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Using Oppositely Charged Ions To Operate a Three-Station [2]Rotaxane in Two Different Switching Modes

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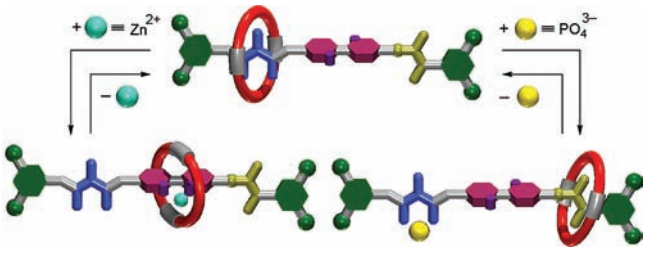
ABSTRACT



A [2]rotaxane undergoes switching of its bis-*p*-xylyl-[26]crown-6 (BPX26C6) component away from its guanidinium station toward its 2,2′-bipyridyl and carbamate stations upon the addition and removal of Zn^{2+} and PO_4^{3-} ions, respectively.

The development of new methods and protocols for the operation of rotaxane-type molecular switches and actuators has attracted much attention because such systems have potential applicability in sensing,[1] organogelation,[2] drug delivery,[3] fluid transportation,[4] and molecular memory.[5] For molecular switches that are operated chemically, the external stimuli are frequently cationic species (e.g., metal ions, protons)[6] because the ion−dipole and/or hydrogen bonding interactions introduced by these additives can be sufficiently strong to invert the interlocked macrocyclic unit's preference for the binding sites. In contrast, anion-controllable interlocked molecular switches are relatively rare[7] because the larger sizes, unique shapes, and higher solvation energies of anions in solution, relative to cations, complicate the molecular design for the recognition process. Although simultaneous recognition of cations and anions in a macrocyclic host is possible,[8] it remains a challenge to operate interlocked molecular switches in different switching modes through the application of ions of opposite charges. In theory, such a dual-mode molecular switch could be constructed by adding two more recognition stations to the thread component of a [2]rotaxane, allowing the interlocked macrocyclic moiety to migrate specifically in the presence of a particular charged species (see abstract image);

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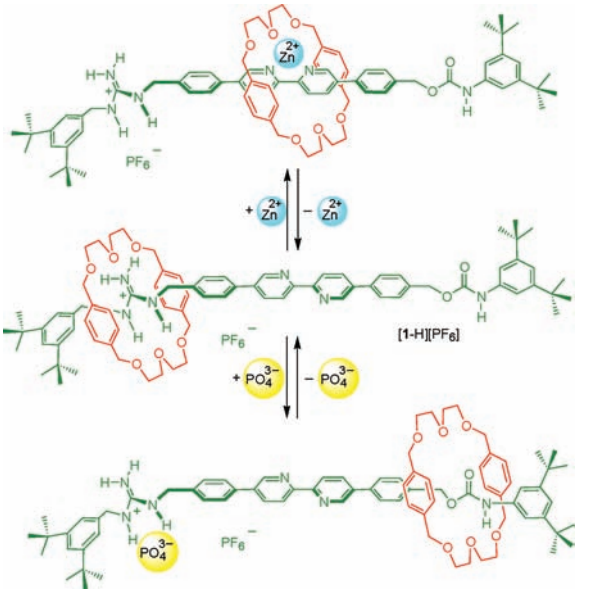
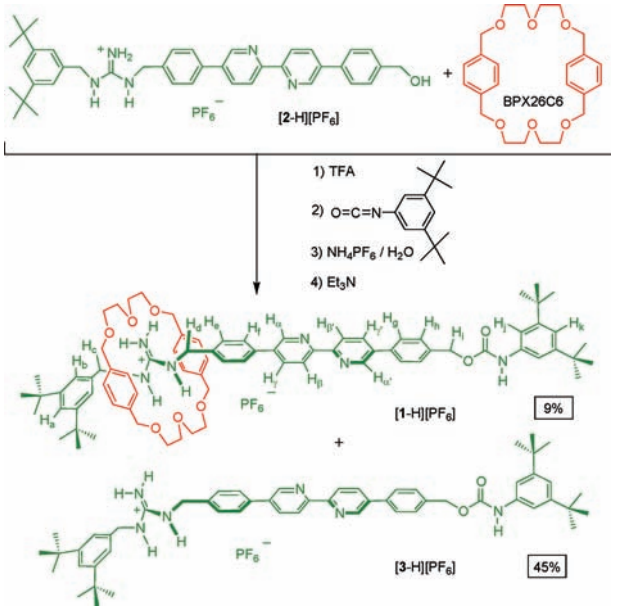
because these ions cannot be added to the solution without complementary counterions, however, fine-tuning of the energetics would be required to maintain the orthogonality of the two operating modes. Herein, we report a three-station [2]rotaxane in which 2,2′-bipyridyl and carbamate units serve as additional recognition stations that allow the bis-*p*-xylyl-[26]crown-6 (BPX26C6)[9] component to migrate away from its originally occupied guanidinium station upon the addition and removal of Zn^{2+} and PO_4^{3-} ions, respectively.

To ensure solubility of the necessary salts, the desired molecular switch would have to be operated in a quite polar solvent (e.g., CH_3CN) or a mixture with a less polar one (e.g., $CHCl_3$, CH_2Cl_2). Because the affinities of these charged species to their binding sites in the [2]rotaxane would be significantly weakened through high solvation in polar solvents, the binding affinity of the macrocyclic component to the original recognition station should not be too strong under such conditions to ensure facile ion-driven switching. Thus, we selected the guanidinium ion, which is also solvated well in more polar solvents but capable of threading through BPX26C6 in CH_2Cl_2,[7g] as a recognition site for assembling the molecular switch. A readily accessible monopyridinium ion would not be a suitable secondary station for the anion-mediated switching process because its binding affinity to BPX26C6 is higher than that of a guanidinium ion in CD_3CN.[7g] Therefore, we chose a carbamate unit as the second station, with the expectation that [N−H···O] hydrogen binding of its NH proton to the oxygen atoms of BPX26C6 and its weaker interaction with anions, relative to that of the guanidinium ion, would allow it to host the macrocycle in the presence of competing anions in solution. In a previous study, we found that the interlocked BPX26C6 macrocyclic moiety and the 2,2′-bipyridyl unit of the thread component of a [2]rotaxane can interact orthogonally to induce the recognition of specific metal ions, thereby providing a ^{1}H NMR spectroscopic probe for the simultaneous identification of physiologically important metal ions in a solution mixture.[10] It seemed reasonable to expect that the interlocked BPX26C6 component might move to the 2,2′-bipyridyl station from the guanidinium station if we were to introduce suitable metal ions into the solution.

Scheme 1



Scheme 2



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Taking all of these factors into consideration, we designed the [2]rotaxane **1**-H·PF_6—featuring guanidinium, bipyridyl, and carbamate units as three stations for the interlocked BPX26C6 component—as a dual cation/anion-operated molecular switch (Scheme 1).

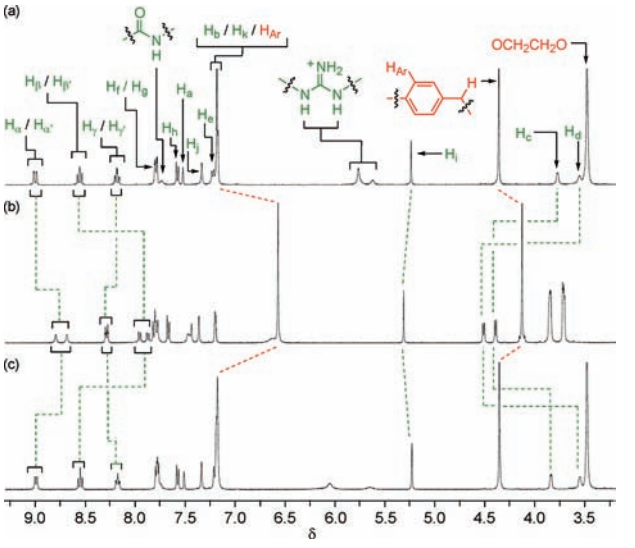

Figure 1. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of (a) the [2]rotaxane **1**-H·PF_6, (b) the mixture obtained after adding TFA (2 equiv) to the solution in (a), and (c) the mixture obtained after adding Et_3N (3 equiv) to the solution in (b).

We synthesized the threadlike guanidinium salt **2**-H·PF_6 in nine steps from 5,5′-dibromo-[2,2′]bipyridyl (see the Supporting Information (SI)). Because the protonated form of 2,2′-bipyridyl can also form complexes with BPX26C6, thereby increasing the efficiency of the assembly of the [2]rotaxane,[9d,10] we reacted the macrocycle BPX26C6, 1-isocyanato-3,5-di-*tert*-butylbenzene,[2b,7d] and the threadlike guanidinium salt **2**-H·PF_6 under acidic conditions, followed by ion exchange and neutralization of the (presumably) protonated 2,2′-bipyridyl station, to afford the desired [2]rotaxane **1**-H·PF_6 and its corresponding dumbbell-shaped threadlike salt **3**-H·PF_6 in 9% and 45% yields, respectively (Scheme 2).

Because BPX26C6 can form complexes with protonated 2,2′-bipyridyl units, we suspected that the [2]rotaxane **1**-H·PF_6 would function as an acid/base-controllable molecular switch. After the addition of 2 equiv of trifluoroacetic acid (TFA) to a CD_3CN solution of the [2]rotaxane, the ^{1}H NMR spectrum revealed significant upfield and downfield shifts of the signal of the xylene protons (H_{Ar}) of BPX26C6 and of the signals of the methylene groups adjacent to the guanidinium ion (H_c, H_d), respectively, suggesting that the macrocycle BPX26C6 had moved away from the guanidinium station to stack with the aromatic motifs of the bipyridyl unit of the threadlike component. A comparison of the signals of the bipyridinium protons in the [2]rotaxane with those in the dumbbell-shaped salt **3**-H·PF_6 in the presence of TFA revealed a more significant upfield shift for the former sample, consistent with the BPX26C6 component residing at the bipyridinium station under these conditions (see the SI). The presence of cross peaks for the signals of the aromatic (H_{Ar}) and diethylene glycol protons of BPX26C6 with the signals for the bipyridinium protons (H_α, $H_{\alpha'}$, H_β) in the 2D NOSY spectrum of a 2:1 mixture of TFA and the [2]rotaxane **1**-H·PF_6 (see the SI) confirmed the encircling of the macrocyclic component around the bipyridinium station under these conditions. The addition of Et_3N (3 equiv) to the solution of the [2]rotaxane **1**-H·PF_6 and TFA resulted in a ^{1}H NMR spectrum (Figure 1c) similar to that of the original (untreated) [2]rotaxane **1**-H·PF_6 (Figure 1a), suggesting that the BPX26C6 unit had moved back to encircle the guanidinium ion. Thus, the [2]rotaxane **1**-H·PF_6 can be operated as an acid/base-controllable molecular switch, in which the interlocked BPX26C6 component can be positioned selectively at the bipyridyl and guanidinium stations through sequential additions of TFA and Et_3N, respectively.

After having proven that the interlocked BPX26C6 unit in the [2]rotaxane **1**-H·PF_6 could be moved from the guanidinium ion to the 2,2′-bipyridyl station through the addition of protons, we suspected that a similar migration would also be possible when driven by the addition of appropriate metal ions. Figure 2 reveals that the addition of $Zn(ClO_4)_2$ to a solution of the [2]rotaxane **1**-H·PF_6 led to significant migrations of the signals in the ^{1}H NMR spectrum. The shifts of the signals of the xylene units (H_{Ar}) of the interlocked BPX26C6 component and of the methylene groups adjacent to the guanidinium ion (H_c, H_d) for **1**-H·PF_6 in the presence of Zn^{2+} ions were similar to those obtained above after adding TFA to the [2]rotaxane, implying that the interlocked BPX26C6 moiety had again migrated to the bipyridyl station. The appearance of cross peaks between the signals of the aromatic protons (H_{Ar}) of the BPX26C6 unit and the signals of the bipyridyl protons (H_α, $H_{\alpha'}$) in the 2D NOSY spectrum of a mixture of the [2]rotaxane **1**-H·PF_6 and $Zn(ClO_4)_2$ (see the SI) was consistent with the BPX26C6 component encircling the bipyridyl station under these conditions. The signals of the protons of the [2]rotaxane **1**-H·PF_6 shifted back (Figure 2c) to their original positions [i.e., prior to the addition of $Zn(ClO_4)_2$] after the introduction of 1 equiv of *N*,*N*,*N*′,*N*′-tetrakis-(2-pyridylmethyl)ethylenediamine (TPEN), a tight sequestering agent for Zn^{2+} ions,[11] suggesting that the BPX26C6 moiety had returned to encircle the guanidinium ion after removing the complexed metal ion. Thus, the [2]rotaxane **1**-H·PF_6 can be switched not only through pH control but also through metal ion control, with the interlocked BPX26C6 component residing at the bipyridyl and guanidinium stations upon the addition and removal of Zn^{2+} ions, respectively.

Having demonstrated that the migration of the BPX-26C6 unit between the guanidinium and bipyridyl stations in the [2]rotaxane **1**-H·PF_6 could be controlled using either H^+ or Zn^{2+} cations, we turned our attention to the

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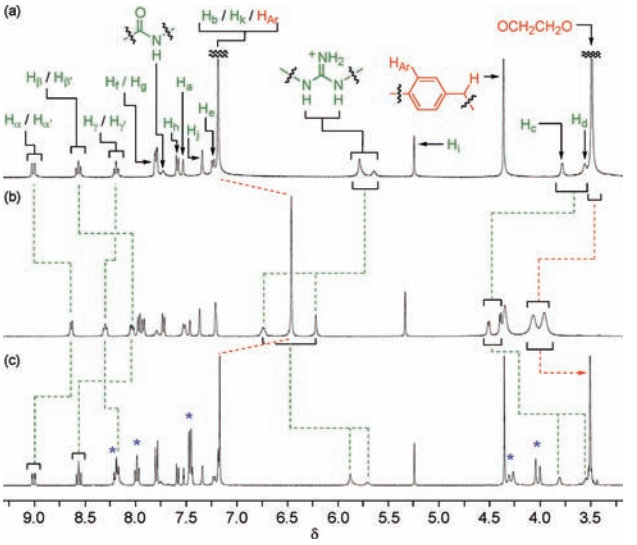

Figure 2. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of (a) the [2]rotaxane **1**-H·PF_6, (b) the mixture obtained after adding $Zn(ClO_4)_2$ (1 equiv) to the solution in (a), and (c) the mixture obtained after adding TPEN (1 equiv) to the solution in (b). Asterisks: Signals from Zn^{2+}-complexed TPEN.

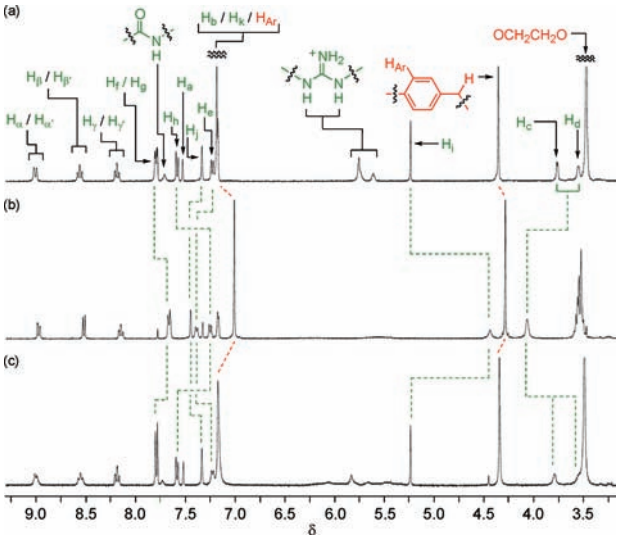

Figure 3. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of (a) the [2]rotaxane **1**-H·PF_6, (b) the mixture obtained after adding $(TBA)_3PO_4$ (2 equiv) to the solution in (a), and (c) the mixture obtained after adding $Ba(ClO_4)_2$ (3 equiv) to the solution in (b).

anion-mediated switching of this system. We suspected that **1**-H·PF_6 would function as an anion-controllable molecular switch, with the interlocked BPX26C6 component migrating between the guanidinium and carbamate stations, if a tightly binding anion were to be introduced to compete with the macrocycle for the guanidinium station (Scheme 1). The singly charged anions Cl^-, F^-, Br^-, and OAc^- failed to provide clean and clear switching in the operation of the [2]rotaxane **1**-H·PF_6, presumably because these anions and the guanidinium ion were highly solvated in the polar solvent, thereby weakening their interactions. Because highly charged anionic species complex more tightly with guanidinium-based anion receptors through stronger electrostatic interactions,[12] we suspected that the PO_4^{3-} anion might, unlike the tested monovalent anions, be capable of displacing the interlocked BPX26C6 unit to reside at the carbamate station. The addition of $(TBA)_3PO_4$ (2 equiv) to a CD_3CN solution of the [2]rotaxane **1**-H·PF_6 resulted in a ^{1}H NMR spectrum revealing the clean and clear migration of the macrocyclic component (Figure 3b). We used 2D COSY and NOSY spectra to identify the signals of the [2]rotaxane **1**-H·PF_6 before and after the addition of $(TBA)_3PO_4$. The negligible shifts of the signals of the 2,2′-bipyridyl unit in the ^{1}H NMR spectra suggested that it was not involved in the complexation of the BPX26C6 moiety under these conditions. The significant upfield and downfield shifts of the benzylic protons adjacent to the carbamate (H_i) and guanidinium (H_c, H_d) stations, respectively, in the ^{1}H NMR spectrum, together with the cross signals between the protons near the carbamate units (H_j, H_h, H_i) and those of the ethylene glycol loops of the BPX26C6 component in the 2D NOSY spectrum, suggested that the macrocycle resided on the carbamate station after the addition of $(TBA)_3PO_4$. Addition of $Ba(ClO_4)_2$ (3 equiv) to this mixture removed the PO_4^{3-} anions from the solution by forming a precipitate of the less-soluble $Ba_3(PO_4)_2$; accordingly, the macrocycle reverted to its original guanidinium station, as evidenced by the restoration of the signals in the ^{1}H NMR spectrum back to their original positions prior to the addition of the PO_4^{3-} anions (Figure 3c). Thus, the [2]rotaxane **1**-H·PF_6 also functions as an anion-controllable molecular switch, with the interlocked macrocycle itinerating between the carbamate and guanidinium stations through the simple addition and removal of PO_4^{3-} anions.

We have constructed a three-station [2]rotaxane in which the macrocyclic component can migrate not only between the guanidinium and 2,2′-bipyridyl stations of the threadlike unit through the addition and removal of suitable cations (H^+, Zn^{2+}) but also between the guanidinium and carbamate motifs through the addition and removal of PO_4^{3-} anions. We believe that such dual-mode molecular switches, which can be controlled orthogonally through the application of oppositely charged ions, will aid in the development of complicated molecular actuators and sensors for specific ion pairs.

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Supporting Information Available. Synthetic procedures and characterization data for the [2]rotaxane **1**-H·PF_6. This material is available free of charge via the Internet at http://pubs.acs.org

The authors declare no competing financial interest.

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