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A Macrocycle/Molecular-Clip Complex that Functions as a Quadruply Controllable Molecular Switch

Pinn-Tsong Chiang,[a] Pin-Nan Cheng,[a] Chi-Feng Lin,[a] Yi-Hung Liu,[a] Chien-Chen Lai,[b] Shie-Ming Peng,[a] and Sheng-Hsien Chiu*[a]

Abstract: Herein, we report the synthesis of a molecular clip with TTF side-walls and its binding behavior towards electron-deficient guests, namely the formation of macrocycle/molecular-clip supramolecular complexes in solution. Four different sets of external stimuli—the K^+/[2.2.2]cryptand, NH_4^+/Et_3N and $(p\text{-BrPh})_3NSbCl_6$/Zn pairs, and heating/cooling cycles—control the movement of this molecular switch between its threaded and unthreaded states and provide color changes that are observable by the naked eye. This macrocycle/molecular-clip complex system can be considered not only as a quadruple-use molecular switch, but can also be operated by three of these stimuli as a three-input molecular NOR-functioning logic gate that may be monitored by UV-visible spectroscopy.

Keywords: macrocycles · molecular devices · molecular switch · pseudorotaxanes

Introduction

Although many elegant pseudorotaxane-like[1] molecular switches[2] have been developed in recent years, the number of recognition motifs that can be exploited in the preparation of these complexes remains limited as a result of structural complexity and/or weak intermolecular interactions. The use of clip-shaped guest molecules and their complementary macrocyclic hosts in the preparation of macrocycle/molecular-clip complexes[3] is a valid approach to increasing the binding affinity between host and guest molecules, because molecular tweezers[4] and clips[5] can exist in preorganized molecular structures that allow the efficient complexation of aromatic guests. We became interested in developing a glycoluril-based molecular clip in which electron-rich tetrathiafulvalene (TTF) units are present as the side-walls; we expected such a molecular clip to possess interesting molecular-recognition properties towards electron-deficient guests as well as redox-controllable switching activity. An additional benefit of 3,4-disubstituted TTF moieties is the structural unity of the molecular clip; as a consequence, some of the complications that arise in the analysis of the binding event may be avoided, particularly those caused by the *cis–trans* photoisomerism[6] of each TTF unit's central carbon–carbon double bond, which occurs in a number of disubstituted TTF units.[7] To the best of our knowledge, only a few examples exist of molecular clips that assemble with macrocycles to form macrocycle/molecular-clip complexes[3] that can be switched between their threaded and unthreaded states by the application of external stimuli.[8] The addition and removal of heat,[9] metal ions,[10] protons,[2c,11] and electrons[12] all allow supramolecular systems to switch efficiently between different states; thus, supramolecular assemblies that can be switched in these ways and which exhibit detectable gains or losses in the optical signals of their different states may be considered as multiple-input molecular logic gates.[13] Although some elegant molecular logic gates that have variable functions have been reported, NOR and NAND (NOR = not or; NAND = not and) logic gates are the most valuable because multiple copies can be wired up to emulate all other types of logic gates.[14] In this paper, we report a new molecular switch based on a macrocycle/molecular-clip complex whose switching behavior can be controlled by 1) the addition of K^+ ions (and their removal with [2.2.2]cryptand), 2) the addition of NH_4^+ ions (and their removal with Et_3N), 3) heating and cooling cycles, and 4) oxidation [$(p\text{-BrPh})_3NSbCl_6$] and reduction (Zn) cycles,

[a] P.-T. Chiang, P.-N. Cheng, C.-F. Lin, Y.-H. Liu, Prof. S.-M. Peng, Prof. S.-H. Chiu
Department of Chemistry, National Taiwan University
No. 1, Sec. 4, Roosevelt Road, Taipei, Taiwan (ROC)
Fax: (+886) 2-2498-0963
E-mail: shchiu@ntu.edu.tw

[b] Prof. C.-C. Lai
Department of Medical Genetics and Medical Research
China Medical University Hospital, Taichung, Taiwan (ROC)

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and which, additionally, provides color changes that are visible to the naked eye. Indeed, based on the absorptions in its UV-visible spectra at 533 nm, this macrocycle/molecular-clip system operates—when stimulated with K^+ and NH_4^+ ions and heat—as a three-input NOR-functioning molecular logic gate.

Results and Discussion

Molecular clips **1a–c** were synthesized from diphenylglycoluril derivative **2**[15] in four steps (Scheme 1). The acid-catalyzed condensation of **2** and the 2-thioxo-1,3-dithiole[16] gave molecular clip **3** in 83% yield. The reaction of molecular clip **3** and the oligo(ethylene glycol) monomethyl ether tosylates **4a–c** under basic conditions afforded the molecular clips **5a–c** with tri-, di-, and mono(ethylene glycol) chains, respectively. Molecular clips **5a–c** were then treated with mercury(II) acetate to provide the corresponding molecular clips **6a–c**. The coupling of molecular clips **6a–c** with 1,3-dithiole-2-thione (**7**) gave the desired molecular clips **1a–c** in moderate yields.

We anticipated that the glycoluril-based molecular clip **1a**, in which two TTF units are positioned at a suitable separation to allow π stacking with guest species, would form complexes with electronically complementary pyridinium motifs between its two aromatic side-walls.[17] We incorporated four tri(ethylene glycol) chains into molecular clip **1a** not only to increase its solubility in organic solvents, but also to partially reduce the free energy of binding during the complexation process by allowing C–H···O hydrogen bonds to form between the guest pyridinium ion's α protons and the oxygen atoms of these tri(ethylene glycol) side-chains.[17a,18] To confirm the enhancement in the solubility of these oligo(ethylene glycol) chains, we synthesized molecular clip **1d** by the same approach (Scheme 1). As anticipated, the molecular clip **1d** has poor solubility in common organic solvents such as CH_2Cl_2 and CH_3CN.

Although molecular clip **1a** is very soluble in CH_2Cl_2, it is only moderately soluble in CH_3CN; the addition of *N*,*N*′-dimethyl-4,4′-bipyridinium bis(hexafluorophosphate) (**8**·2PF_6, see Scheme 2) to a solution of **1a** helped to dissolve any remaining insoluble molecular clip **1a** and led to an immedi-

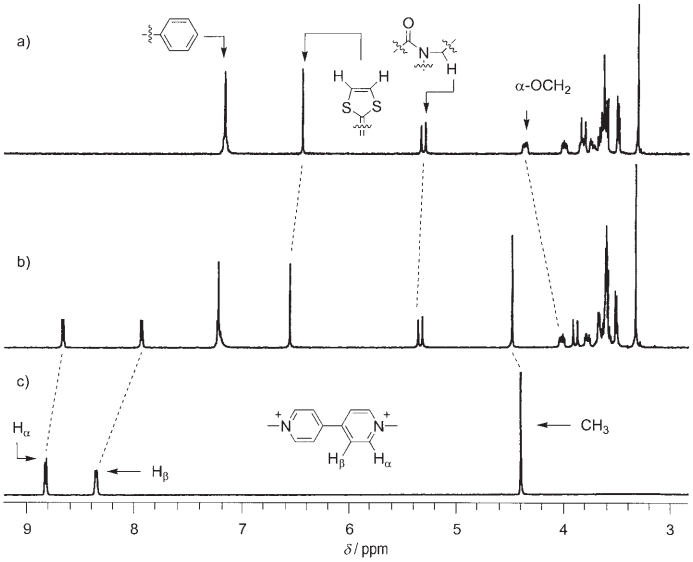
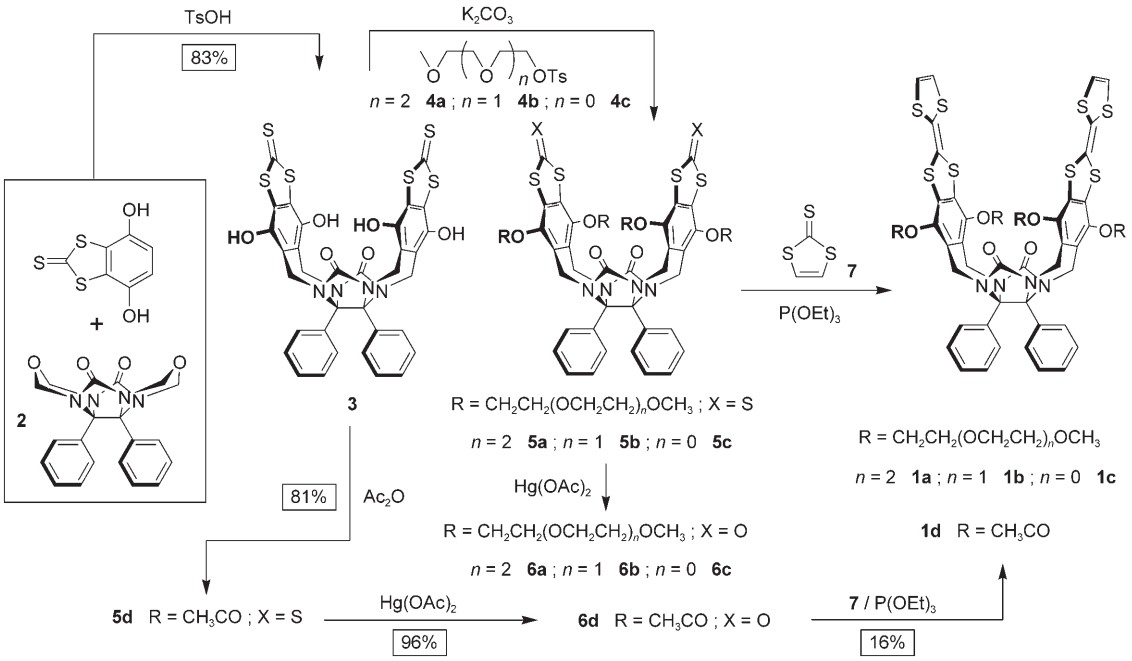


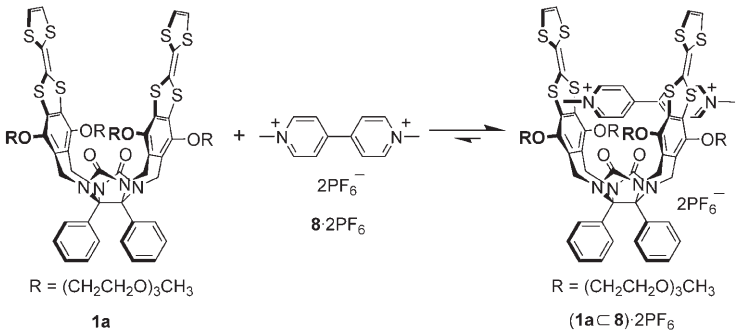
Figure 1. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of a) molecular clip **1a**, b) an equimolar mixture of **1a** and salt **8**·2PF_6 (10 mM), and c) salt **8**·2PF_6.



Scheme 1. Syntheses of the molecular clips **1a–d**.

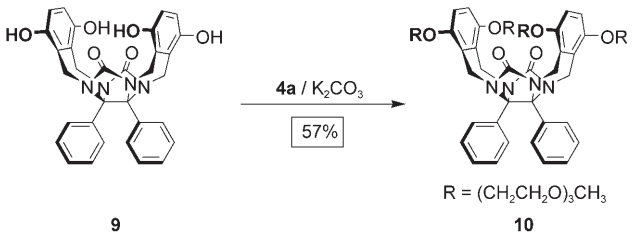
ate change in the color of the solution from light-yellow to green.[19] The green color, which results from the absorption of visible light at 653 nm, is characteristic of the charge-transfer absorption that results from the interactions between electron-rich TTF derivatives and electron-deficient *N*,*N*′-dialkylated bipyridinium ions. As indicated in Figure 1b, the ^{1}H NMR spectrum of an equimolar mixture of molecular clip **1a** and the bipyridinium salt **8**·2PF$_6$ in CD_3CN (10 mM) displays significant shifts in the positions of its signals relative to those of its free components (cf. Figure 1a and c). The upfield shifts of the α and β protons of the bipyridinium ion guest and of the CH_2OAr protons of the host suggest that π-stacking aryl–aryl interactions possibly play an important role in stabilizing the (**1a**⊂**8**)·2PF$_6$ complex.

The downfield shift of the signal arising from the MeN$^+$ protons of the bipyridinium ion suggests the existence of possible C–H···O hydrogen bonding between these protons and the tri(ethylene glycol) side-chains. A Job plot obtained from ^{1}H NMR spectra recorded in CD_3CN affords conclusive evidence of 1:1 complexation (see the Supporting Information), that is, the formation of a 1:1 supramolecular assembly, (**1a**⊂**8**)·2PF$_6$ (Scheme 2). We determined the association constant (K_a) for the interaction between the molecular clip **1a** and the bipyridinium salt **8**·2PF$_6$ in CD_3CN to be $5600 \pm 300\ M^{-1}$ based on the results of a ^{1}H NMR spectroscopic dilution experiment.[20]



Scheme 2. Formation of the complex (**1a**⊂**8**)·2PF$_6$.

To elucidate the importance of the electron-rich TTF side-arms in the recognition of **8**·2PF$_6$, we synthesized molecular clip **10** by alkylating tri(ethylene glycol) monomethyl ether tosylate **4a** and molecular clip **9**[21] under basic conditions (Scheme 3). We used the ^{1}H NMR spectroscopic dilution method to obtain the value of

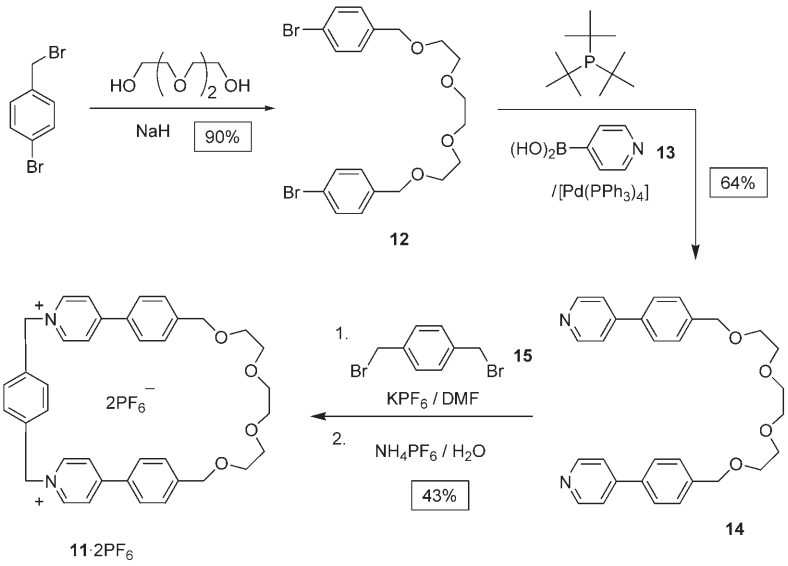


Scheme 3. Synthesis of molecular clip **10**.

K_a ($370 \pm 30\ M^{-1}$) for the interaction in CD_3CN between molecular clip **10**, whose side-walls contain only alkylated hydroquinone units, and the bipyridinium salt **8**·2PF$_6$; this value is about 15-fold weaker than that for the binding between the TTF-containing molecular clip **1a** and **8**·2PF$_6$. The side-walls of both of these glycoluril-based molecular clips (**1a** and **10**) consist of rigid aromatic rings, which we believe impart on these two molecules similar conformational rigidities and π-stacking distances upon guest reception. Thus, the 15-fold increase in the binding affinity of **1a** to **8**·2PF$_6$ is probably the result of the increased area and charge density of the π-electron-rich aromatic moieties of this molecular clip's side-walls.

To test the formation of a macrocycle/molecular-clip complex, we synthesized macrocycle **11**·2PF$_6$ in three steps (Scheme 4). The reaction of 4-bromobenzyl bromide with tri(ethylene glycol) under basic conditions gave the dibromide **12**. A subsequent Suzuki coupling reaction[22] with 4-pyridineboronic acid (**13**) afforded the dipyridine **14**, which we then treated with α,α′-dibromo-*p*-xylene (**15**) to give the desired macrocycle **11**·2PF$_6$ in 43% yield.

We grew single crystals of **11**·2PF$_6$ suitable for X-ray crystallographic analysis by liquid diffusion of diisopropyl ether into a solution of the macrocycle in CH_3CN. The solid-state structure (Figure 2) of **11**$^{2+}$ reveals that the separations be-



Scheme 4. Synthesis of the macrocycle **11**·2PF$_6$.

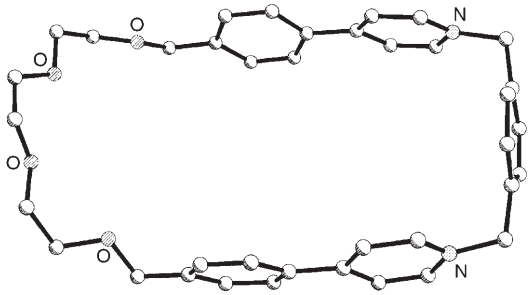


Figure 2. Ball-and-stick representation of the solid-state structure of macrocycle $\mathbf{11}^{2+}$.

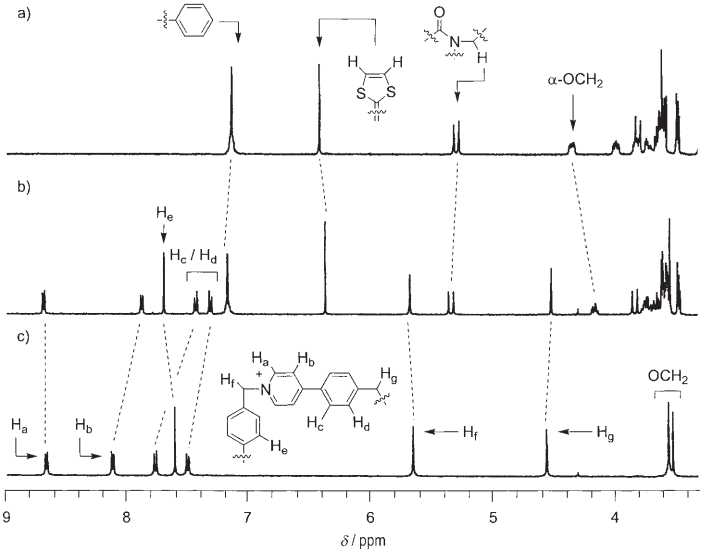
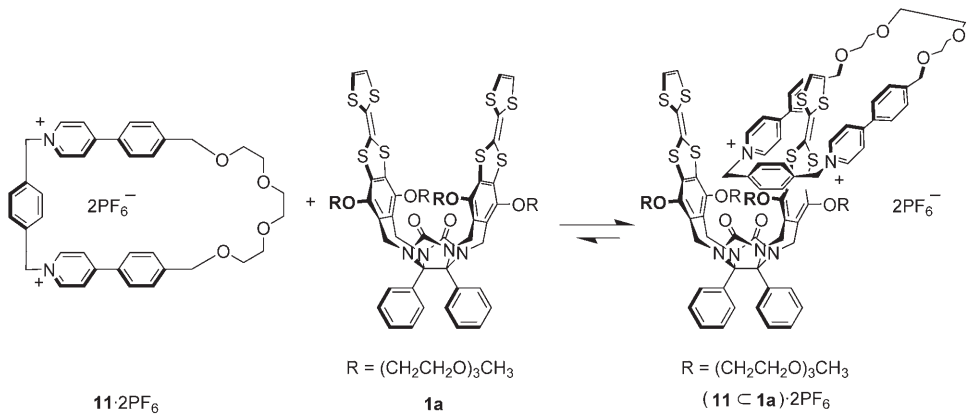


Figure 3. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of a) molecular clip **1a**, b) a mixture of **11**·2 PF_6 and **1a** (10 mM each), and c) macrocycle **11**·2 PF_6.

tween the mean planes of the pairs of pyridinium and phenyl residues are approximately 6.8 and 7.2 Å, respectively. The dimensions of the pseudorectangular $\mathbf{11}^{2+}$ are approximately 13.2×7.0 Å and thus, the insertion of a π-electron-rich TTF guest unit between the two π-electron-deficient pyridinium units seemed promising (cf. the accepted[18b,23] aromatic π-stacking distance of 3.5 Å).

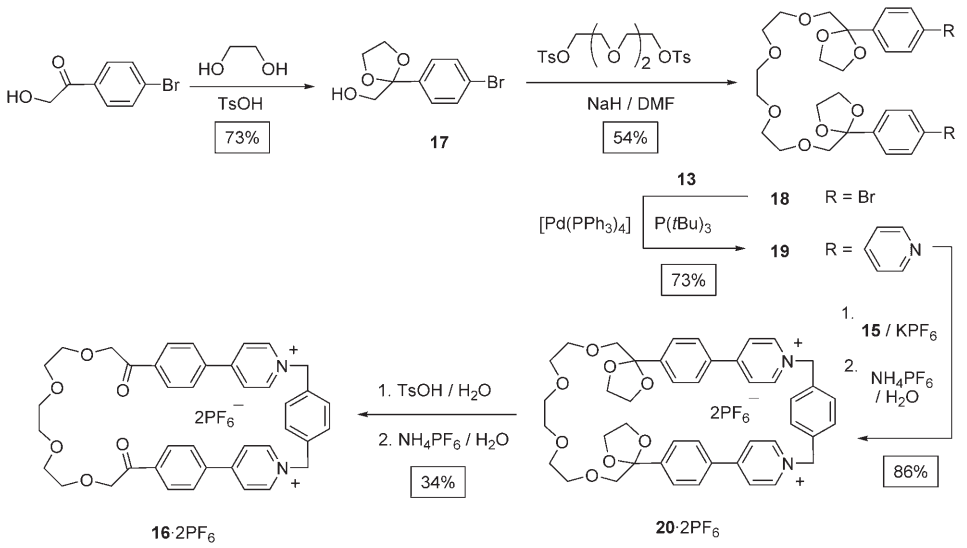
As was the case when we mixed molecular clip **1a** with the bipyridinium salt **8**·2 PF_6, the addition of macrocycle **11**·2 PF_6 to a suspension of **1a** in CH_3CN helped to dissolve any remaining insoluble **1a**; more interestingly, this process resulted in an immediate change in the color of the solution from light-yellow to puce. The ^{1}H NMR spectrum of an equimolar mixture of **1a** and **11**·2 PF_6 in CD_3CN (10 mM) displays significant shifts in the positions of its signals relative to those of its free components (Figure 3). The upfield shifts of protons H_c and H_d in macrocycle **11**·2 PF_6 and the protons of the TTF and CH_2OAr units of molecular clip **1a** imply the existence of aryl–aryl interactions between the two electronically complementary components. These results suggest that the macrocycle/molecular-clip complex (**11**⊂**1a**)·2 PF_6 is generated in solution (Scheme 5). Based on the results of a ^{1}H NMR dilution experiment, we determined the binding constant for the formation of this complex to be $1600 \pm 100\ M^{-1}$.

We used macrocycle **11**·2 PF_6 to elucidate the importance of the chain lengths of the oligo(ethylene glycol) motifs in these molecular clips. Because molecular clips **1b** and **1c**, which feature di(ethylene glycol) and ethylene glycol side-chains, respectively, are very soluble in $CHCl_3$ but not in CD_3CN, we examined their complexation with macrocycle **11**·2 PF_6 in a $CDCl_3$/CD_3CN (4:1) mixture. The ^{1}H NMR spectrum of an equimolar mixture of molecular clip **1c** and macrocycle **11**·2 PF_6 in such a solution displays only negligible changes in the positions of its signals relative to the spectra of its free components and no distinct color change occurred, that is, the affinity of **1c** for **11**·2 PF_6 is negligible under these conditions. In contrast, when we mixed equimolar amounts of molecular clip **1b** and **11**·2 PF_6 in $CDCl_3$/CD_3CN (4:1), we observed both signal movement in the ^{1}H NMR spectrum and a color change. Through ^{1}H NMR spectroscopic dilution experiments we determined the association constant for this system to be $70 \pm 10\ M^{-1}$. In comparison, the association constant for the complex formed between molecular clip **1a** and **11**·2 PF_6 under the same conditions is $170 \pm 30\ M^{-1}$, that is, about tenfold weaker than the affinity between these two species in pure CD_3CN. This result suggests that aryl–aryl π-stacking interactions may play an important role in the stabilization of these complexes, because π-stacking interactions are generally stronger in polar solvents; the addition of a less-polar solvent, for



Scheme 5. Formation of the complex (**11**⊂**1a**)·2 PF_6.

example, $CDCl_3$, to a solution of the complex in CD_3CN tends to weaken these interactions even though it may increase the strength of any hydrogen-bonding interactions. The stronger binding affinity of molecular clip **1a** to **11**·2 PF_6 relative to those of **1b** and **1c** towards this macrocycle confirms the benefits of incorporating sufficiently long oligo(ethylene glycol) chains into the constitution of these molecular clips: not only do they help to increase the solubility of the molecular clip but they also enhance the degree of guest complexation through stronger C–H···O hydrogen bonding.



Scheme 6. Synthesis of the macrocycle **16**·2 PF_6.

We grew single crystals of **5c** suitable for X-ray crystallographic analysis by slow evaporation of a solution of the clip in CH_3CN. The solid-state structure (Figure 4) of **5c** reveals the existence of a slight structural twist in the diphenylglycoluril unit; the relative displacement of the centers of the two alkoxybenzene rings is 1.2 Å. These dialkoxybenzene moieties define a tapering cavity and the mean planes through the cavity walls are aligned at a relative angle of 44.5°.[24] The centers of the alkoxybenzene rings are 6.5 Å apart.

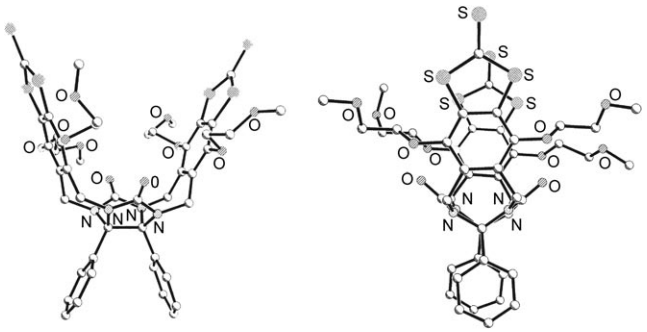


Figure 4. Ball-and-stick representations of the solid-state structure of molecular clip **5c**.

Having established the feasibility of forming macrocycle/molecular-clip complexes, we turned our attention towards switchable versions of this system. To do so, we designed a new macrocycle (**16**·2 PF_6, Scheme 6) in which the tri(ethylene glycol) motif of macrocycle **11**·2 PF_6 is replaced by a ring-expanded [18]crown-6 unit.

We synthesized macrocycle **16**·2 PF_6 from (4-bromobenzoyl)methanol in five steps. The carbonyl group of (4-bromobenzoyl)methanol was protected by reaction with ethylene glycol under acidic conditions to give the alcohol **17** in 73% yield. The alkylation of **17** with tri(ethylene glycol) bis(*p*-toluenesulfonate) under basic conditions afforded the dibromide **18** in 54% yield. Subsequent Suzuki coupling of **18** with 4-pyridineboronic acid (**13**) gave the dipyridine **19**. Macrocycle **20**·2 PF_6 was obtained after [1+1] macrocyclization of **19** with α,α′-dibromo-*p*-xylene (**15**) followed by anion exchange. Removal of the ketal protecting group of macrocycle **20**·2 PF_6 under acidic conditions and exchange of the anions with NH_4PF_6/H_2O afforded the desired macrocycle **16**·2 PF_6.

The structure of macrocycle **16**·2 PF_6 is reminiscent of a combination of a ring-expanded [18]crown-6 (18C6) unit, which we expect to bind alkali-metal ions, and the π-electron-deficient aromatic motif of macrocycle **11**·2 PF_6. We anticipated that 1) the complementary electronic structures of the TTF and pyridinium motifs, 2) the separation between the two aromatic side-walls of the macrocycle suitable for π stacking of a TTF unit, and 3) the π-stacking interactions between the nonthreaded "*exo*" TTF arm of the molecular clip and a pyridinium ring of the macrocycle would all assist **1a** to complex with **16**·2 PF_6 with reasonable affinity.

The addition of macrocycle **16**·2 PF_6 to a suspension of **1a** in MeCN dissolved any remaining insoluble molecular clip and led to an immediate change in the color of the solution from light-yellow to puce, just as we had observed upon mixing **1a** and **11**·2 PF_6. The UV-visible spectrum of the complex formed between **11**·2 PF_6 and **1a** in MeCN (Figure 5a) displays a charge-transfer band at 533 nm that suggests the formation of the macrocycle/molecular-clip complex (**16**⊂**1a**)·2 PF_6. A Job plot based on this absorption in MeCN affords conclusive evidence for 1:1 complexation (see the Supporting Information). From the results of ^1H NMR spectroscopic dilution experiments, we determined the association constant for the binding between macrocycle **16**·2 PF_6 and molecular clip **1a** in CD_3CN to be 4900 ± 200 M^{-1}.

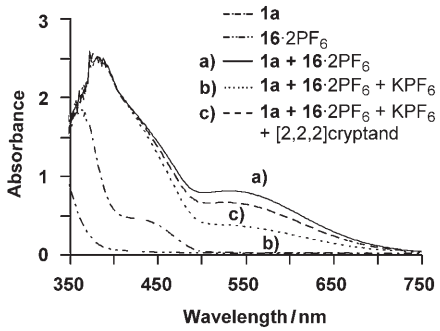


Figure 5. The UV-visible spectra (MeCN, 1.5 mM, 298 K) of a) an equimolar mixture of **16**·2 PF_6 and **1a**, b) the mixture obtained after adding KPF_6 (20 equiv) to solution (a), c) the mixture obtained after adding [2.2.2]cryptand (20 equiv) to solution (b).

The addition of 20 equivalents of potassium hexafluorophosphate (KPF_6) to the puce solution of a mixture of **16**·2 PF_6 and **1a** in MeCN switched the color of the solution back to its original yellow hue (see the Supporting Information). The significant decrease in the intensity of the charge-transfer band in the UV-visible spectrum (Figure 5b) and the appearance of signals characteristic of the free molecular clip **1a** (Figure 6b) in the ^{1}H NMR spectrum both suggest the dissociation of complex (**16**⊂**1a**)·2 PF_6. This phenomenon may be the result of negative allosteric behavior[25] that arises because the 18C6-like motif of macrocycle **16**·2 PF_6 recognizes the K^+ ions and, through a conformational change in the aromatic units of macrocycle **16**·2 PF_6, repels the threaded molecular clip (Scheme 7).[26] However, we cannot be certain whether this effect arises mostly through conformational, steric, or repulsive electrostatic effects.

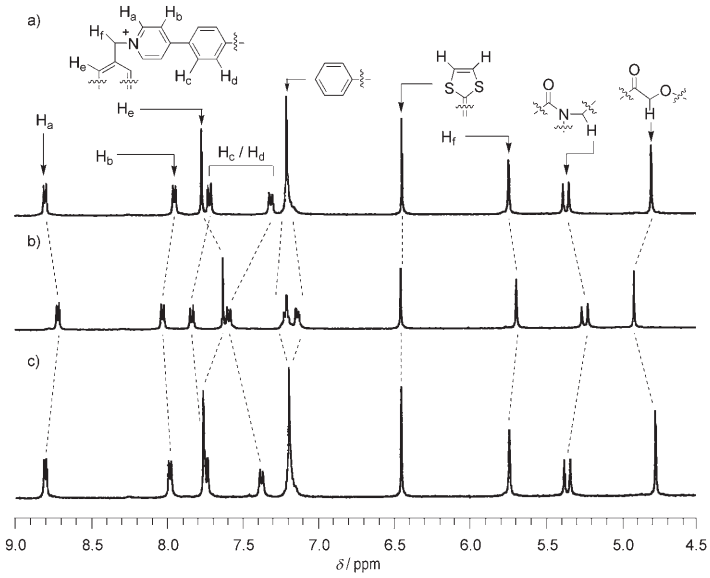
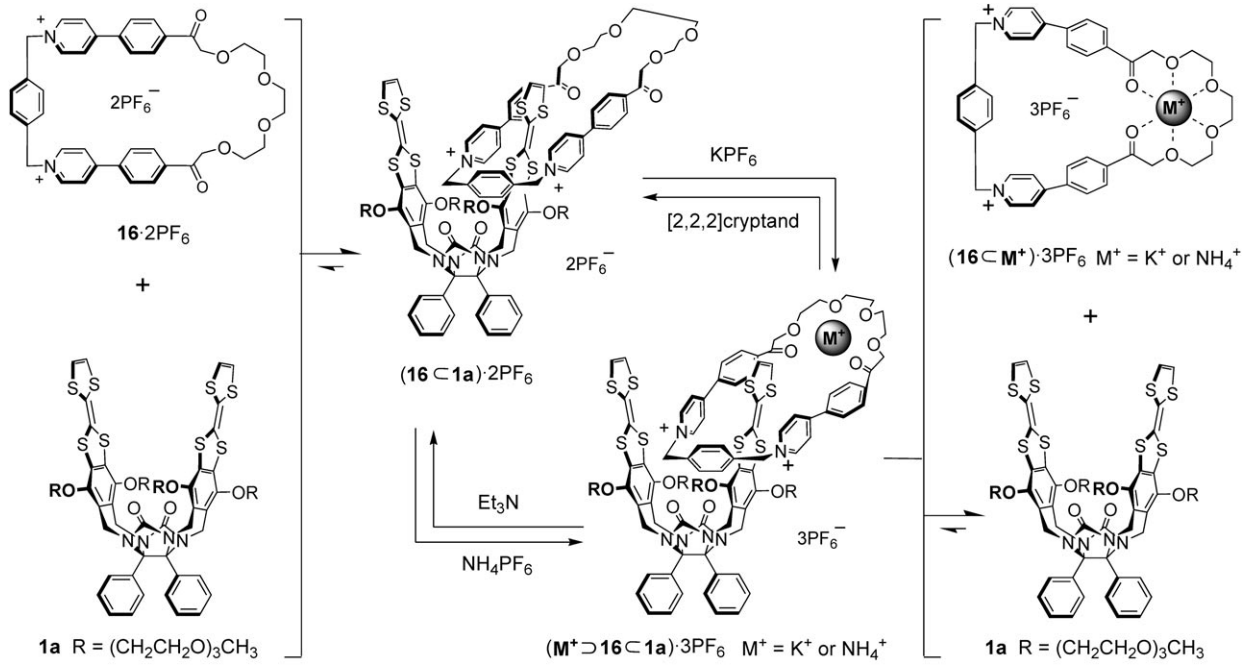


Figure 6. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of a) a mixture of **16**·2 PF_6 and **1a** (10 mM each), b) the mixture obtained after the addition of KPF_6 (20 equiv) to the solution in (a), and c) the mixture obtained after adding [2.2.2]cryptand (20 equiv) to the solution in (b).

To remove the K^+ ions complexed to macrocycle **16**·2 PF_6, we added an excess amount of [2.2.2]cryptand, a very strong binder of K^+ ions, to the solution. As anticipated, the puce color of the solution returned instantly upon addition of [2.2.2]cryptand. The ^{1}H NMR spectrum (Figure 6c) of this mixture appears to be similar to that of the original solution of macrocycle **16**·2 PF_6 and molecular clip **1a** (Figure 6a); this observation implies that the original (**16**⊂**1a**)·2 PF_6 complex is regenerated in this solution. The threading/unthreading process can be repeated several times by adding excess amounts of K^+ ions and [2.2.2]cryptand sequentially; moreover, the reversible color changes allow us to monitor the switching process directly by the naked eye.

Because of the similar sizes and binding affinities of NH_4^+ and K^+ ions towards 18C6,[27] we hypothesized that this [2]pseudorotaxane-like macrocycle/molecular-clip system may be switchable through the sequential addition of NH_4^+ ions and base. The addition of ammonium hexafluorophosphate (NH_4PF_6) to the puce solution of macrocycle **16**·2 PF_6 and molecular clip **1a** in MeCN also causes the color of the solution to turn light yellow. The addition of an excess of Et_3N to the mixture immediately switches the color of the solution back to puce (see the Supporting Information), that is, addition of the base leads to the formation of NH_3 and Et_3NH^+ ions, neither of which binds strongly to the 18C6 motif of **16**·2 PF_6, and, thus, molecular clip **1a** once again threads through the macrocycle to regenerate the complex (**16**⊂**1a**)·2 PF_6. Again, the switching process can be visualized by observing the color of the solution of the macrocycle/molecular-clip complex; this process can be operated reversibly by the sequential addition of NH_4PF_6 and Et_3N.

Because we expected the formation of the macrocycle/molecular-clip complex (**16**⊂**1a**)·2 PF_6 to be an enthalpy-driven process, we believed that elevating the temperature of the solution would cause the complex to dissociate and so the intensity of the charge-transfer absorption at 533 nm would be reduced. To test this hypothesis, we heated an equimolar solution of molecular clip **1a** and macrocycle **16**·2 PF_6 in CH_3CN (1 mM) from 298 to 353 K. The color of the solution gradually switched from puce to light-yellow as the temperature increased (see the Supporting Information). Figure 7 indicates that the partial variable-temperature ^{1}H NMR spectrum of the mixture of **1a** and **16**·2 PF_6 at 353 K is a superimposition of the ^{1}H NMR spectra of the two free species; that is, the degree of complexation between **1a** and **16**·2 PF_6 is negligible at 353 K. As anticipated, when we cooled the solution to ambient temperature, the absorptions in both the UV-visible and ^{1}H NMR spectra returned to their original positions suggesting that the components of complex (**16**⊂**1a**)·2 PF_6 are stable in solution over this temperature range. Thus, complex (**16**⊂**1a**)·2 PF_6 can be considered to display thermal chromism[28] in solution, because the



Scheme 7. The complexation and switching behavior of the macrocycle/molecular-clip complex (**16**⊂**1a**)·2 PF_6.

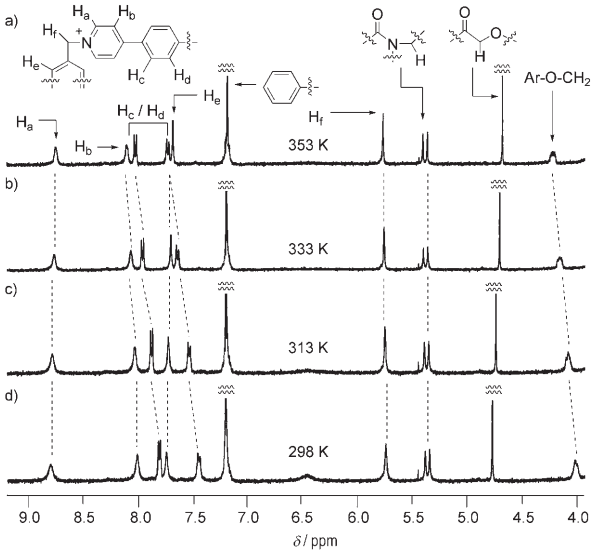


Figure 7. Partial ^{1}H NMR spectra (400 MHz, CD_3CN) displaying the dissociation of complex (**16**⊂**1a**)·2 PF_6 at elevated temperatures: a) 353 K, b) 333 K, c) 313 K, and d) 298 K.

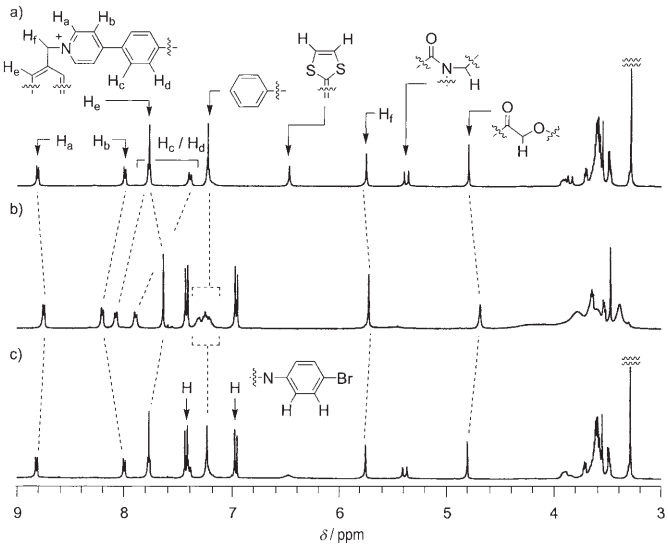


Figure 8. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of a) a mixture of **16**·2 PF_6 and **1a** (2 mM each), b) the mixture obtained after addition of (p-BrPh)$_3$$NSbCl_6$ (1 equiv) to the solution in (a), and c) the mixture obtained after the addition of excess zinc powder to the solution in (b).

reversible color changes of the macrocycle/molecular-clip complex can be triggered thermally.

The rich redox chemistry of TTF units provides a very efficient tool with which to control the switching of supramolecular assemblies between their different states.[12f,29] We wished to examine the possibility of using such a process to drive our macrocycle/molecular-clip complex between its complexed and uncomplexed states. The (p-BrPh)$_3$$NSbCl_6$ species can oxidize TTF units into their corresponding TTF$^{\cdot+}$ radical cations.[7c,30] The addition of one equivalent of (p-BrPh)$_3$$NSbCl_6$ to a mixture of molecular clip **1a** and macrocycle **16**·2 PF_6 switched the color of the solution to black (see the Supporting Information). The appearance of signals characteristic of the free macrocycle **16**·2 PF_6 in the ^{1}H NMR spectrum (Figure 8b) suggests that dissociation of the (**16**⊂**1a**)·2 PF_6 complex occurred presumably as a result of

electrostatic repulsion between the positively charged pyridinium units of **16**·2 PF_6 and the radical cationic $TTF^{\cdot+}$ moieties of the oxidized molecular clip. The addition of zinc powder to this solution reduces the $TTF^{\cdot+}$ motifs back to their neutral form and results in a color and ^{1}H NMR spectrum (Figure 8c) that are almost identical to those of the original mixture of molecular clip **1a** and macrocycle **16**·2 PF_6 (Figure 8a).

These observations indicate that the complex (**16**⊂**1a**)·2 PF_6 is stable to these switching conditions. Interestingly, and in contrast to our observations during the previous three switching processes, the intensity of the UV-visible absorption at 533 nm did not decrease upon dissociation of complex (**16**⊂**1a**)·2 PF_6. After the addition of the oxidant, which the ^{1}H NMR spectrum in Figure 8 proves leads to almost complete dissociation of the complex, the UV-visible absorption at 533 nm increased (Figure 9b) as a result of the intensity of the characteristic $TTF^{\cdot+}$ absorption at 580 nm.[31]

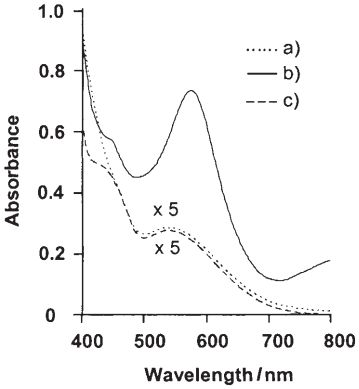


Figure 9. Partial UV-visible spectra (MeCN, 298 K) of a) a mixture of **16**·2 PF_6 and **1a** (1 mM each), b) the mixture obtained after addition (*p*-$BrPh)_3NSbCl_6$ (1 equiv) to the solution in (a), and c) the mixture obtained after the addition of excess zinc powder to the solution in (b).

We have demonstrated that the degree of complexation of this new macrocycle/molecular-clip complex (**16**⊂**1a**)·2 PF_6 can be controlled reversibly through the use of K^+/[2.2.2]cryptand, NH_4^+/Et_3N, and (*p*-$BrPh)_3NSbCl_6$/Zn pairs and heating/cooling cycles. This molecular switch can also be considered to operate as a three-input NOR-functioning molecular logic gate, because the addition of any one of three stimuli (i.e., one of K^+, NH_4^+, or heat) to a solution of **16**·2 PF_6 and **1a** results in the dissociation of the complex (**16**⊂**1a**)·2 PF_6 and a decrease in its UV-visible absorption at 533 nm. Thus, we can consider the intensity of the absorbance at 533 nm in the UV-visible spectrum of complex (**16**⊂**1a**)·2 PF_6 as the output and KPF_6, NH_4PF_6, and heat as the inputs in the operation of a three-input NOR logic gate (Figure 10).[32] We note, however, that the practical difficulties involved in connecting chemically controlled logic gates and the signal disruption caused by the accumulation of side-products during the switching process certainly limit their potential applications in complicated electronic circuitry when compared with the potential suitability of related electronically or photonically controllable systems.

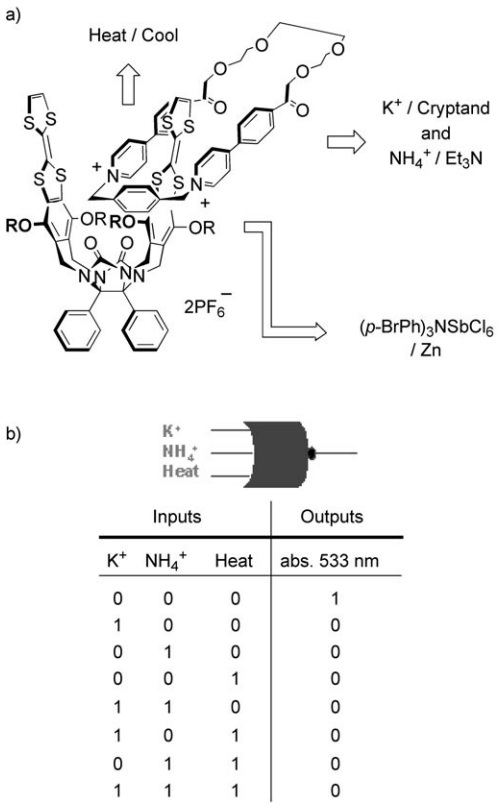


Figure 10. a) The quadruply controllable molecular switch that can be operated as b) a three-input NOR functioning molecular logic gate.

Conclusions

We have prepared a new macrocycle/molecular-clip complex that functions as a molecular switch. Four different external stimuli—the K^+/[2.2.2]cryptand, NH_4^+/Et_3N and (*p*-$BrPh)_3NSbCl_6$/Zn pairs, and heating/cooling cycles—control the movement of this molecular switch between its threaded and unthreaded states. The design of this supramolecular macrocycle/molecular-clip complex has allowed us to operate a molecular switch through three fundamentally different processes: 1) the recognition of K^+ and NH_4^+ ions by the 18C6-like motif of macrocycle **16**·2 PF_6 leads to dissociation as a result of steric hindrance or conformational changes, 2) oxidation of the TTF side-walls of molecular clip **1a** leads to dissociation through electrostatic repulsion, and 3) heating the complex leads to dissociation as a result of the enthalpic dominance of the binding event. These dissociation processes lead to color changes that are observable by the naked eye. The addition of K^+, NH_4^+, or heat not only causes dissociation of the macrocycle/molecular-clip complex, but also reduces the intensity of its charge-transfer absorption band at 533 nm; thus, these three inputs and one

output characterize this macrocycle/molecular-clip complex system as a functioning three-input molecular NOR logic gate.

Experimental Section

General: All glassware, stirrer bars, syringes, and needles were either oven- or flame-dried prior to use. All reagents, unless otherwise indicated, were obtained from commercial sources. Anhydrous CH_2Cl_2 and MeCN were obtained by distillation from CaH_2 under nitrogen. Anhydrous THF was obtained by distillation from Na/Ph_2CO under nitrogen. Reactions were conducted under nitrogen or argon. Thin-layer chromatography (TLC) was performed on Merck 0.25 mm silica gel (Merck Art. 5715). Column chromatography was performed on Kieselgel 60 (Merck, 70–230 mesh). The melting points were determined by using a Fargo MP-2D Mel-Temp apparatus and are uncorrected. In the NMR measurements, deuteriated solvent was used as the lock, while either the solvent's residual protons or TMS was employed as the internal standard. Chemical shifts are reported in parts per million (ppm). Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad).

X-ray crystallographic analysis: CCDC-274909 (**5c**) and CCDC-274910 (**11**·2PF_6) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Molecular clip 3: Molecular clip **2** (12.0 g, 31.7 mmol), TsOH (12.0 g, 70 mmol), and 1,2-dichloroethane (240 mL) were refluxed for 10 min in a two-neck flask equipped with a Dean–Stark apparatus. 1,3-Benzodithiole-2-thione (26.4 g, 120 mmol) was added and then the mixture was refluxed for 24 h. The mixture was poured into MeOH (450 mL), the precipitate was filtered off, suspended in DMSO (450 mL), heated to 90 °C for 30 min, and then poured into MeOH (450 mL). The resulting precipitate was filtered off, washed with MeOH (150 mL), and dried to give molecular clip **3** as a light-yellow solid (20.3 g, 83 %). M.p. >305 °C (decomp); ^{1}H NMR (400 MHz, CD_3SOCD_3, 298 K): δ = 3.79 (d, J = 16 Hz, 4H), 5.36 (d, J = 16 Hz, 4H), 7.04–7.22 (m, 10H), 9.66 ppm (s, 4H); ^{13}C NMR (100 MHz, CD_3SOCD_3, 298 K): δ = 37.0, 84.5, 126.6, 127.6, 128.5, 128.6, 129.9, 133.0, 140.6, 156.6, 212.3 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{34}H_{23}N_4O_6S_6$): 774.9942; found: 774.9932.

Molecular clip 5a: K_2CO_3 (13.8 g, 100 mmol) was added to a solution of molecular clip **3** (5.0 g, 6.5 mmol) in DMF (180 mL). After stirring at room temperature for 30 min, a solution of tosylate **4a** (9.5 g, 30.0 mmol) in DMF (20 mL) was added and the mixture was stirred for another 12 h at 70 °C. The solvent was evaporated under reduced pressure and the residue was partitioned between water (150 mL) and CH_2Cl_2 (150 mL). The organic layer was washed with water (2×100 mL), dried ($MgSO_4$), and concentrated to give a crude product, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 2:98) to provide a yellow solid (4.0 g, 46 %). M.p. 129–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.36 (s, 12H), 3.54–3.56 (m, 8H), 3.65–3.84 (m, 32H), 3.89–3.94 (m, 4H), 4.02–4.07 (m, 4H), 4.44–4.49 (m, 4H), 5.44 (d, J = 16 Hz, 4H) 7.05–7.13 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 37.9, 59.0, 70.2, 70.6, 70.8, 71.9, 73.4, 85.1, 127.9, 128.8, 129.0, 130.9, 132.7, 135.2, 145.6, 157.0, 211.5 ppm (one carbon is missing, possibly because of signal overlap); HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{62}H_{79}N_4O_{18}S_6$): 1359.3713; found: 1359.3695.

Molecular clip 5b: The procedure described above for the preparation of **5a** was followed, but in this case the reaction of K_2CO_3 (13.8 g, 100 mmol), molecular clip **3** (5.5 g, 7.1 mmol), and tosylate **4b** (8.2 g, 30 mmol) afforded a light-yellow solid (3.1 g, 37 %). M.p. 173–174 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.38 (s, 12H), 3.56–3.63 (m, 8H), 3.66–3.85 (m, 16H), 3.90–3.95 (m, 4H), 4.05–4.10 (m, 4H), 4.45–4.49 (m, 4H), 5.45 (d, J = 16 Hz, 4H), 7.05–7.15 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 38.1, 59.3, 70.3, 70.7, 72.0, 73.4, 85.1, 127.7, 128.5, 128.8, 130.6, 132.4, 135.0, 145.3, 156.6, 210.9 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{54}H_{63}N_4O_{14}S_6$): 1183.2665; found: 1183.2681.

Molecular clip 5c: The procedure described above for the preparation of **5a** was followed, but in this case the reaction of K_2CO_3 (13.8 g, 100 mmol), molecular clip **3** (5.5 g, 7.1 mmol), and tosylate **4b** (6.44 g, 28 mmol) afforded a light-yellow solid (2.7 g, 38 %). M.p. >311 °C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.46 (s, 12H), 3.69–3.73 (m, 4H), 3.81–3.86 (m, 8H), 4.04–4.09 (m, 4H), 4.50–4.54 (m, 4H), 5.46 (d, J = 16 Hz, 4H), 7.06–7.14 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 38.1, 59.3, 71.6, 73.1, 85.1, 127.7, 128.6, 128.8, 130.7, 132.5, 135.0, 145.3, 156.7, 210.7 ppm; HRMS (ESI): m/z calcd. for $[M+H]^+$ $C_{46}H_{47}N_4O_{10}S_6$): 1007.1616; found: 1007.1600.

Molecular clip 5d: Acetic anhydride (7.1 mL) was added to a solution of molecular clip **3** (2.2 g, 2.9 mmol) in DMSO (22 mL) and pyridine (7.1 mL); the mixture was then stirred for 2 h. The resulting suspension was poured into water (150 mL), filtered, washed with water (50 mL) and acetone (20 mL), and then dried under vacuum to afford a light-yellow solid (2.1 g, 81 %). M.p. >325 °C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 2.41 (s, 12H), 3.90 (d, J = 16 Hz, 4H), 5.00 (d, J = 16 Hz, 4H), 6.98–7.13 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 20.6, 38.0, 85.0, 127.7, 128.9, 129.3, 130.5, 132.0, 135.0, 138.2, 156.7, 167.4, 209.0 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{42}H_{31}N_4O_{10}S_6$): 943.0364; found: 943.0386.

Molecular clip 6a: A mixture of molecular clip **5a** (200 mg, 150 μmol) and $Hg(OAc)_2$ (250 mg, 0.8 mmol) in glacial acetic acid (1.1 mL) and CH_2Cl_2 (1.5 mL) was stirred at ambient temperature for 15 min. The suspension was filtered through Celite and the organic solution was washed with saturated aqueous $NaHCO_3$ (2×75 mL) and water (75 mL). The organic layer was dried ($MgSO_4$) and concentrated to give molecular clip **6a** as a white solid (160 mg, 80 %). M.p. 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.36 (s, 12H), 3.53–3.55 (m, 8H), 3.64–3.85 (m, 32H), 3.89–3.94 (m, 4H), 4.01–4.06 (m, 4H), 4.43–4.48 (m, 4H), 5.44 (d, J = 16 Hz, 4H), 7.05–7.15 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 37.8, 58.9, 70.1, 70.5, 70.5, 70.7, 71.8, 72.9, 85.0, 127.0, 127.8, 128.6, 128.9, 130.0, 132.7, 147.0, 156.9, 189.1 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{62}H_{79}N_4O_{20}S_4$): 1327.4171; found: 1327.4199.

Molecular clip 6b: The procedure described above for the preparation of **6a** was followed; in this case, the reaction of molecular clip **5b** (180 mg, 150 μmol) and $Hg(OAc)_2$ (250 mg, 0.8 mmol) afforded a white solid (136 mg, 79 %). M.p. 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.38 (s, 12H), 3.55–3.62 (m, 8H), 3.66–3.86 (m, 16H), 3.90–3.95 (m, 4H), 4.03–4.08 (m, 4H), 4.44–4.49 (m, 4H), 5.45 (d, J = 16 Hz, 4H), 7.05–7.15 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 38.2, 59.2, 70.4, 70.7, 72.0, 73.0, 85.1, 126.9, 127.7, 128.5, 128.7, 129.9, 132.6, 146.7, 156.7, 188.7 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{54}H_{63}N_4O_{16}S_4$): 1151.3122; found: 1151.3170.

Molecular clip 6c: The procedure described above for the preparation of **6a** was followed; in this case, the reaction of molecular clip **5c** (150 mg, 150 μmol) and $Hg(OAc)_2$ (250 mg, 0.8 mmol) afforded a white solid (118 mg, 81 %). M.p. 265–266 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.46 (s, 12H), 3.68–3.72 (m, 4H), 3.82–3.86 (m, 8H), 4.03–4.08 (m, 4H), 4.49–4.54 (m, 4H), 5.47 (d, J = 16 Hz, 4H), 7.08–7.13 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 38.2, 59.3, 71.7, 72.7, 85.1, 126.9, 127.7, 128.5, 128.7, 129.9, 132.6, 146.7, 156.7, 188.5 ppm; HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{46}H_{47}N_4O_{12}S_4$): 975.2073; found: 975.2086.

Molecular clip 6d: The procedure described above for the preparation of **6a** was followed; in this case, the reaction of molecular clip **5d** (560 mg, 0.6 mmol) and $Hg(OAc)_2$ (950 mg, 3.1 mmol) afforded a white solid (0.52 g, 96 %). M.p. >325 °C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 2.40 (s, 12H), 3.91 (d, J = 16 Hz, 4H), 4.99 (d, J = 16 Hz, 4H), 6.98–7.13 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 20.6, 38.1, 84.9, 127.1, 127.7, 128.9, 129.2, 129.8, 132.1, 140.0, 156.8, 167.5, 187.0 ppm; HRMS (FAB): m/z calcd for $[M]^+$ ($C_{42}H_{30}N_4O_{12}S_4$): 911.0821; found: 911.0790.

Molecular clip 1a: Triethyl phosphite (28.6 mL) was added to a mixture of molecular clip **6a** (1.4 g, 1.1 mmol) and 1,3-dithiole-2-thione **7** (2.1 g, 15.7 mmol). The mixture was stirred at 130 °C for 3.5 h, cooled to room temperature, and filtered. The filtrate was washed with hexane (40 mL) to afford molecular clip **1a** as a light-yellow solid (500 mg, 31 %). M.p. 222–223 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K): δ = 3.33 (s, 12H), 3.53–

3.55 (m, 8H), 3.63–3.81 (m, 32H), 3.89–3.94 (m, 4H), 4.03–4.08 (m, 4H), 4.39–4.43 (m, 4H), 5.38 (d, 4H), 6.35 (s, 4H), 7.10–7.17 ppm (m, 10H); ^{13}C NMR (100 MHz, CD_2Cl_2, 298 K): δ = 38.4, 59.2, 70.9, 71.0, 71.1, 71.2, 72.4, 72.8, 85.5, 106.5, 115.4, 119.0, 128.4, 128.7, 128.8, 130.2, 131.6, 133.6, 146.5, 157.1 ppm; HRMS (FAB): *m/z* calcd for $[M]^+$ ($C_{68}H_{82}N_4O_{18}S_8$): 1498.3390; found: 1498.3381.

Molecular clip 1b: The procedure described above for the preparation of **1a** was followed; in this case, the reaction of molecular clip **6b** (115 mg, 0.1 mmol), 1,3-dithiole-2-thione **7** (160 mg, 1.2 mmol), and triethyl phosphite (3.2 mL) afforded a light-yellow solid (42 mg, 32%). M.p. 274–275 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 298 K): δ = 3.38 (s, 12H), 3.57–3.61 (m, 8H), 3.66–3.81 (m, 16H), 3.88–3.93 (m, 4H), 4.03–4.08 (m, 4H), 4.39–4.43 (m, 4H), 5.38 (d, J = 16 Hz, 4H), 6.35 (s, 4H), 7.10–7.15 ppm (m, 10H); ^{13}C NMR (100 MHz, CD_2Cl_2, 298 K): δ = 38.3, 59.3, 70.8, 71.0, 72.4, 72.7, 85.5, 106.4, 115.4, 119.0, 128.3, 128.6, 128.7, 130.2, 131.6, 133.5, 146.4, 157.0 ppm; HRMS (FAB): *m/z* calcd for $[M+H]^+$ ($C_{60}H_{67}N_4O_{14}S_8$): 1323.2419; found: 1323.2400.

Molecular clip 1c: The procedure described above for the preparation of **1a** was followed; in this case, the reaction of molecular clip **6c** (160 mg, 120 μmol), 1,3-dithiole-2-thione **7** (200 mg, 1.5 mmol), and triethyl phosphite (3.1 mL) afforded a light-yellow solid (46 mg, 24%). M.p. >312 °C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.50 (s, 12H), 3.72–3.76 (m, 8H), 3.86–3.88 (m, 4H), 4.15–4.18 (m, 4H), 4.41–4.44 (m, 4H), 5.40 (d, J = 16 Hz, 4H), 6.28 (s, 4H), 7.05–7.10 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 38.0, 59.3, 71.7, 72.0, 85.1, 106.2, 116.0, 118.5, 127.8, 128.4, 128.5, 129.3, 131.5, 133.1, 146.1, 156.7 ppm; HRMS (FAB): *m/z* calcd for $[M]^+$ ($C_{52}H_{50}N_4O_{10}S_8$): 1146.1293; found: 1146.1344.

Molecular clip 1d: The procedure described above for the preparation of **1a** was followed; in this case, the reaction of molecular clip **6d** (180 mg, 0.2 mmol), 1,3-dithiole-2-thione **7** (420 mg, 3.1 mmol), and triethyl phosphite (8.4 mL) afforded a light-yellow solid (35 mg, 16%). M.p. >312 °C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 2.40 (s, 12H), 3.83 (d, J = 16 Hz, 4H), 4.85 (d, J = 16 Hz, 4H), 5.97 (s, 4H), 6.96–7.08 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 20.7, 38.0, 85.0, 103.3, 118.2, 127.8, 128.7, 128.8, 129.1, 132.6, 132.7, 139.2, 156.9, 168.0 ppm (one carbon is missing, possibly because of signal overlap); HRMS (FAB): *m/z* calcd for $[M]^+$ ($C_{48}H_{34}N_4O_{10}S_8$): 1082.0041; found: 1082.0013.

Molecular clip 10: K_2CO_3 (1.5 g, 10.9 mmol) was added to a solution of molecular clip **9** (0.5 g, 0.9 mmol) and tosylate **4a** (1.4 g, 4.2 mmol) in DMF (14 mL) at ambient temperature. The mixture was stirred at 90 °C for 12 h before the solvent was evaporated under reduced pressure. The residue was partitioned between water (500 mL) and CH_2Cl_2 (500 mL) and the organic layer was washed with water (2×500 mL), dried ($MgSO_4$), and concentrated to give a crude product, which was then purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 4:96) to provide clip **10** as a yellow solid (580 mg, 57%). M.p. 149–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.36 (s, 12H), 3.50–4.20 (m, 52H), 5.49 (d, J = 16 Hz, 4H), 6.71 (s, 4H), 7.00–7.06 ppm (m, 10H); ^{13}C (100 MHz, $CDCl_3$, 298 K): δ = 37.4, 59.1, 70.2, 70.3, 70.5, 70.7, 70.8, 71.9, 85.1, 114.4, 127.8, 127.9, 128.0, 133.7, 150.4, 157.2 ppm (the signal of one carbon atom is missing, possibly because of signal overlap); HRMS (FAB): *m/z* calcd for $[M]^+$ ($C_{60}H_{82}N_4O_{18}$): 1147.5702; found: 1147.5704.

1,2-Bis[2-(4-bromophenylmethoxy)ethoxy]ethane (12): NaH (60%; 1.0 g, 24 mmol) was added in small portions to a solution of tri(ethylene glycol) (1.2 g, 8.0 mmol) in DMF (80 mL) and then the resulting mixture was stirred at room temperature for 1 h. 4-Bromobenzyl bromide (6.0 g, 24 mmol) was added and then the mixture was stirred at ambient temperature for 18 h. MeOH (5 mL) was added to quench the reaction and then the organic solvent was evaporated under reduced pressure. The residue was partitioned between H_2O (50 mL) and CH_2Cl_2 (50 mL) and the organic layer was dried ($MgSO_4$) and concentrated to give a crude product, which was purified by column chromatography (SiO_2; EtOAc/hexane, 3:7) to give compound **12** as a yellow oil (3.49 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.59–3.61 (m, 4H), 3.65–3.67 (m, 8H), 4.83 (s, 4H), 7.19 (d, J = 8 Hz, 4H), 7.43 ppm (d, J = 8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 69.6, 70.6, 70.6, 72.4, 121.3, 129.1, 131.3, 137.1 ppm; HRMS (ESI): *m/z* calcd for $[M+H]^+$ ($C_{20}H_{25}Br_2O_4$): 487.0120; found: 487.0119.

1,2-Bis{2-[4-(4-pyridyl)phenylmethoxy]ethoxy}ethane (14): 4-Pyridineboronic acid (**13**) (0.7 g, 5.5 mmol), MeOH (18 mL), and saturated aqueous Na_2CO_3 (9 mL) were added in turn to a mixture of **12** (1.1 g, 2.2 mmol), $[Pd(PPh_3)_4]$ (130 mg, 0.11 mmol), and tri-*tert*-butylphosphine (25 mM, 4.5 mL, 110 μmol) in toluene (28 mL). The mixture was then refluxed for 24 h. After being cooled to room temperature, the mixture was partitioned between aqueous NH_4OH (0.1 M, 80 mL) and CH_2Cl_2 (80 mL). The organic phase was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 2.5:97.5) to give compound **14** as a light-yellow oil (680 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.64–3.70 (m, 12H), 4.60 (s, 4H), 7.42–7.48 (m, 8H), 7.58 (d, J = 8 Hz, 4H), 8.61 ppm (d, J = 6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 69.7, 70.7, 70.7, 72.9, 121.4, 126.9, 128.2, 137.0, 139.4, 148.1, 149.7 ppm; HRMS (ESI): *m/z* calcd for $[M+Na]^+$ ($C_{30}H_{32}N_2O_4Na$): 507.2260; found: 507.2259.

Macrocycle 11·2PF$_6$: A mixture of **14** (700 mg, 1.4 mmol), α,α′-dibromo-*p*-xylene (380 mg, 1.4 mmol), and KPF_6 (270 mg, 1.4 mmol) was stirred in DMF (200 mL) at room temperature for 7 days. The organic solvent was evaporated under reduced pressure, the residue was dissolved in MeCN (20 mL), and then saturated aqueous NH_4PF_6 (30 mL) was added. The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to afford a white solid, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 3:97) to afford macrocycle **11**·2PF$_6$ as a yellow solid (550 mg, 43%). M.p. >272 °C (decomp); ^{1}H NMR (400 MHz, CD_3CN, 298 K): δ = 3.53 (s, 4H), 3.55–3.58 (m, 8H), 4.56 (s, 4H), 5.67 (s, 4H), 7.50 (d, J = 8 Hz, 4H), 7.62 (s, 4H), 7.77 (d, J = 8 Hz, 4H), 8.13 (d, J = 7 Hz, 4H), 8.68 ppm (d, J = 7 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 64.4, 70.7, 71.1, 71.4, 72.7, 125.9, 128.9, 129.5, 131.1, 133.1, 136.6, 144.5, 144.6, 157.1 ppm; HRMS (ESI): *m/z* calcd for $[\mathbf{11}\cdot PF_6]^+$ ($C_{38}H_{40}F_6N_2O_4P$): 733.2624; found: 733.2678.

[2-(4-Bromophenyl)-1,3-dioxolan-2-yl]methanol (17): (4-Bromobenzoyl)-methanol (6.45 g, 30 mmol), ethylene glycol (9.3 g, 0.15 mol), and TsOH (200 mg, 11.6 mmol) were dissolved in benzene (300 mL) and then refluxed for 3 h in glassware equipped with a Dean–Stark apparatus. The reaction mixture was then cooled to room temperature and the organic solvent was evaporated. The residue was partitioned between H_2O (300 mL) and CH_2Cl_2 (300 mL) and the organic layer was dried ($MgSO_4$) and concentrated. The crude product was then purified by column chromatography (SiO_2; hexane/CH_2Cl_2, 4:7) to give alcohol **17** as a white solid (5.65 g, 73%). M.p. 93–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.68 (s, 2H), 3.83–3.86 (m, 2H), 4.08–4.12 (m, 2H), 7.34 (d, J = 6 Hz, 2H), 7.47 ppm (d, J = 6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 65.8, 67.2, 109.2, 122.9, 128.0, 131.5, 138.7 ppm; HRMS (FAB): *m/z* calcd for $[M+H]^+$ ($C_{10}H_{12}BrO_3$): 258.9970; found: 259.0000.

2,2′-(2,5,8,11-Tetraoxadodecane-1,12-diyl)bis[2-(4-bromophenyl)-1,3-dioxolane] (18): Alcohol **17** (2.26 g, 8.8 mmol) and NaH (60%; 370 mg, 15 mmol) were added to DMF (70 mL). The mixture was stirred at room temperature for 1 h before tri(ethylene glycol) ditosylate (1.36 g, 3 mmol) was added slowly. The resulting mixture was stirred for 4 h and then the reaction was quenched by the addition of MeOH (5 mL). The organic solvent was evaporated under reduced pressure and the residue was partitioned between H_2O (100 mL) and CH_2Cl_2 (100 mL). The organic layer was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was purified by column chromatography (SiO_2; MeCN/CH_2Cl_2, 3:97) to give compound **18** as a yellow oil (1.02 g, 54%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.49 (s, 4H), 3.53–3.55 (m, 4H), 3.63–3.67 (m, 8H), 3.79–3.83 (m, 4H), 4.06–4.09 (m, 4H), 7.35 (d, J = 6 Hz, 4H), 7.43 ppm (d, J = 6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ = 65.2, 70.5, 70.5, 71.6, 75.2, 108.4, 122.0, 127.6, 130.7, 138.8 ppm; HRMS (FAB): *m/z* calcd for $[M+H]^+$ ($C_{26}H_{33}Br_2O_8$): 631.0542; found: 631.0500.

4,4′-[2,5,8,11-Tetraoxadodecane-1,12-diylbis(1,3-dioxolane-2,2-diyl-4,1-phenylene)]dipyridine (19): 4-Pyridineboronic acid **13** (0.22 g, 1.8 mmol), MeOH (6 mL), and saturated aqueous Na_2CO_3 (3 mL) were added in turn to a mixture of **18** (0.4 g, 630 μmol), $[Pd(PPh_3)_4]$ (42 mg, 40 μmol), and tri-*tert*-butylphosphine (25 mM, 1.44 mL, 40 μmol) in toluene (9 mL).

This mixture was then refluxed for 24 h. After cooling to room temperature, the mixture was partitioned between aqueous NH_4OH (0.1 M, 20 mL) and CH_2Cl_2 (20 mL). The organic phase was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 4:96) to give compound **19** as a light-yellow oil (290 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): $\delta = 3.51$ (s, 4H), 3.54–3.66 (m, 4H), 3.67–3.69 (m, 4H), 3.70 (s, 4H), 3.84–3.87 (m, 4H), 4.10–4.13 (m, 4H), 7.49 (d, $J = 6$ Hz, 4H), 7.60 (s, 8H), 8.63 ppm (br, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): $\delta = 65.2$, 71.5, 75.2, 108.6, 121.4, 126.5, 126.8, 137.7, 141.1, 147.8, 149.8 ppm (the signals of two carbon atoms are missing, possibly because of signal overlap); HRMS (FAB): m/z calcd for $[M+H]^+$ ($C_{36}H_{41}N_2O_8$): 629.2863; found: 629.2900.

Macrocycle 20·2PF$_6$: A mixture of **19** (1.0 g, 1.6 mmol), α,α′-dibromo-*p*-xylene (0.4 g, 1.6 mmol), and KPF_6 (0.33 g, 1.6 mmol) in DMF (230 mL) was stirred at room temperature for 7 days. The solvent was evaporated under reduced pressure, the residue was dissolved in MeCN (20 mL), and then saturated aqueous NH_4PF_6 (30 mL) was added. The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to afford a white solid, which was purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 5:95) to afford macrocycle **20**·2PF$_6$ as a yellow solid (1.40 g, 86%). M.p. 179–182 °C; ^{1}H NMR (400 MHz, CD_3CN, 298 K): $\delta = 3.33$–3.36 (m, 8H), 3.47–3.49 (m, 4H), 3.66 (s, 4H), 3.83–3.85 (m, 4H), 4.03–4.05 (m, 4H), 5.70 (s, 4H), 7.60 (s, 4H), 7.66 (d, $J = 9$ Hz, 4H), 7.82 (d, $J = 9$ Hz, 4H), 8.19 (d, $J = 7$ Hz, 4H), 8.69 ppm (d, $J = 7$ Hz, 4H); ^{13}C NMR (100 MHz, CD_3CN, 298 K): $\delta =$ 64.2, 65.9, 68.2, 70.6, 70.7, 71.8, 75.6, 108.8, 126.1, 128.5, 131.1, 133.9, 136.1, 145.0, 146.0, 157.0 ppm; HRMS (FAB): m/z calcd for $[\mathbf{20}\cdot PF_6]^+$ ($C_{44}H_{48}O_8N_2F_6P$): 877.3052; found: 877.3062.

Macrocycle 16·2PF$_6$: Macrocycle **20**·2PF$_6$ (0.4 g, 0.4 mmol) and TsOH (8.5 mg, 40 μmol) were dissolved in a mixture of H_2O (1 mL) and acetone (2 mL) and then refluxed for 3 days. The organic solvent was evaporated under reduced pressure, the residue was dissolved in MeCN (20 mL), and then saturated aqueous NH_4PF_6 (30 mL) was added. The organic solvent was evaporated and the resulting precipitate was collected and washed with H_2O (3 mL) to give a crude product, which was then purified by column chromatography (SiO_2; MeOH/CH_2Cl_2, 5:95) to afford the macrocycle **16**·2PF$_6$ as a light-yellow solid (127 mg, 34%). M.p. >245 °C (decomp); ^{1}H NMR (400 MHz, CD_3CN, 298 K): $\delta = 3.46$ (s, 4H), 3.51–3.54 (m, 4H), 3.63–3.65 (m, 4H), 4.67 (s, 4H), 5.71 (s, 4H), 7.62 (s, 4H), 7.89 (d, $J = 8$ Hz, 4H), 8.08 (d, $J = 8$ Hz, 4H), 8.19 (d, $J = 8$ Hz, 4H), 8.74 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, CD_3CN, 298 K): $\delta =$ 65.1, 71.3, 71.6, 71.9, 76.2, 127.3, 129.8, 130.9, 131.8, 136.9, 138.9, 139.1, 145.6, 156.9, 198.2 ppm; HRMS (FAB): m/z calcd for $[\mathbf{16}\cdot PF_6]^+$ ($C_{40}H_{40}O_6N_2F_6P$): 789.2528; found: 789.2540.

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