A switchable macrocycle–clip complex that functions as a NOR logic gate†

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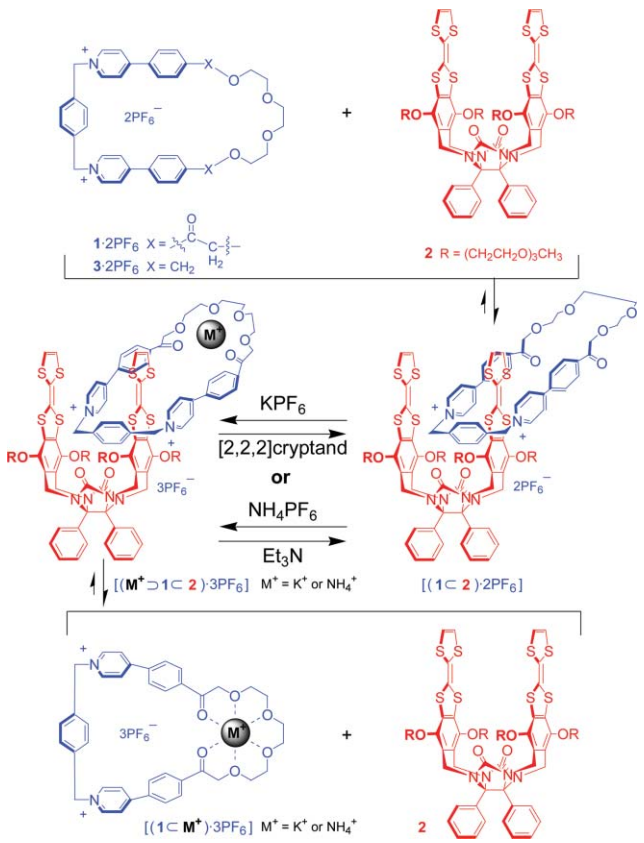
We have synthesized a new molecular switch—based on a macrocycle–clip complex—whose switching behavior not only can be controlled through the use of either K^+–[2,2,2]cryptand or NH_4^+–Et_3N systems but also provides color changes that are visible to the naked eye; consequently, this system operates as a two-input NOR functioning molecular logic gate.

Although many elegant pseudorotaxane-like[1] molecular switches[2] have been developed in recent years, the number of recognition motifs that can be exploited for the preparation of these complexes remains limited because of structural complexity and/or weak intermolecular interactions. Thus, we became interested in preparing new supramolecular assemblies by taking advantage of the increased binding affinities that clip-shaped guest molecules exert toward their macrocyclic hosts. Although many molecular tweezers[3] and clips[4] have been prepared as effective synthetic receptors, there are only a few examples of molecular clips that form complexes with macrocycles;[5] of these macrocycle–clip complexes, we are unaware of any that can be switched between their threaded and unthreaded states by the application of external stimuli.[6] The addition and removal of metal ions[6b,7] and protons[6b,8] are efficient methods for switching supramolecular systems between different states; such systems that can be switched in two different ways and exhibit detectable gains or losses of the optical signals of their different states may be considered as molecular logic gates.[9] In this paper, we report a new molecular switch—based on a macrocycle–clip complex—whose switching behavior not only can be controlled through the use of either K^+–[2,2,2]cryptand or NH_4^+–Et_3N systems but also provides color changes that are visible to the naked eye; consequently, this system operates as a two-input NOR[10] functioning molecular logic gate.

We synthesized macrocycle **1**·$2PF_6$ in five steps from 2,4′-dibromoacetophenone. The structure of **1**·$2PF_6$ is reminiscent of a combination of a ring-expanded [18]crown-6 (18C6) unit—which we expected to bind to alkali metal ions—and a π-electron-deficient aromatic system, which we expected would bind π-electron-rich units, such as tetrathiafulvalene (TTF) (Scheme 1). Because of its flexible molecular structure, relative to those of 18C6 itself and other effective cyclophane-based π-electron acceptors,[11] we expected that **1**·$2PF_6$ would have quite low affinities for both alkali metal ions and π-electron-rich aromatic rings. Thus, we synthesized the glycoluril-based compound **2** in which two TTF molecules are positioned parallel to each other as the side walls of a molecular clip. We anticipated that the complementary electronic nature of the TTF and pyridinium motifs, the good separation (6.7 Å) for π-stacking of a pyridinium moiety between the two parallel aromatic side walls of the glycoluril-based molecular clip, and π-stacking interactions between the non-threaded "*exo*" TTF arm of clip **2** and the pyridinium rings of the macrocycle **1**·$2PF_6$ would all assist molecular clip **2** to complex with **1**·$2PF_6$ with reasonable affinity. The four triethylene glycol chains of clip **2** are present not only to increase its solubility but also to allow [C–H···O] hydrogen bonds to form between the pyridinium α-protons and the oxygen atoms of these triethylene glycol side chains, which are interactions that may partially decrease the free energy of binding during the complexation process.

Although clip **2** is only moderately soluble in MeCN, the addition of macrocycle **1**·$2PF_6$ to the solution helped to dissolve any remaining insoluble clip **2**; more interestingly, this process



Scheme 1 Schematic representation of the complexation and switching behavior of the macrocycle–clip complex.

† Electronic supplementary information (ESI) available: Experimental procedures for the preparation of **1**·$2PF_6$, **2**, and **3**·$2PF_6$ and their characterization data. See http://www.rsc.org/suppdata/cc/b4/b417823h/

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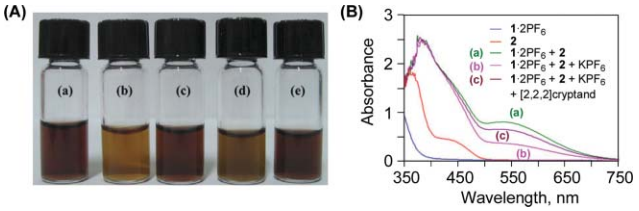

Fig. 1 (A) A photograph depicting the color changes (MeCN, 3 mM, 298 K) that occur in the switching process and (B) the corresponding partial UV-vis spectra (MeCN, 1.5 mM, 298 K) of (a) an equimolar mixture of **1**·2PF$_6$ and **2**; (b) the mixture obtained after adding KPF$_6$ (20 equiv.) to solution (a); (c) the mixture obtained after adding [2,2,2]cryptand (20 equiv.) to solution (b); (d) the mixture obtained after adding NH_4PF_6 (20 equiv.) to solution (a); (e) the mixture obtained after adding Et_3N (20 equiv.) to solution (d).

immediately changed the color of the solution from light-yellow to puce (Fig. 1A-a). The UV spectrum of the complex formed between **1**·2PF$_6$ and **2** in MeCN (Fig. 1B-a) displays a charge transfer band at 533 nm, which suggests the formation of the macrocycle–clip complex [(**1**⊂**2**)·2PF$_6$]. A Job plot based on this absorption in MeCN affords conclusive evidence for 1 : 1 complexation (see supporting information†). From a ^{1}H NMR spectroscopic dilution experiment, we determined the binding constant between macrocycle **1**·2PF$_6$ and molecular clip **2** in CD_3CN to be 4900 ± 180 M^{-1}.[12] Adding 20 equiv. of potassium hexafluorophosphate (KPF$_6$) to the puce solution of a mixture of **1**·2PF$_6$ and **2** in MeCN switched the color of the solution back to its original yellow hue (Fig. 1A-b). The significant decrease in the intensity of the charge transfer band in the UV-vis spectrum (Fig. 1B-b) and the appearance of the characteristic absorptions of the free clip **2** (Fig. 2b) in the ^{1}H NMR spectrum both suggest that dissociation of the complex [(**1**⊂**2**)·2PF$_6$] occurred. The macrocycle **3**·2PF$_6$, whose structure differs from that of **1**·2PF$_6$ by the absence of the carbonyl groups, also generates a puce solution when mixed with clip **2**, but the color of the solution of [(**3**⊂**2**)·2PF$_6$] did not switch back to light yellow upon adding an

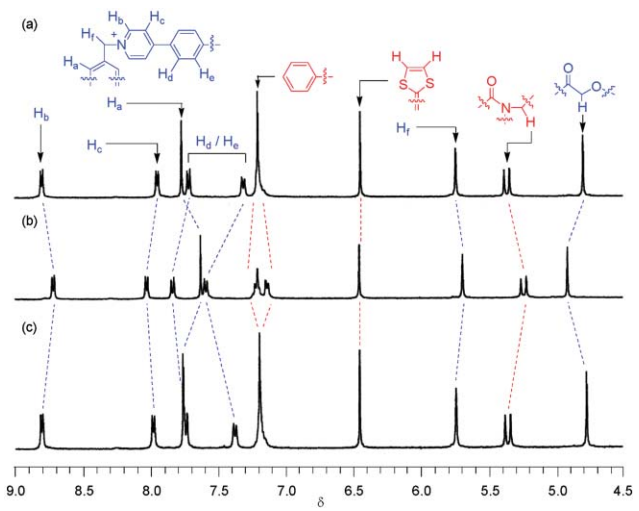

Fig. 2 Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of (a) a mixture of **1**·2PF$_6$ and **2** (10 mM each); (b) the mixture obtained after adding KPF$_6$ (20 equiv.) to the solution in (a); and (c) the mixture obtained after adding [2,2,2]cryptand (20 equiv.) to the solution in (b).

excess amount of KPF$_6$. This observation suggests that the 18C6-like motif of macrocycle **1**·2PF$_6$ is likely to be the one that recognizes the K^+ ions; the conformational changes that this binding event causes the aromatic units of macrocycle **1**·2PF$_6$ to undergo may be the source of the negative allosteric effect.[13]

To remove the complexed K^+ ions from macrocycle **1**·2PF$_6$, we added an excess of a very strong binder, [2,2,2]cryptand, to the solution. As we anticipated, the puce color of the solution returned instantly (Fig. 1A-c) upon the addition of [2,2,2]cryptand. The ^{1}H NMR spectrum (Fig. 2c) of this mixture appears to be similar to that of the original solution of macrocycle **1**·2PF$_6$ and clip **2** (Fig. 2a); this observation implies that the original [(**1**⊂**2**)·2PF$_6$] complex has regenerated in the solution. This threading–unthreading process can be repeated several times by adding excess amounts of K^+ ion and [2,2,2]cryptand sequentially; the reversible color changes allow us to monitor the switching process by the naked eye.

Alternatively, this [2]pseudorotaxane-like macrocycle–clip molecular switch can be switched by the sequential addition of NH_4^+ ions and base. Adding ammonium hexafluorophosphate (NH_4PF_6) to the puce solution of macrocycle **1**·2PF$_6$ and clip **2** in MeCN also causes the color of the solution to turn light-yellow (Fig. 1A-d). The similar sizes and binding affinities of NH_4^+ and K^+ ions toward 18C6 may explain these phenomena.[14] Adding an excess of Et_3N to the mixture switches the color of the solution back to puce immediately (Fig. 1A-e). The addition of the base leads to the formation of NH_3 and the Et_3NH^+ ion, neither of which binds strongly to the 18C6 motif of **1**·2PF$_6$, and, thus, the threading of clip **2** through the macrocycle regenerates the complex [(**1**⊂**2**)·2PF$_6$]. Again, the switching process can be visualized by observing the color of the solution of the macrocycle–clip complex, which can also be operated reversibly when adding NH_4PF_6 and Et_3N sequentially.

As anticipated, the addition of both KPF$_6$ and NH_4PF_6 to the mixture of **1**·2PF$_6$ and **2** also switches the color of the solution from puce to light yellow. Thus, if we consider the intensity of the absorbance at 533 nm in the UV-vis spectrum of complex [(**1**⊂**2**)·2PF$_6$] as the output and the K^+ and NH_4^+ ions as the inputs, the switching of the macrocycle–clip system reflects the operation of a two-input NOR logic gate.

We have prepared a new macrocycle–clip complex that functions as a molecular switch. Both K^+–[2,2,2]cryptand and NH_4^+–Et_3N stimuli control the movement of this molecular switch between its threaded and unthreaded states.[15] The color changes, which are observable to the naked eye during switching by either of these two different methods, allows the macrocycle–clip complex system to function as a two-input molecular NOR logic gate.

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