumstances, the controllable [2]rotaxane acts as a good molecular switch, while in others, it starts to become less well-defined in its action, i.e., switching becomes imposed on top of shuttling.

Results and Discussion

Shuttle and Switch Design. On the basis of the K_a values[10b,12a] for the complexation processes shown in Figure 2, the difference in the free energies of complexation by DB24C8 of dibenzylammonium hexafluorophosphate and 1,2-bis(pyridinium)ethane hexafluorophosphate is 0.6 kcal mol^{-1} in favor of the former in CD_3CN at room temperature. This $\Delta\Delta G°$ value suggests that, in a molecular shuttle containing these two recognition

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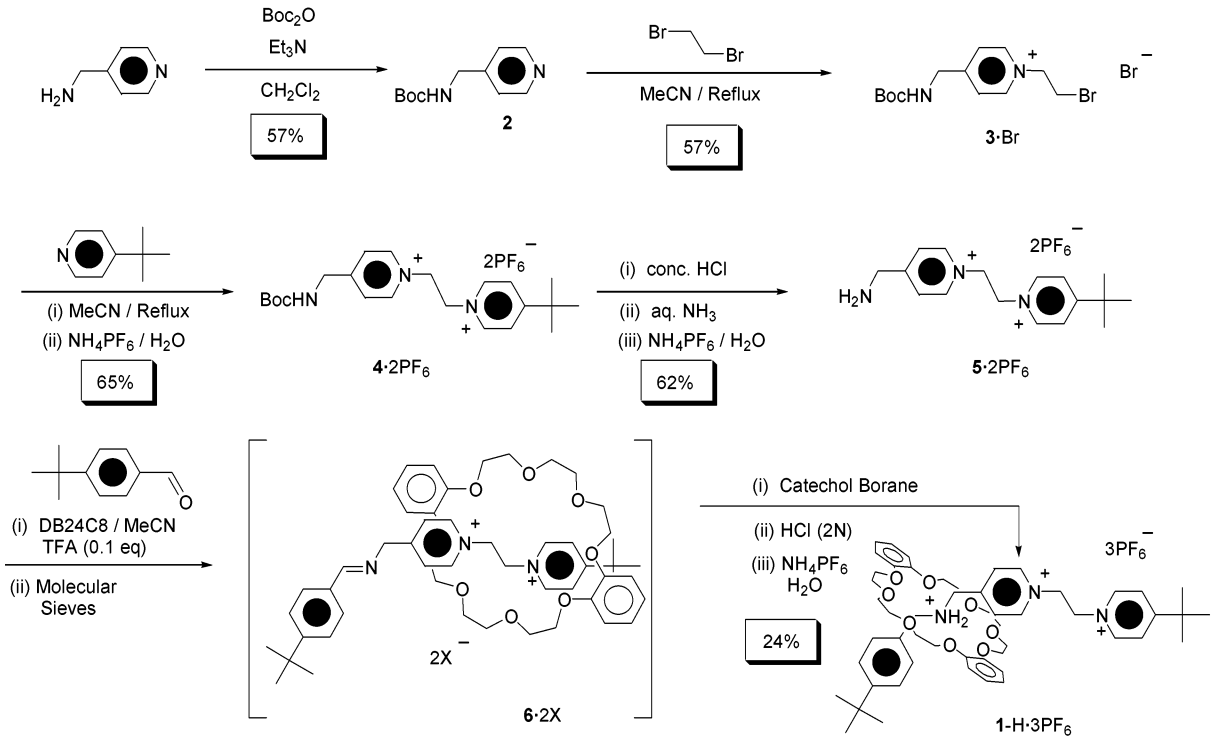
SCHEME 1. Synthesis of the Switchable [2]Rotaxane 1·3PF$_6$



motifs, the equilibrium constant for shuttling would be 2.1, i.e., for every molecule where the bis(pyridinium)-ethane site is encircled by the DB24C8 ring, there should be 2.1 times as much of the other translational isomer where the more highly favored dibenzylammonium ion center is encircled. This analysis assumes, to a first approximation, that the occupation ratio by the ring of the two sites within the dumbbell component is similar to the ratio of K_a values obtained for the two separate model 1:1 complexes. We reasoned that it might be possible to change the proportion of the two translational isomers to favor the major one even more so by exploiting both solvent and temperature effects upon the equilibrium.

Our strategy for the synthesis (Scheme 1) of the [2]-rotaxane **1**-H·3PF$_6$, which incorporates two recognition sites but only one ring, was to ensure that only one active recognition site is present at the time of the formation of the mechanical bond under template control. Thus, the 1,2-bis(pyridinium)ethane-containing derivative **5**·2PF$_6$ carries a *tert*-butyl stopper at one end and an amino function at the other. This semidumbbell can undergo imine condensation with a bulky aldehyde—of sufficient size so as to act as the second stopper for DB24C8 in a rotaxane—to form the dumbbell-shaped component of the [2]rotaxane. Since this condensation is a reversible reaction, introduction of the DB24C8 component during this step should lead to the formation of a dynamic rotaxane.[13] In principle, it should be possible to drive the reaction toward a high yield of rotaxane by removing the water formed during the reaction. When the imine found in the dynamic [2]rotaxane[14] is reduced, the mechanically interlocked molecule enters a fixed state in which the dumbbell-shaped component has a secondary amine function (not a binding site) in addition to its original 1,2-bis(pyridinium)ethane recognition site. The second NH_2^+ recognition center can then be unmasked by treating the amine with acid. This logical stepwise procedure allows the two-station [2]rotaxane to be constructed in a highly controlled manner around one recognition site, before activating the second recognition site for shuttling and switching.

Synthesis and Characterization. The implementation of the synthetic strategy, outlined above, is shown in Scheme 1 for the synthesis of the [2]rotaxane **1**-H·3PF$_6$. During the preparation of **3**·Br and **4**·2PF$_6$, the amino group of 4-aminomethylpyridine has to be protected in order to shield it from reaction with electrophiles: thus, its reaction with di-*tert*-butyl carbonate yielded the Boc-protected derivative **2**. The pyridinium salt **3**·Br was obtained by subjecting **2** to reaction with an excess of 1,2-dibromoethane. Subsequent reaction of **3**·Br with 4-*tert*-butylpyridine, followed by counterion exchange (NH_4PF_6), gave the bis(pyridinium)ethane salt **4**·2PF$_6$, which incorporates one of the two recognition sites for DB24C8. Removal of the Boc protecting group from **4**·2PF$_6$ yielded the semidumbbell **5**·2PF$_6$—a key intermediate with its one recognition site for DB24C8 and the amine functionality necessary for the dynamic formation of the [2]rotaxane. The amine **5**·2PF$_6$ was then mixed with 4-*tert*-butylbenzaldehyde in the presence of an

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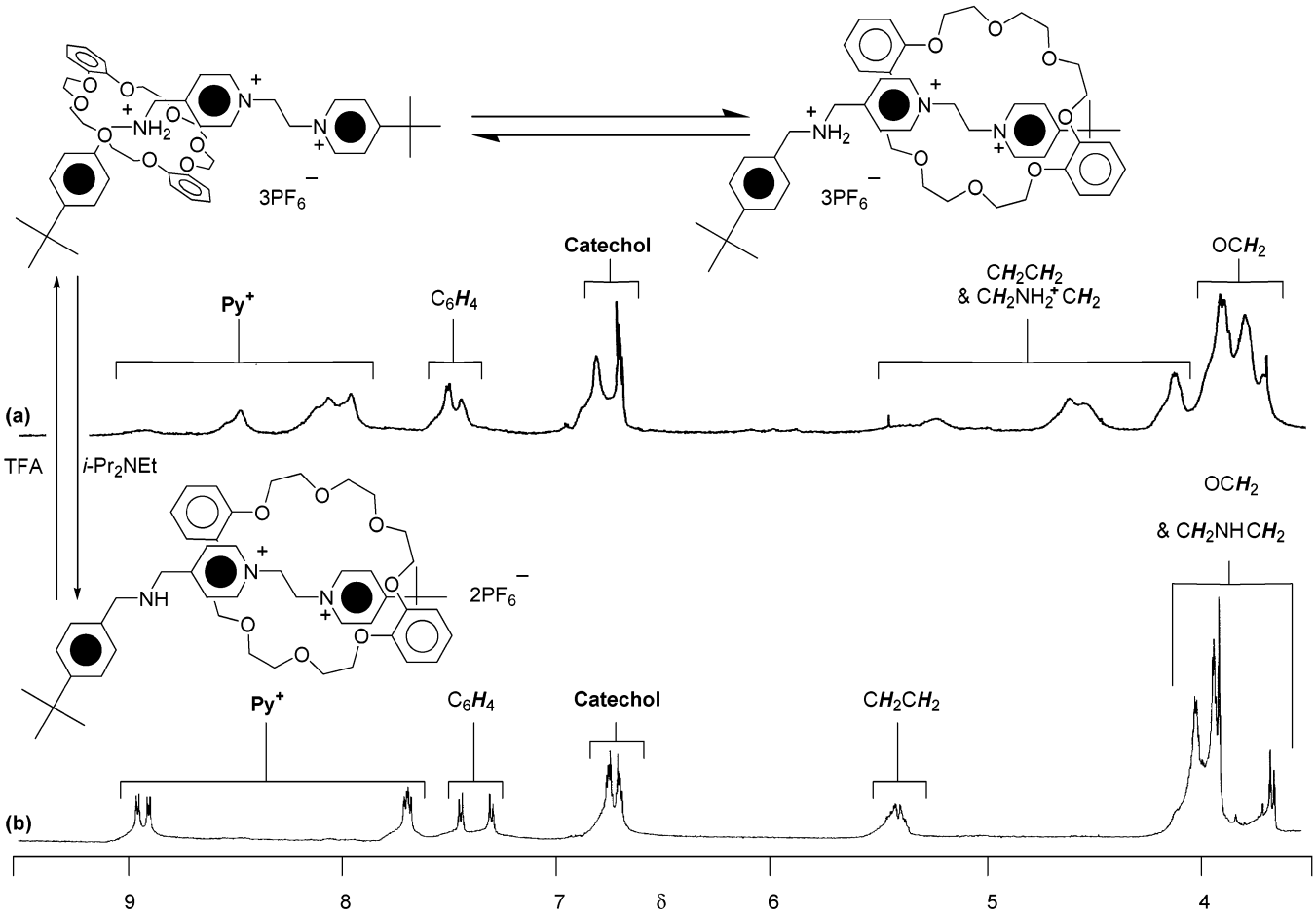

FIGURE 3. Shuttling observed in **1**-H·3PF_6 in CD_3CN (a) can be stopped by turning off the binding at the NH_2^+ site and producing **1**·2PF_6 (b). This process is followed by ^{1}H NMR spectroscopy (500 MHz, CD_3CN, 298 K).

excess of DB24C8 and a catalytic amount of trifluoroacetic acid to form the imine in CD_3CN solution to which molecular sieves were subsequently added. This dynamic reaction was followed by ^{1}H NMR spectroscopy by focusing on the relative intensities of the signals for the formyl and imine protons. When it was judged that the equilibrium had been reached between the intermediate **6**·X (where X^- is a mixture of PF_6^- and $CF_3CO_2^-$ counterions) and its starting materials (after ca. 4 h), catechol borane was added to the reaction mixture in order to reduce the imine. Subsequent acidification (HCl) of the secondary amine function created the new NH_2^+ recognition site and counterion exchange (NH_4PF_6) led to the isolation of the two-station [2]rotaxane **1**-H·3PF_6. The ^{1}H NMR spectrum of **1**-H·3PF_6 confirms the presence of both the dumbbell and ring (DB24C8) components in 1:1 proportions in agreement with its [2]rotaxane constitution, which was also supported by a singly charged peak observed at *m*/*z* 1056.3 for the [M − HPF_6] ion in its ESMS.

Shuttling. The ^{1}H NMR spectrum (Figure 3a) recorded in CD_3CN at 298 K for the [2]rotaxane **1**-H·3PF_6 is characterized by substantial line broadening, a phenomenon that would be consistent with the presence of two translational isomers undergoing slow exchange on the ^{1}H NMR time scale. This observation did not come as a surprise since we had anticipated occupancy of both the $CH_2NH_2^+CH_2$ and 1,2-bis(pyridinium)ethane recognition sites in the dumbbell component of **1**-H·3PF_6 by the DB24C8 ring component. On cooling the CD_3CN solution to 233 K, the signals became somewhat better resolved. However, an ambiguous assignment of these signals to one translational isomer — where we suspect the CH_2-$NH_2^+CH_2$ recognition site is preferentially encircled by the DB24C8 ring—or, more likely, to this isomer as the major one in admixture with a small amount of some other isomer(s) which may or may not include the other translational isomer, where the DB24C8 ring encircles the 1,2-bis(pyridinium)ethane recognition site—was not possible because of the sheer complexity of the spectrum. Accordingly, we decided to investigate the ^{1}H NMR spectum of **1**-H·3PF_6 in $CDCl_3$ solution where the interaction between the $CH_2NH_2^+CH_2$ recognition site and the DB24C8 ring is known[15] to be very much stronger[16] than when the solvent is CD_3CN. The result was the observation (Figure 4a) of a much simpler and better-resolved

(15) It is known that (ref 10a) the [2]pseudorotaxane formed between DB24C8 and dibenzylammonium hexafluorophosphate has a much higher association constant (K_a = 27 000 M^{-1}) in $CDCl_3$ than that (K_a = 420 M^{-1}) obtained in CD_3CN.

(16) The change from CD_3CN to $CDCl_3$ seems to stabilize significantly one translational isomer relative to the other. The solvent effect is apparently more marked for the $CH_2NH_2^+CH_2$ recognition site than it is for the 1,2-bis(pyridinium)ethane recognition site. This observation might find an explanation in the much stronger [N^+−H···O] hydrogen bonding that is at stake in the former recognition site compared with the weaker [C−H···O] interactions that characterize the latter recognition site.

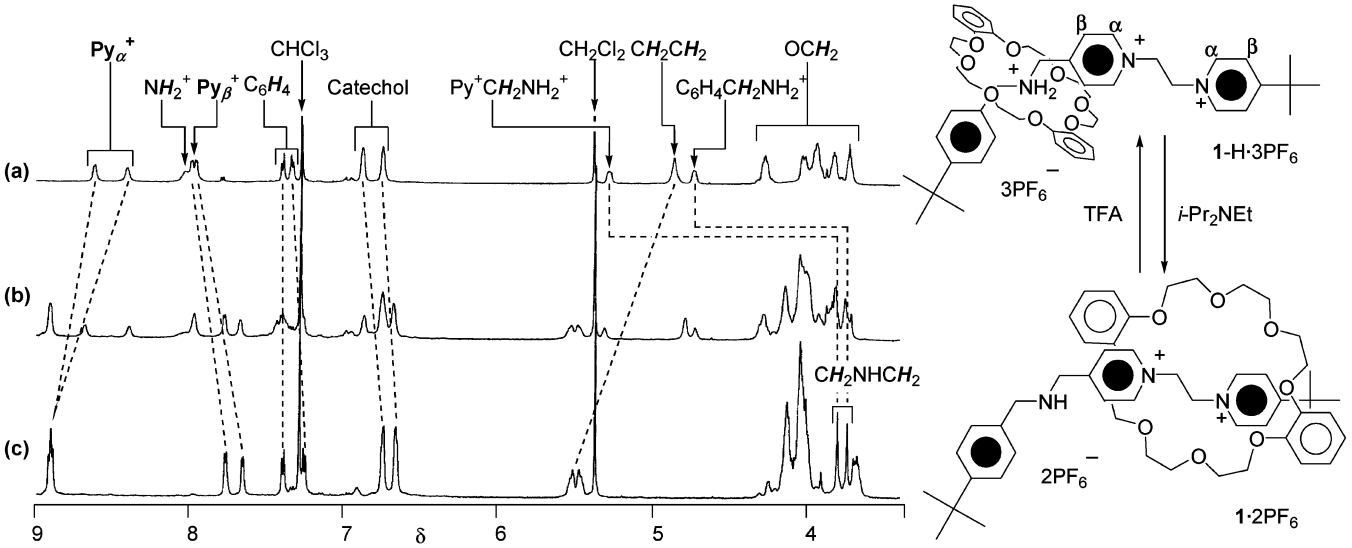

FIGURE 4. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of switching between [2]rotaxanes **1**·3PF$_6$ (a) and **1**·2PF$_6$ (c) driven by acid−base chemistry. The spectrum shown in part b represents the mixture of **1**·3PF$_6$ and **1**·2PF$_6$, observed upon incomplete deprotonation of **1**·3PF$_6$.

spectrum.[17] A key resonance in this spectrum is the multiplet centered on δ 4.63 for the protons associated with the benzylic methylene group adjacent to the NH_2^+ center. This chemical shift can be compared very favorably with that[18] of δ 4.58 for the benzylic methylene protons in dibenzylammonium hexafluorophosphate (DBA·PF$_6$) when it is complexed by DB24C8 to form the [2]-pseudorotaxane in $CDCl_3$ solution (Figure 2a). It represents an upfield shift of 0.38 ppm relative to the signal observed[18] at δ 4.20 for the corresponding protons in the free DBA·PF$_6$, which is only very sparingly soluble in $CDCl_3$. These observations, taken together, suggest very strongly that the DB24C8 ring in **1**-H·3PF$_6$ encircles the $CH_2NH_2^+CH_2$ recognition site exclusively; i.e., the [2]-rotaxane exists as only one translational isomer in $CDCl_3$ solution, making it an ideal system to switch by controlling the pH of the solution.

Switching. When the [2]rotaxane **1**-H·3PF$_6$ in $CDCl_3$ solution was treated with 0.90 molar equiv of EtN^iPr$_2$, the ^{1}H NMR spectrum (Figure 4b) indicates the presence of just more than 60% of a new compound in addition to some unreacted starting material. The addition of a further 0.60 molar equiv of EtN^iPr$_2$ resulted in complete conversion to a new compound, as indicated by the ^{1}H NMR spectrum (Figure 4c). All the spectroscopic evidence points to this compound being the [2]rotaxane **1**·2PF$_6$ in which (i) the NH_2^+ center has been deprotonated and (ii) the DB24C8 ring has migrated to the 1,2-bis(pyridinium)-ethane recognition site. The protons on the methylene groups, which are now adjacent to a secondary amine function, are shifted upfield by more than 1 ppm and resonate at δ 3.56 and 3.63. When the same base is added in $CDCl_3$ to the [2]pseudorotaxane comprising DB24C8 and DBA·PF$_6$, the corresponding *N*-methylene protons resonate at δ 3.83. The structure of **1**·2PF$_6$ in which the DB24C8 ring encircles the 1,2-bis(pyridinium)ethane recognition site is confirmed by (i) the downfield shifts of the Py$_\alpha^+$ protons from two multiplets centered on δ 8.43 and 8.65 to one centered on δ 8.92, (ii) the upfield shifts of the Py$_\beta^+$ protons from one multiplet centered on δ 7.98 to two multiplets centered on δ 7.74 and 7.64, and (iii) the downfield shifts of the bismethylene protons in the ethano linkage between the two pyridinium rings from a "tight" multiplet centered on δ 4.76 to a very broad multiplet spanning the range from δ 5.32 to 5.43. These observations are all consistent with the ^{1}H NMR spectroscopic data reported by Loeb et al.[12c] in their investigation[19] of the complexation of 1,2-bis(pyridinium)ethane dications by DB24C8. Further compelling evidence that the [2]rotaxane **1**-H·3PF$_6$ experiences migration of its DB24C8 ring from the $CH_2NH_2^+CH_2$ to the 1,2-bis-(pyridinium)ethane recognition site on deprotonation with Hunig's base comes from the fact that both **1**-H·3PF$_6$ and **1**·2PF$_6$ are clearly present (see the ^{1}H NMR spectrum in Figure 4b) as different species undergoing slow exchange on the ^{1}H NMR time scale, when insufficient base has been added to deprotonate **1**-H·3PF$_6$ completely.[20] Finally, when trifluoroacetic acid (TFA) is added to the fully deprotonated **1**·2PF$_6$, the original [2]-rotaxane **1**-H^{3+} is regenerated, indicating that the switching process is pH-controlled and completely (quantitatively) reversible.[21]

Switching of this [2]rotaxane is not a process that is observed only in a $CDCl_3$ solution. It occurs in other solvents, including CD_3CN, where the ^{1}H NMR spectrum (Figure 3b), obtained on addition of EtN^iPr$_2$, is clearly

(17) The assignment of peaks in Figure 4a was made on the basis of a TROESY NMR experiment (500 MHz, $CDCl_3$, 298 K) carried out on the [2]rotaxane **1**-H·3PF$_6$.

(18) The chemical shifts of δ 4.58 and 4.20, corresponding to the methylene protons of DBA·PF$_6$, were obtained from ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) spectra of DBA·PF$_6$ recorded in the presence and in the absence of DB24C8, respectively.

(19) Loeb et al. (ref 12c) have reported on the changes in chemical shifts of selected protons when ^{1}H NMR spectra are recorded at 298 K in CD_3CN solutions of the free 1,2-bis(pyridinium)ethane bis(hexafluorophosphate) and when it is the thread component of the [2]pseudorotaxane formed with DB24C8. On complexation, the signals for the Py$_\alpha^+$ protons are shifted downfield by 0.34 ppm while those for the Py$_\beta^+$ protons are shifted upfield by 0.33 ppm. These changes in chemical shifts are analogous to those we have observed in the switching experiment performed in $CDCl_3$ at 298 K and followed by ^{1}H NMR spectroscopy.

also that of the [2]rotaxane **1**·2PF_6. In this case, however, the switching involves a protonated [2]rotaxane **1**-H·3PF_6 that is comprised of more than one isomeric form.[22]

Conclusions

The development and construction of working molecular machinery is attracting a lot of attention in the scientific literature[1] these days. There are many reasons for this scurry of activity: one is certainly the desire to be able to turn chemical into mechanical energy at a molecular level. This paper describes how a chemically driven molecular machine has been designed—based on a switchable [2]rotaxane with two different recognition sites, one of which is pH-addressable, in its dumbbell-shaped component—and then put through its paces in solution. The bistable rotaxane described herein may be considered as a prototype of a linear motor-molecule which, with appropriate structural modifications, could be self-assembled on surfaces or self-organized as monolayers at interfaces. It is now apparent that the fabrication of such NanoChemoMechanical Systems (NCMS) can be contemplated as an obvious pathway to be followed in the further development of this particular kind of research.

Experimental Section

General. All solvents were used as purchased. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F. The plates were examined under UV light. Column chromatography was carried out using silica gel 60 F (230−400 mesh). Fast atom bombardment and electrospray mass spectra (FAB-MS and ES-MS, respectively) were obtained from a mass spectrometer. ^{1}H NMR spectra were recorded at 400 and 500 MHz with residual solvent as calibrant. ^{13}C NMR spectra were recorded at 100 and 125 MHz. The chemical shifts are expressed in ppm and the coupling constants from the ^{1}H NMR spectra are given in hertz (Hz) and are within a ca. ±0.5 Hz error range. The following abbreviations are used to explain the multiplicities: s, singlet; br s, broad singlet; d, doublet; t, triplet; m, multiplet.

4-(*tert*-Butyloxycarbonylaminomethyl)pyridine (2). Di-*tert*-butyl dicarbonate (9.00 g, 42 mmol) was added to a solution of 4-aminomethylpyridine (4.54 g, 42 mmol) and Et_3N (10.12 g, 100 mmol) in CH_2Cl_2 (340 mL) and the reaction mixture was stirred for 20 h at ambient temperature. After evaporation of the solvent, the residue was subjected to column chromatography (SiO_2; EtOAc/hexanes, 7:3), and the product was obtained as a white solid (6.98 g, 80%). Mp 89−90 °C; ^{1}H NMR (500 MHz, CD_3CN, 298 K) δ 1.45 (s, 9H), 4.25 (d, J = 6 Hz, 2H), 5.94 (br s, 1H), 7.24 (d, J = 6 Hz, 2H), 8.51 (d, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, CD_3CN, 298 K) δ 28.6, 43.7, 45.2, 79.7, 122.3, 150.2, 150.5, 157.2; HR-MS (FAB) $C_{11}H_{16}N_2O_2$ [**2**-H]$^+$ calcd m/z 209.1290, found m/z 209.1289.

1-(2-Bromoethyl)-4-(*tert*-butyloxycarbonylaminomethyl)pyridinium Bromide (3·Br). A solution of 1,2-dibromoethane (4.14 mL, 48 mmol) and **2** (1.00 g, 4.8 mmol) in MeCN (60 mL) was heated under reflux for 25 h. Upon evaporation of the solvent, the residue was subjected to column chromatography (SiO_2; MeCN/3 g/L NH_4Cl in MeOH, 95:5), and the product was isolated as a white foam (1.07 g, 57%): ^{1}H NMR (500 MHz, CD_3CN, 298 K) δ 1.42 (s, 9H), 3.90 (t, J = 6 Hz, 2H), 4.48 (d, J = 6 Hz, 2H), 4.86 (t, J = 6 Hz, 2H), 6.05 (br s, 1H), 7.91 (d, J = 6 Hz, 2H), 8.59 (d, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, CD_3CN, 298 K) δ 28.6, 31.7, 44.4, 62.3, 80.8, 126.7, 145.7, 157.8, 163.1; HR-MS (MALDI) $C_{13}H_{20}N_2O_2Br$ [**3**]$^+$ calcd m/z 315.0712, found m/z 315.07027.

Boc-Protected Semidumbbell 4·2PF_6. The following procedure was derived from a literature[23] method. A solution of 4-*tert*-butylpyridine (0.128 mL, 0.87 mmol) and **3**·Br (0.140 g, 0.37 mmol) in MeCN (5.0 mL) was heated under reflux for 3 d. Upon evaporation of the solvent, the residue was subjected to column chromatography (SiO_2; MeCN/3 g/L NH_4Cl in MeOH, 9:1). A pale-yellow solid was isolated, which was dissolved in H_2O (15 mL) and treated with NH_4PF_6 (0.60 g, 3.7 mmol). The pale-yellow solid that precipitated was collected by filtration and dried under high vacuum to yield **4**·2PF_6 (160 mg, 65%): ^{1}H NMR (500 MHz, CD_3CN, 298 K) δ 1.39 (s, 9H), 1.43 (s, 9H), 4.48 (d, J = 6 Hz, 2H), 4.95 (m, 4H), 6.06 (br s, 1H), 7.91 (d, J = 6 Hz, 2H), 8.04 (d, J = 6 Hz, 2H), 8.46 (d, J = 6 Hz, 2H), 8.48 (d, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, CD_3CN, 298 K) δ 27.4, 28.8, 58.6, 58.9, 126.0, 126.4, 144.0, 144.3, 174.0, 174.9; HR-MS (FAB) $C_{22}H_{33}N_3O_2PF_6$ [**4**·PF_6]$^+$ calcd m/z 516.2215, found m/z 516.2201.

Semidumbbell 5·2PF_6. Compound **4**·2PF_6 (330 mg, 0.50 mmol) was dissolved in concentrated HCl (2.0 mL) and stirred for 15 min. Aqueous NH_3 was then added slowly until the solution became blue at neutral pH. At this point, NH_4PF_6 (0.60 g, 3.7 mmol) was added and the blue solid that precipitated was collected by filtration and dried under high vacuum to yield the semidumbbell **5**·2PF_6 (238 mg, 85%): ^{1}H NMR (500 MHz, CD_3CN, 298 K) δ 1.39 (s, 9H), 4.19 (s, 2H), 4.99 (m, 4H), 8.06 (m, 4H), 8.45 (d, J = 6 Hz, 2H), 8.49 (d, J = 6 Hz, 2H); ^{13}C NMR (125 MHz, CD_3CN, 298 K) δ 29.9, 37.6, 45.5, 59.9, 60.1, 127.2, 127.7, 145.0, 145.1, 167.6, 174.2; HR-MS (MALDI) $C_{17}H_{24}N_3$ [**5**]$^+$ calcd m/z 270.1976, found m/z 270.1965.

[2]Rotaxane 1-H·3PF_6. Dibenzo[24]crown-8 (0.210 g, 0.47 mmol) was dissolved in a solution of semidumbbell **5**·2PF_6 (33 mg, 0.047 mmol) and trifluoroacetic acid (0.005 mmol) in CD_3CN (1.0 mL). 4-*tert*-Butylbenzaldehyde (0.008 mL, 0.047 mmol) was added and the reaction mixture was stirred for 4 h, before being treated with catechol borane (0.05 mL, 0.47 mmol). The solution was stirred for 5 min before being treated with 2 M HCl (0.1 mL). The solvents were evaporated and the residue was subjected to column chromatography (SiO_2; EtOAc/MeOH, 9:1, then Me_2CO/MeOH/2M aq NH_4Cl/$MeNO_2$, 80:17:2:1). A pale-yellow solid was isolated that was then dissolved in H_2O (15 mL) and treated with NH_4PF_6 (0.60 g, 3.7 mmol). A pale-yellow solid precipitated, which was collected by filtration and dried under high vacuum to yield the [2]rotaxane **1**-H·3PF_6 (14 mg, 24%): ^{1}H NMR (500 MHz, CD_3Cl, 298 K) δ 1.29 (s, 9H), 1.40 (s, 9H), 3.55−4.20 (m, 24H), 4.63 (m, 2H), 4.76 (br s, 8H), 5.20 (m, 2H), 6.71 (m, 4H), 6.85 (m, 4H), 7. 32 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.96−8.00 (m, 4H), 8.04 (br s, 2H), 8.44 (m, 2H), 8.65 (m, 2H). HR-MS (ES) $C_{52}H_{71}N_3O_8$ [**1**]$^{2+}$ calcd m/z 432.7621, found m/z 432.7623. (Running this experiment on a larger scale (without monitoring it by ^{1}H NMR) resulted in drastically diminished yields.)

(20) A control experiment was performed on a sample of the free dumbbell-shaped compound, obtained in 41% yield by reacting **5**·2PF_6 with *p-tert*-butylbenzaldehyde, followed by reduction with catechol borane, protonation with HCl, and counterion exchange (NH_4PF_6/H_2O). Addition of base to this compound caused deprotonation and migration of the methylene peaks upfield: addition of acid caused them to move downfield again. However, in contrast with the [2]rotaxane, the exchange between the protonated and deprotonated species was fast on the ^{1}H NMR time scale, and at no point were separate peaks observed for protonated and deprotonated species. (The latter experiment was performed in CD_3CN because the hexafluorophosphate salt of the dumbbell-shaped compound was not soluble in $CDCl_3$.)

(21) The resulting spectrum was ever so slightly different from that shown in Figure 4a, presumably because the counterions are now a mixture of PF_6^- and $CF_3CO_2^-$.

(22) Unlike the protonated [2]rotaxane **1**-H·3PF_6, which is capable of undergoing some shuttling action in CD_3CN, the deprotonated [2]-rotaxane **1**·2PF_6 is only capable of existing as one translational isomer and so it gives a sharp, well-resolved ^{1}H NMR spectrum as shown in Figure 3b.

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Supporting Information Available: Selected ^{1}H and ^{13}C NMR and mass spectra of **2**, **3**·Br, **4**·$2PF_6$, **5**·$2PF_6$, and **1**-H·$3PF_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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