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Operating Molecular Elevators

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Abstract: Inspired by the concept of multivalency in living systems, two mechanically interlocked molecules have been conceived that incorporate not once or twice but thrice the features of a pH-switchable [2]rotaxane with two orthogonal recognition sites for dibenzo[24]crown-8 (DB24C8), and 2,3-dinaphtho[24]crown-8 (DN24C8)—one a dialkylammonium ion ($CH_2NH_2^+CH_2$) and the other a bipyridinium dication ($BIPY^{2+}$). Whereas at low pH, the $CH_2NH_2^+CH_2$ sites bind the DB24C8/DN24C8 macrocycles preferentially, at high pH, deprotonation occurs with loss of hydrogen bonding and the macrocycles will move to the $BIPY^{2+}$ sites, where they can acquire some stabilizing [$\pi-\pi$] stacking interactions. Such mechanically interlocked molecules have been assembled from a trifurcated rig-like component wherein the dumbbell-like components of three [2]rotaxanes have one of their ends fused onto alternate positions (1,3,5) around a benzenoid core. The rig is mechanically interlocked by a platform based on a tritopic receptor, wherein either three benzo[24]crown-8 or three 2,3-naphtho[24]crown-8 macrocycles are fused onto a hexaoxatriphenylene core. The synthesis of these molecular elevators involves 1:1 complexation, followed by stoppering, i.e., feet are added to the rig. ^{1}H NMR spectroscopy and cyclic voltammetry, aided and abetted by absorption spectroscopy, have been employed to unravel the details of the mechanism by which the rig and platform components move on the alternate addition of base and acid. For each molecular elevator, the platform operates by taking three distinct steps associated with each of the three deprotonation/reprotonation processes. Thus, molecular elevators are more reminiscent of a legged animal than they are of passengers on freight elevators.

Introduction

Natural molecular machines,[1,2] such as ATP synthase, myosin, kinesin, or dynein, are complex and inspiring assemblies[3] whose structures and working mechanisms have been elucidated in a few cases.[4,5] These intriguing systems have prompted scientists to design and build artificial molecular machines[6] by mimicking their biological counterparts. In this sense, phenomena that control the form and function of living systems, such as self-assembly,[7] molecular recognition,[8] and multivalency,[9] have been employed in supramolecular chemistry[10] and template-directed synthesis[11] in order to construct functional molecular devices. Attempts to extend the concept of a machine to the molecular

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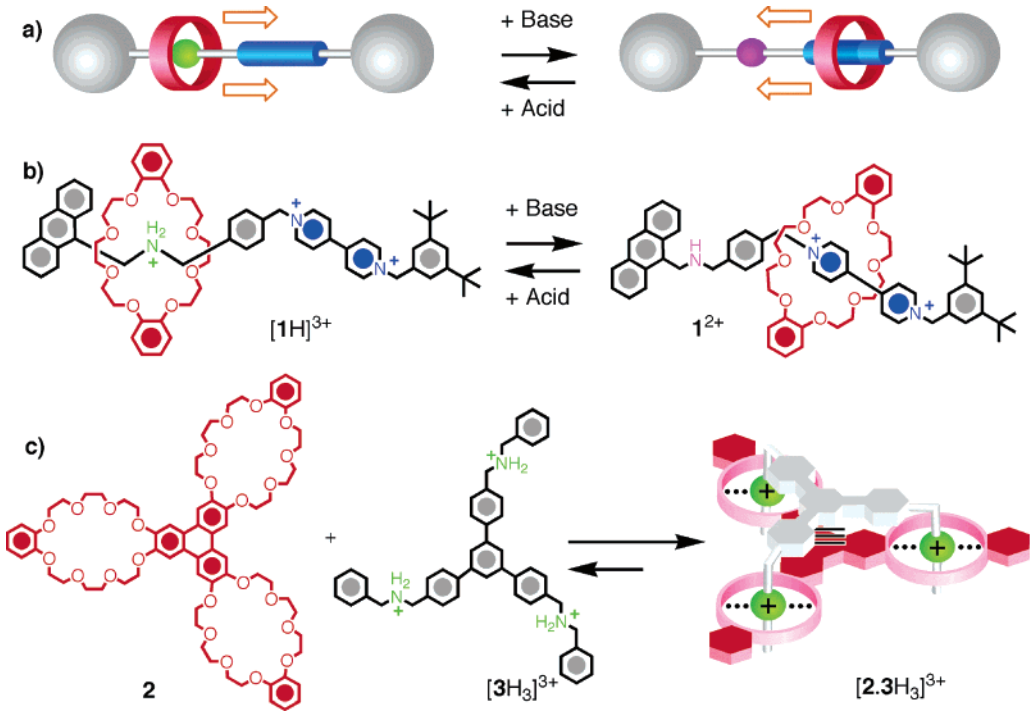
Scheme 1 [a]



[a] Part a) depicts a schematic representation of a switchable [2]rotaxane composed of a rod-shaped component bearing two different recognition sites, encircling a dumbbell-shaped component. As shown in part b), the recognition sites are a dialkylammonium center ($-NH_2^+-$) and a bipyridinium ($BIPY^{2+}$) unit, which serve as stations for the dibenzo[24] crown-8 (DB24C8) component.[22b] The preferred $-NH_2^+-$ center for the DB24C8 is related to the formation of strong hydrogen bonds. On addition of base, the $-NH_2^+-$ center is deprotonated and the DB24C8 moves to the $BIPY^{2+}$ unit, where donor−acceptor interactions become stabilizing. In part c) is shown the equilibrium between the tris-crown ether **2** and the tris-ammonium ion $[\mathbf{3}H_3]^{3+}$, which lies to the right in favor of the superbundle in solvents.[25a]

level, by taking advantage of biomimicry, have yielded a plethora of switches,[12,13] tweezers,[14] shuttles,[15] and even molecular muscles,[16] walkers,[17] and rotary motors.[18] Each of these molecular machines has been designed specifically to perform particular functions upon application of an external energy input.[19]

The concept of multivalency[9] is exemplified in many living systems. The recognition of carbohydrate ligands by bacterial and mammalian lectins is only one example of this phenomenon. Specific inhibition of recognition events of this type has been proposed as therapeutic modalities for the neutralization of bacterial toxins, the prevention of viral and bacterial infections, and the treatment of cancer. Transferring this concept from natural settings into an unnatural, wholly synthetic one has already been investigated during the preparation of some intricate supramolecular assemblies.[20] Stimulated by the potential of the multivalency in building stable and yet complex molecular assemblies, we have recently constructed, using the bottom-up approach, a nanoscale molecular elevator that incorporates and expresses multivalency in its structure and operation.[21] This molecular elevator derives from a switchable [2]rotaxane[22] which comprises a ring component encircling a dumbbell-shaped component bearing two different recognition centers (Scheme 1). One of the recognition centers is a

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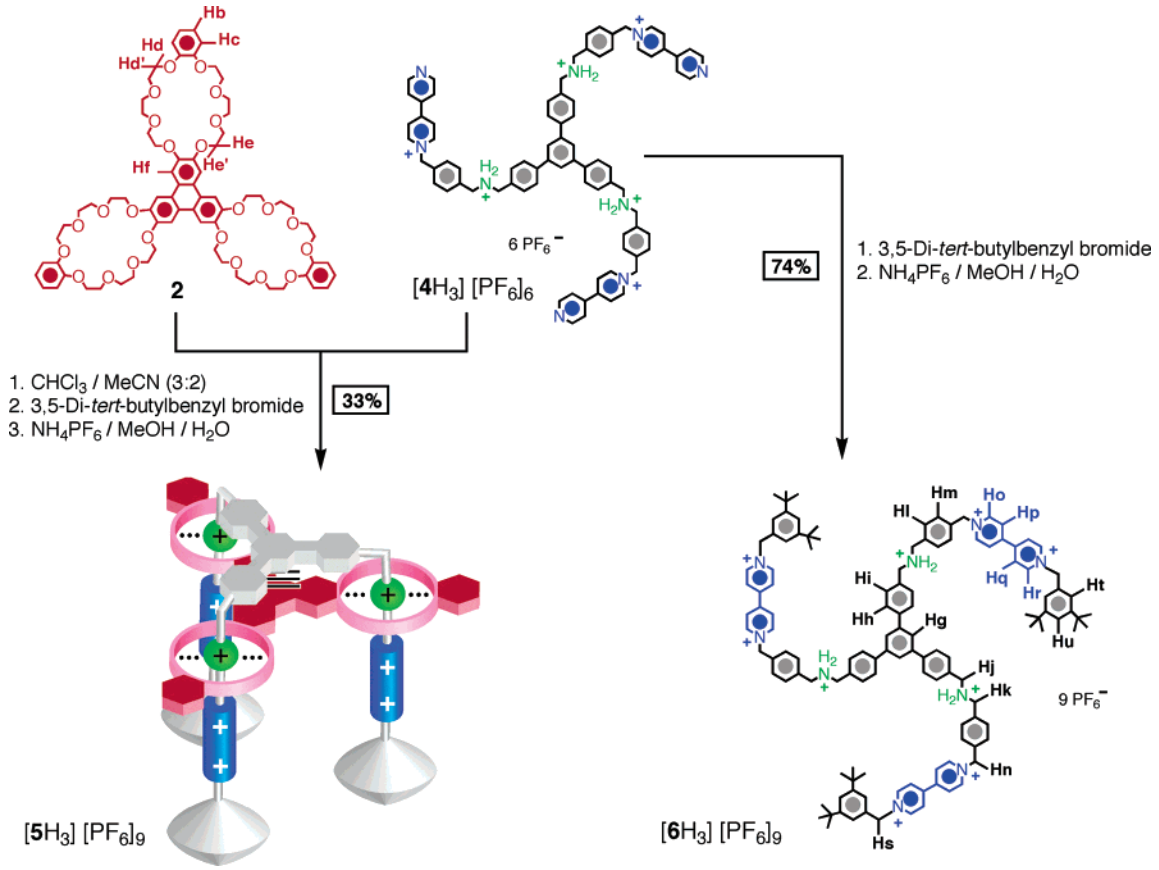
Scheme 2 [a]



[a] The trifurcated guest salt $[\mathbf{4}H_3][PF_6]_6$ and the tritopic host **2** in a $CHCl_3$/MeCN solution (3.0 mL, 2:1) form a 1:1 adduct (superbundle) that was converted to the molecular elevator $[\mathbf{5}H_3][PF_6]_9$ in the reaction with (i) 3,5-di-*tert*-butylbenzyl bromide, followed by (ii) counterion exchange (NH_4PF_6/MeOH/H_2O).

secondary dialkylammonium ($-NH_2^+-$) center and the other is a bipyridinium ($BIPY^{2+}$) unit. They show different affinities toward dibenzo[24]crown-8 (DB24C8), the ring component present in the [2]rotaxane. Previously, we have demonstrated, using a variety of techniques, that in both Me_2CO and MeCN, the DB24C8 ring resides exclusively around the ($-NH_2^+-$) center. X-ray crystallography has revealed[23] that this preference results from a combination of strong [$^+$N—H···O] hydrogen-bonding and weak [C—H···O] interactions, amplified by some stabilizing [$\pi-\pi$] stacking forces between the components. Upon addition of an excess of the base iPr$_2$NEt to the [2]rotaxane in $(CD_3)_2CO$ solution, deprotonation of the ammonium recognition site occurs. As a result, the intercomponent hydrogen bonds are destroyed and the DB24C8 ring moves to the $BIPY^{2+}$ recognition site as a consequence of Brownian motion.[24] However, the original co-conformation can be restored by the addition of the acid CF_3CO_2H, since the protonation of the ($-NH_2^+-$) recognition site is followed by shuttling of the ring by means of further Brownian movement back to the reformed ($-NH_2^+-$) center. The switching of the ring between the two recognition sites can be monitored by ^{1}H NMR spectroscopy and by electrochemical techniques.

The synthesis of the [2]rotaxane was achieved by the formation of a stable 1:1 complex by threading of a precursor thread containing the ($-NH_2^+-$) center with the ring, followed by stoppering at the threads' open ends to interlock the ring mechanically into place. In pursuit of a yet more intricate threaded structure than the switchable [2]rotaxane (Scheme 1a), we designed a molecular elevator.[21] The enhanced stability offered by the molecular elevator can be achieved in two different ways: (1) by clustering together multiple copies of the recognition centers in order to act in a multivalent fashion[25] and (2) by modifying one of the components in order to effect stronger hydrogen bonding and/or [$\pi-\pi$] stacking interactions. For our initial investigations on multivalency using the two nondegenerate recognition centers, we synthesized the first

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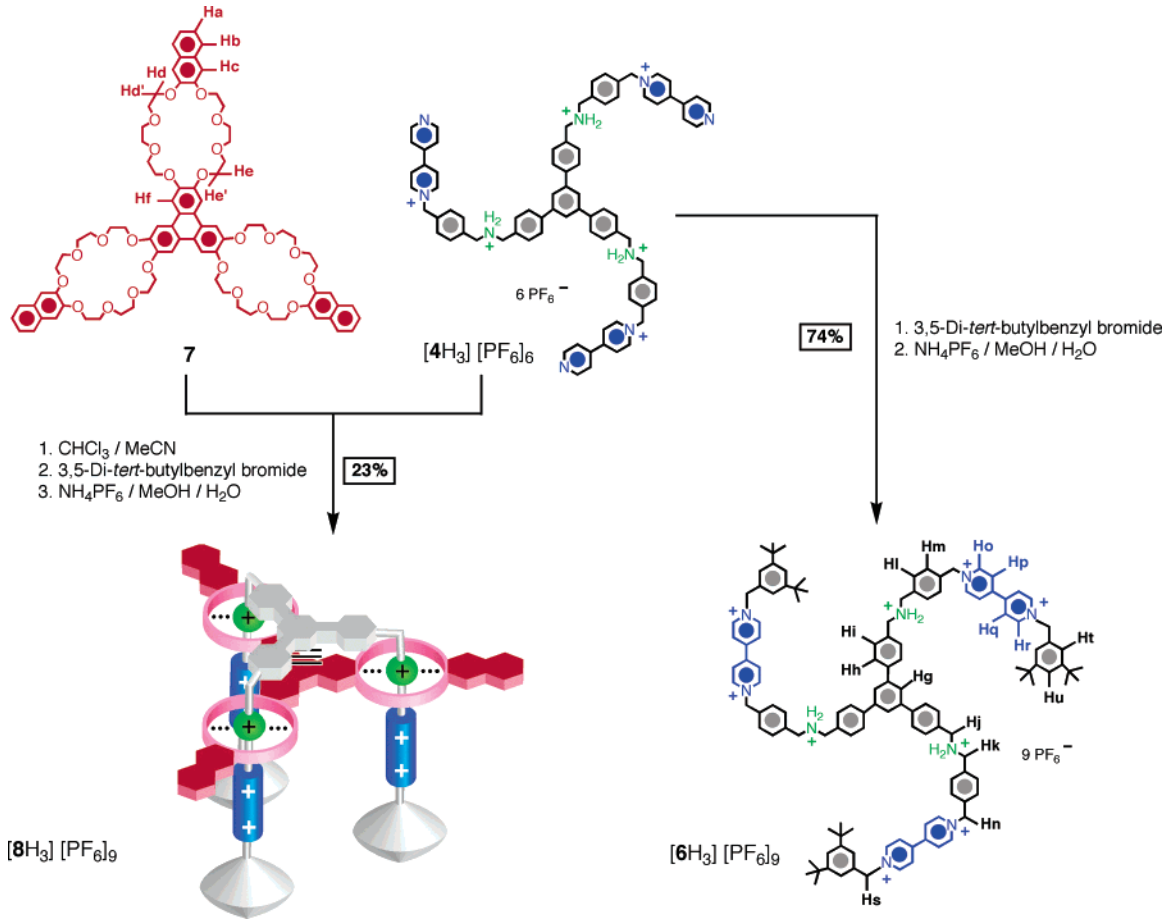
Scheme 3 [a]



[a] The trifurcated guest salt [**4**H$_3$][PF$_6$]$_6$ and the tritopic host **7** in a CHCl$_3$/MeCN solution (3.0 mL, 2:1) form a 1:1 adduct (superbundle) that was converted to the molecular elevator [**8**H$_3$][PF$_6$]$_9$ in the reaction with (i) 3,5-di-*tert*-butylbenzyl bromide, followed by (ii) counterion exchange (NH$_4$PF$_6$/MeOH/H$_2$O).

generation molecular elevator from two components. A trifurcated rig-like component bears three of the dumbbell-like components of the [2]rotaxane fused at one of their ends to a central aromatic core. The rig is interlocked by a tritopic receptor in the form of a tris-crown ether derivative **2**. This tris-crown ether consists of three benzo[24]crown-8 macrorings fused onto a triphenylene core. Once the molecular elevator has been formed, the tris-crown ether can be induced to stop at the two different levels, following the protocol of the addition of acid and base established for the [2]rotaxane (Scheme 1).

The objective of this work was to study and compare the preparation, characterization, and operation of two generations of the trivalent mechanically interlocked molecular machines—molecular elevators—in order to understand the properties and operational mechanisms of these kinds of artificial machines as a prelude to optimizing their performance. To achieve this goal we have modified the tritopic receptor in the [**5**H$_3$][PF$_6$]$_9$ by introducing dioxynaphthalene π-electron-rich units onto the termini. The extended aromatic units confer stronger electron-donating power compared with the simple benzo units. These additional structural features should direct and enhance the formation of [$\pi-\pi$] stacking and charge-transfer (CT) interactions with the electron-acceptor bipyridinium (BIPY^{2+}) units.[26] Herein, we report specifically (1) the synthesis of two tris-crown ether derivatives containing catechol and 2,3-dioxynaphthalene π-electron-rich units, respectively, to give the first and second generations of the molecular machines that act like nanometer-scale elevators; (2) the elevators' characterization by mass spectrometry and ^{1}H NMR spectroscopy; (3) the chemical switching processes by ^{1}H NMR spectroscopy; and (4) fluorescence titration (Job plots), UV−vis spectroscopy, and electrochemical switching of these molecular elevators in solution.

Results and Discussion

Synthesis. The molecular elevators [**5**H$_3$][PF$_6$]$_9$ and [**8**H$_3$][PF$_6$]$_9$ were synthesized[27] using a template-directed approach (Schemes 2 and 3) in 33 and 23% yield, respectively. The superbundles were first assembled as 1:1 adducts between the trifurcated rig-like component [**4**H$_3$][PF$_6$]$_6$ and the tris-crown ethers **2** and **7**, respectively, in CHCl$_3$/MeCN (3:2). These 1:1 adducts in CHCl$_3$/MeCN (3:2) were next reacted with 3,5-di-*tert*-butylbenzyl bromide followed by counterion exchange (NH$_4$PF$_6$/MeOH/H$_2$O) to afford the molecular elevators [**5**H$_3$]-

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(27) Full experimental procedures for all synthetic steps are available in the Supporting Information.

$[PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$ which, along with the rig component $[\mathbf{6}H_3][PF_6]_9$, were characterized by mass spectrometry, ^1H and ^{13}C NMR spectroscopies, and also absorption and fluorescence spectroscopies and electrochemistry.

Characterization. High-resolution electrospray ionization (HR-ESI) mass spectrometry revealed (Figure 1) that the most intense peaks in the spectra occurred at $m/z = 1331.1704$ and 1381.1919 for the $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, respectively, with an isotope distribution corresponding to the $[M - 3PF_6]^{3+}$ ion. This result supports the structural assignments of the mechanically interlocked bundles shown in Schemes 2 and 3.

The compounds **2**, **7**, $[\mathbf{6}H_3][PF_6]_9$, $[\mathbf{5}H_3][PF_6]_9$, and $[\mathbf{8}H_3][PF_6]_9$ were all characterized by ^1H NMR spectroscopy (Figure 2), including $^1H-^1H$ COSY and TROESY two-dimensional experiments in order to achieve full assignments in the cases of $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$. The ^1H NMR spectra of $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$ reveal (Figure 2a,b) a complex array of resonances corresponding to triply threaded, mechanically interlocked molecules with averaged C_{3v} symmetry. Three more features are highlighted by the ^1H NMR spectroscopic results, namely (i) the interlocked nature of the two components in both molecular elevators, (ii) the stabilization in both molecular elevators by $[\pi-\pi]$ stacking interactions between the aromatic cores of the individual components, and (iii) the diastereotopicities of the OCH_2 protons in crown ethers **2** and **7** as soon as they form 1:1 adducts. These points are now discussed in turn.

The characteristic downfield shifts and multiplicities[25] of the resonances for the methylene protons adjacent to the secondary dialkylammonium ($-NH_2^+-$) centers—specifically, H_j and H_k resonating at δ 4.92 and 4.79 ppm in the case of $[\mathbf{5}H_3][PF_6]_9$, and at δ 4.92 and 4.83 ppm in the case of $[\mathbf{8}H_3][PF_6]_9$—demonstrate that the platforms' tris-crown ethers bind selectively with the three $-NH_2^+-$ centers in the legs of the trifurcated rigs. The resonances of the trifurcated rigs' aromatic core protons—namely, H_g in $[\mathbf{6}H_3][PF_6]_9$ ($\Delta\delta = -0.54$ and -0.59 for the molecular elevators $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, respectively) and H_f in **2** and **7** ($\Delta\delta = -0.33$ and -0.40 for molecular elevators $\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, respectively)—are shifted upfield significantly relative to the chemical shifts of the analogous protons in the separate components, indicating that there are some $[\pi-\pi]$ stacking interactions of the central aromatic cores of the components with each other.

Inspection of the region between δ 3.8 and 4.6 ppm in the ^1H NMR spectra (Figure 2a,b) reveals that the protons $H_{d/d'}$ and $H_{e/e'}$ in the tris-crown ether derivatives **2** and **7** separate into two different sets of signals as a consequence of losing their planes of symmetry orthogonal to the principal axes in the molecules. In other words, the pairs of protons in each of the *O*-methylene groups that are directed toward the hub of $[\mathbf{6}H_3][PF_6]_9$ become diastereotopic with respect to those which are directed away from the hub. Thus, all the ^1H NMR spectroscopic evidence supports the mechanically interlocked, triply threaded structures proposed in Schemes 2 and 3 for the molecular elevators $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$.

Incorporation of naphtho groups into the tris-crown ether derivative **7** provides the possibility of $[\pi-\pi]$ stacking interactions between the bipyridinium units of the rigs and the dioxynaphthalene units in the tris-crown ether. The ^1H NMR spectra (Figure 2) of the two molecular elevators indicate evidence for $[\pi-\pi]$ stacking interactions in solution: the signals for the H_o protons in bipyridinium units are successively shifted upfield, that is, from δ 9.0 to 8.82 to 8.70 ppm for $[\mathbf{6}H_3][PF_6]_9$

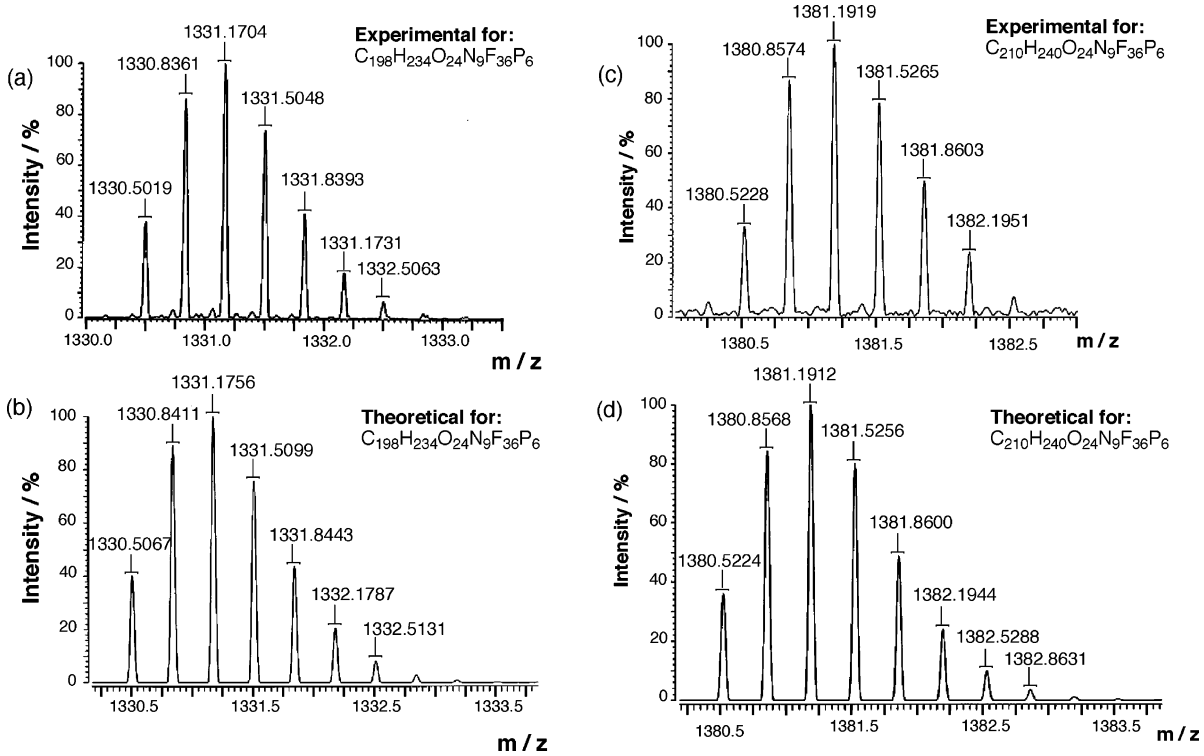


Figure 1. High-resolution electrospray ionization (HR-ESI) mass spectrometry: (a,c) experimental isotopic distribution with peaks at $m/z = 1331.1704$ and 1381.1919 corresponding to the $[M - 3PF_6]^{3+}$ ions for the molecular elevators $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, respectively; (b,d) calculated isotopic distribution with peaks at $m/z = 1331.1756$ and 1381.5256 corresponding to the $[M - 3PF_6]^{3+}$ ions of the molecular elevators $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, respectively.

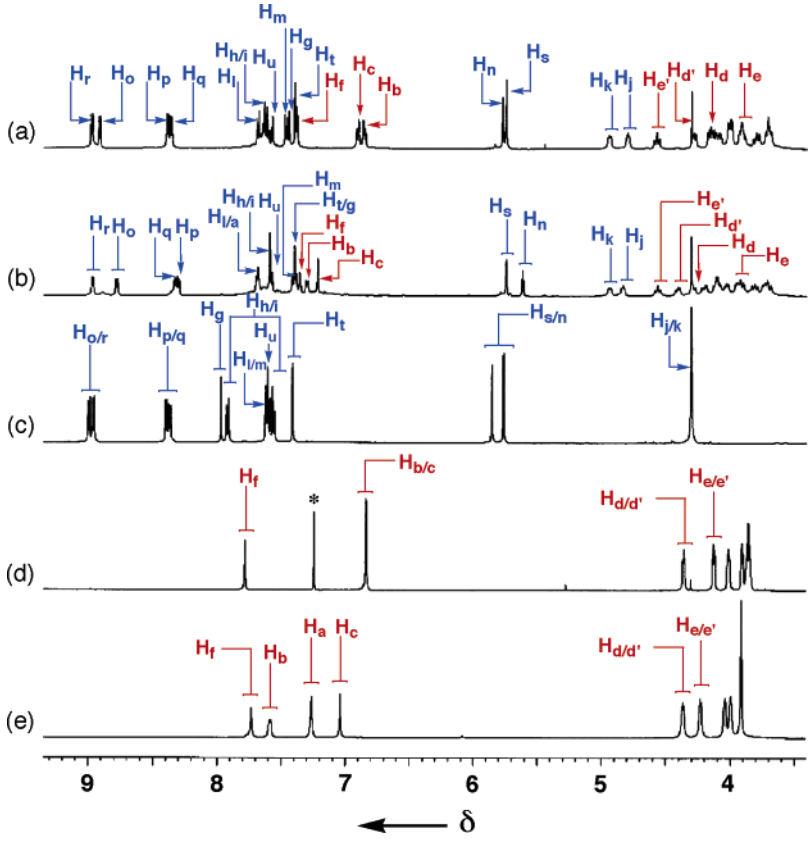


Figure 2. ^{1}H NMR spectra (500 MHz, 298 K) recorded on (a) [**5**H$_3$][PF$_6$]$_9$ (in CD$_3$CN), (b) [**8**H$_3$][PF$_6$]$_9$ (in CD$_3$CN), (c) [**6**H$_3$][PF$_6$]$_9$ (in CD$_3$CN), (d) the tris-crown ether **2** (in CDCl$_3$), and (e) the tris-crown ether **7** (in CDCl$_3$).

and the molecular elevators [**5**H$_3$][PF$_6$]$_9$ and [**8**H$_3$][PF$_6$]$_9$, respectively.

Absorption and Fluorescence Spectra. The electronic absorption spectra of the molecular elevators [**5**H$_3$]$^{9+}$ and [**8**H$_3$]$^{9+}$ in MeCN solution (see Supporting Information) show bands in the near-UV region that can be assigned to transitions localized on the various chromophoric units[28] contained in the molecular components, namely 1,3,5-triphenylbenzene, hexaoxytriphenylene, and 1,2-dioxybenzene or 2,3-dioxynaphthalene in the case of [**5**H$_3$]$^{9+}$ or [**8**H$_3$]$^{9+}$, respectively. The absorption spectra of the molecular elevators, however, differ from the sum of the spectra of their separated rig and tris-crown ether components, indicating the presence of intercomponent electronic interactions. However, no new absorption band at wavelengths longer than 400 nm, typical of donor−acceptor interactions between the electron-rich units of the tris-crown ether components and the electron-deficient bipyridinium units of the rig, can be seen.

The intense fluorescence band of the 1,3,5-triphenylbenzene unit (λ_{max} = 359 nm for model compound [**3**H$_3$]$^{3+}$)[25] is strongly quenched in the rig compound [**6**H$_3$]$^{9+}$, most likely because of an electron-transfer process from the excited state of the triphenylbenzene core to a BIPY^{2+} unit in one of the three legs. Both tris-crown ethers **2** and **7** exhibit the typical[28] fluorescence of their hexaoxytriphenylene core (λ_{max} = 383 nm) and no emission from their 1,2-dioxybenzene or 2,3-dioxynaphthalene units. Fluorescence excitation spectra show that an efficient energy transfer from the peripheral chromophoric groups to the central hexaoxytriphenylene unit takes place, as can be expected on the basis of their excited-state energies. The luminescence bands of **2** or **7** can still be observed in the corresponding molecular elevators, but their intensities are reduced by factors of more than 200 in the case of [**5**H$_3$]$^{9+}$ and of about 70 in the case of [**8**H$_3$]$^{9+}$. The fluorescence band, originating from [$\pi-\pi$] stacking of the hexaoxytriphenylene and triphenylbenzene units, that was observed[25] for related superbundle systems cannot be seen for the molecular elevators. Such quenching phenomena are most likely related to electron-transfer processes involving the bipyridinium units, which are easily reducible (vide infra).

Electrochemical Properties. The molecular elevators contain several electroactive units in their molecular components, and are therefore expected to exhibit a rich redox behavior. In the potential window examined (from −2 to +2 V vs SCE), the rig component [**6**H$_3$]$^{9+}$ shows two reversible reduction processes and no oxidation (Table 1). Chronoamperometric experiments indicate that each reduction process involves the exchange of three electrons. Since it is well known[29] that the 4,4′-bipyridinium unit undergoes two successive, reversible monoelectronic reduction processes at about −0.4 and −0.8 V versus SCE, we conclude that the three BIPY^{2+} units of [**6**H$_3$]$^{9+}$ are equivalent and behave independently of one another. The tris-crown ethers **2** and **7** show three irreversible oxidation processes and no reduction (Table 1).

(28) (a) Berlman, I. B. *Handbook of Fluorescence Spectra of Aromatic Molecules*; Academic Press: New York, 1965. (b) Montalti, M.; Credi, A.; Prodi, L.; Gandolfi, M. T. *Handbook of Photochemistry*, 3rd ed.; CRC Press: Boca Raton, FL, in press.

(29) Monk, P. M. S. *The Viologens. Physicochemical Properties, Synthesis and Application of the Salts of 4,4′-Bipyridine*; Wiley: Chichester, U.K., 1995.

Table 1. Electrochemical Data for the Molecular Elevators, Their Molecular Components, and Model Compounds[a]

compound	reduction $E_{1/2}'$ [b]	reduction $E_{1/2}''$ [b]	oxidation E_p[c]
HMTP[d]			+1.02
2[e]			+0.99
7[e]			+0.94
DBV^{2+} [e,f]	−0.342	−0.779	
$[\mathbf{6}H_3]^{9+}$	−0.347	−0.793	
$\mathbf{6}^{6+}$ [g]	−0.350	−0.795	
$[\mathbf{5}H_3]^{9+}$	−0.340	−0.764	+1.08[h]
$\mathbf{5}^{6+}$ [g]	−0.528	−0.879	+1.09[h,i]
$[\mathbf{8}H_3]^{9}$	−0.343	−0.764	+1.09[h]
$\mathbf{8}^{6+}$ [g]	−0.542	−0.897	+1.10[h,i]

[a] MeCN solution, 5.0×10^{-4} mol L^{-1}, 0.05 mol L^{-1} tetraethylammonium hexafluorophosphate, glassy carbon, 298 K. [b] Half-wave potential values of reversible processes in volts versus SCE; experimental error, ±5 mV. [c] Irreversible processes, potential values in volts versus SCE obtained from DPV peaks; experimental error, ±10 mV. [d] 2,3,6,7,10,11-Hexamethoxytriphenylene. [e] The redox behavior is not affected by the addition of P_1-*t*-Bu base and trifluoroacetic acid. [f] 1,1′-Dibenzyl-4,4′-bipyridinium. [g] Obtained by deprotonation of the corresponding protonated form with 3.3 equiv of P_1-*t*-Bu base. [h] First oxidation process; see text for details. [i] Process characterized by a much lower current intensity compared to the corresponding protonated species.

Comparison with model compounds allows for a safe assignment of each process to a specific redox-active unit. In both cases, the first oxidation process is attributed to the hexaoxytriphenylene core, and the two successive oxidation processes are attributed to the dioxybenzene (in the case of **2**) or dioxynaphthalene (in the case of **7**) units interacting with one another. The molecular elevators $[\mathbf{5}H_3]^{9+}$ and $[\mathbf{8}H_3]^{9+}$ show both reduction and oxidation processes. On reduction, they exhibit two successive reversible three-electron processes (Table 1 and Figure 3), at potential values very similar to those found for the rig component $[\mathbf{6}H_3]^{9+}$. This observation indicates that in the molecular elevators the three $BIPY^{2+}$ units are again equivalent, behave independently from one another, and are not engaged[30] in electron donor−acceptor interactions with the dioxyaromatic units of the tris-crown ether platform. Such a result is fully consistent with the location of the platform component on the upper level, with its three crown ether rings encircling the $-NH_2^+-$ centers, in agreement with the ^1H NMR spectroscopic data. On the oxidation side, the molecular elevators show one irreversible process (Table 1), assigned to oxidation of the hexaoxybenzene core, and other broad voltammetric peaks at potential values higher than +1.3 V, assigned to irreversible oxidation of the peripheral dioxyaromatic units. Because of their irreversible nature and poor definition, these processes will not be further discussed.

Chemical Switching. One of the reasons for assembling mechanically interlocked compounds, such as the molecular elevators $[\mathbf{5}H_3][PF_6]_9$ and $[\mathbf{8}H_3][PF_6]_9$, is to construct machines on the nanoscale level, wherein their operation can be controlled through acid/base external input. We have already established that the tris-crown ether components **2** and **7** reside exclusively on the $-NH_2^+-$ recognition centers (upper level). Bases that can deprotonate these centers could act as chemical inputs, promoting the movement of the tris-crown ethers toward the bipyridinium ($BIPY^{2+}$) units (lower level).

The choice of the base for deprotonation of $-NH_2^+-$ centers in $[\mathbf{5}H_3][PF_6]_9$ was complicated on the account of our experimental observations, in line with our previous report[22a] that $BIPY^{2+}$ units can undergo a structural change if they are subjected to basic conditions. Addition of a slight excess of weakly nucleophilic bases, e.g., 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2,2,2]octane (DABCO), hexamethyldisilazane (HMDSZ), quinuclinide, 2,6-lutidine, and potassium *tert*-butoxide (*t*-BuOK), to $[\mathbf{5}H_3][PF_6]_9$ in different solvents (Table 2) led to either incomplete deprotonation of the $-NH_2^+-$ centers or decomposition of the $[\mathbf{5}H_3][PF_6]_9$. Incomplete deprotonations were reflected in complicated ^1H NMR spectra, whereas decomposition was signaled by the development of a dark blue color and ill-defined ^1H NMR spectra. In the case of incomplete deprotonation, subsequent addition of an equivalent amount of trifluoroacetic acid (TFA) regenerated the ^1H NMR spectrum of $[\mathbf{5}H_3][PF_6]_9$, fully suggesting the reversibility of the protonation/deprotonation process and indicating that these particular bases were simply not strong enough to cause deprotonation at all three $-NH_2^+-$ centers. These results are in agreement with our previous observation[25b] that a mechanically interlocked molecular bundle can be fully deprotonated when it is subjected to very strong base (*t*-BuOK). By contrast, the triply threaded supramolecular bundle can be easily deprotonated[25a] using a range of weak bases. The tris-crown ether hosts affect significantly the pK_a values of the trisammonium guest within the mechanically interlocked mo-

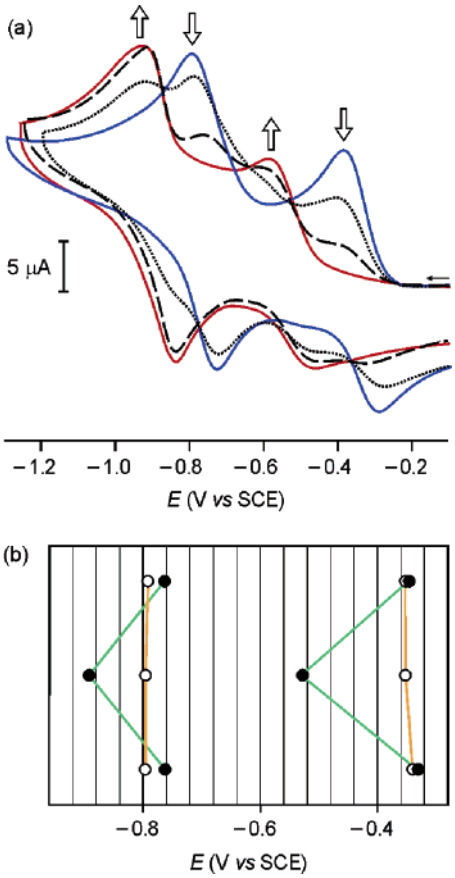


Figure 3. (a) Cyclic voltammetric curves for the reduction of the $BIPY^{2+}$ units in $[\mathbf{8}H_3]^{9+}$ (blue line), and in the deprotonated species $[\mathbf{8}H_2]^{8+}$ (dotted line), $[\mathbf{8}H]^{7+}$ (dashed line), and $\mathbf{8}^{6+}$ (red line), obtained from $[\mathbf{8}H_3]^{9+}$ on successive additions of P_1-*t*-Bu base. Conditions: MeCN solution, 5.0×10^{-4} mol L^{-1} molecular elevator, 0.05 mol L^{-1} tetraethylammonium hexafluorophosphate, glassy carbon electrode, 0.2 V s^{-1}, 298 K. (b) Diagram of the potential values for the reduction processes of the $BIPY^{2+}$ units of $[\mathbf{8}H_3]^{9+}$ (●) and $[\mathbf{6}H_3]^{9+}$ (○) (top), on addition of base to afford $\mathbf{8}^{6+}$ and, respectively, $\mathbf{6}^{6+}$ (middle), and after reprotonation with an acid, a stoichiometric amount with respect to the added base (bottom).

Table 2. Switching Process Using Different Bases

base	pK_a MeCN	solvent	temperature/ K	deprotonation
1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU)	18.3	CD_3CN	298	decomposition of $BIPY^{2+}$ units
1,4-diazabicyclo[2,2,2]-octane (DABCO)	18.3	CD_3CN	298	incomplete, reversible[a,b]
potassium hexamethyldisilazane (KHMDSZ)	26.0[a]	CD_3CN	298	decomposition of $BIPY^{2+}$ units
quinuclinide	9.80[a]	CD_3CN	298	incomplete, reversible[b]
2,6-lutidine	14.0	CD_3CN	298	incomplete, reversible[b]
potassium *tert*-butoxide (*t*-BuOK)	19.0[a]	CD_3CN	298	decomposition of $BIPY^{2+}$ units
N-ethyldiisopropylamine (EDIPA)	11.4[a]	$(CD_3)_2CO$, CD_3CN, $(CD_3)_2SO$	235−298	incomplete, reversible[b]
tributylamine (TBA)	18.0	CD_3CN	298	incomplete, reversible[b]
N,N,N′,N′-tetramethyl-1,8-naphthalene-diamine (proton-sponge)	18.2	$(CD_3)_2CO$	298	incomplete, reversible[b]
N-*tert*-butyl-*N′,N′,N″,N″,N‴,N‴*-hexamethyl-phosphorimidic triamide (P_1-*t*-Bu)	26.5	CD_3CN	298	complete, reversible[b]

[a] In DMSO. [b] Upon addition of TFA.

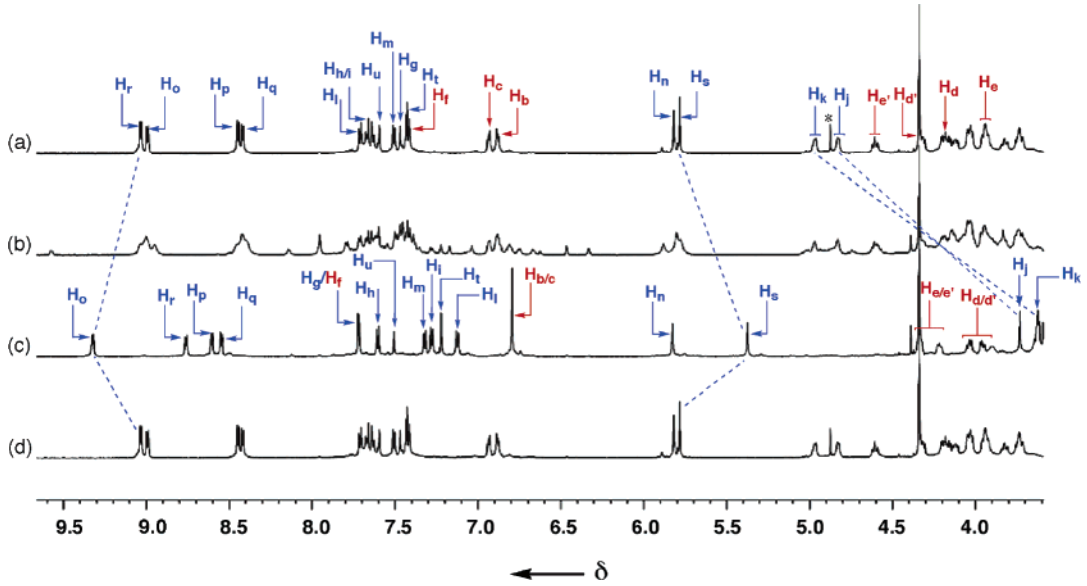


Figure 4. ^1H NMR spectra (600 MHz, in CD_3CN, 4.3 mM, and 298 K) recorded on $[\mathbf{5}H_3][PF_6]_9$ before (a) and after addition of (b) 1.7 and (c) 3.4 equiv of the phosphazene (*N*-*tert*-butyl-*N′,N′,N″,N″,N‴,N‴*-hexamethylphosphorimidic triamide) base. The original spectrum is regenerated (d) on addition of 3.4 equiv of trifluoroacetic acid.

lecular elevator $[\mathbf{5}H_3][PF_6]_9$ or bundle,[25] a phenomenon that will be a subject for discussion in a future paper.

On addition of 1.7 equiv of the strong phosphazene base (P_1-*t*-Bu) to a solution of $[\mathbf{5}H_3][PF_6]_9$ in CD_3CN, extensive broadening of peaks occurred, indicating the presence of more than one species, undergoing slow exchange[31] on the ^1H NMR time scale (Figure 4b). Upon addition of a slight excess (3.4 equiv) of the phosphazene base, significant changes were observed (Figure 4c) in the spectrum. The resonances for the methylene protons H_j and H_k in $[\mathbf{5}H_3][PF_6]_9$ were shifted upfield from δ 4.92 and 4.79 ppm to δ 3.62 and 3.53 ppm, respectively, indicating complete deprotonation of all three $-NH_2^+-$ centers. The chemical shifts of all the other protons in both the **2** and $[\mathbf{6}H_3][PF_6]_9$ components of the molecular elevator $[\mathbf{5}H_3][PF_6]_9$ changed (Figure 4c) dramatically as well. In particular, the resonances for the central aromatic core protons, H_g in the $[\mathbf{6}H_3]$-$[PF_6]_9$ component and H_f in the hexaoxytriphenylene core of the tris-crown ether component **2**, were shifted downfield from δ 7.42 to 7.70 ppm in the case of H_g, and from δ 7.35 to 7.70 ppm in the case of H_f. These results demonstrate the absence of any [$\pi-\pi$] stacking interactions upon addition of base. Moreover, the *O*-methylene protons ($H_{d/d'}$ and $H_{e/e'}$) retain their diastereotopicities, indicating that the two components are still interacting intimately with each other.

^1H NMR spectroscopic studies revealed that the affinity of tris-crown ether component **2** for the $-NH_2^+-$ centers decreases noticeably upon addition of 3.4 equiv of the phosphazene base—which deprotonates the NH_2^+ centers— and the tris-crown ether **2** moves (Figure 4c) to the $BIPY^{2+}$ recognition sites. This movement is indicated by the remarkable chemical shifts associated with the $BIPY^{2+}$ and *p*-xylyl methylene protons, demonstrating that the tris-crown ether **2** is now associated with the $BIPY^{2+}$ recognition sites. In addition, the H_o protons in the $BIPY^{2+}$ units are shifted downfield from δ 9.0 to 9.3 ppm, a trend which is indicative of the formation of [C—H···O] interactions with the oxygen atoms in the tris-crown ether. The original ^1H NMR spectrum was regenerated in every detail upon addition of a slight excess of TFA to the NMR sample previously treated with base, indicating that the switching process is pH-controlled and completely (quantitatively) reversible.

(30) It is well known that when $BIPY^{2+}$ units are surrounded by electron donors such as the dioxybenzene units of DB24C8, their reduction potentials become displaced to more negative values by more than 150 mV because of donor−acceptor interactions. See ref 22b.
(31) Elizarov, A. M.; Chiu, S. H.; Stoddart, J. F. *J. Org. Chem.* **2002**, *67*, 9175−9181.

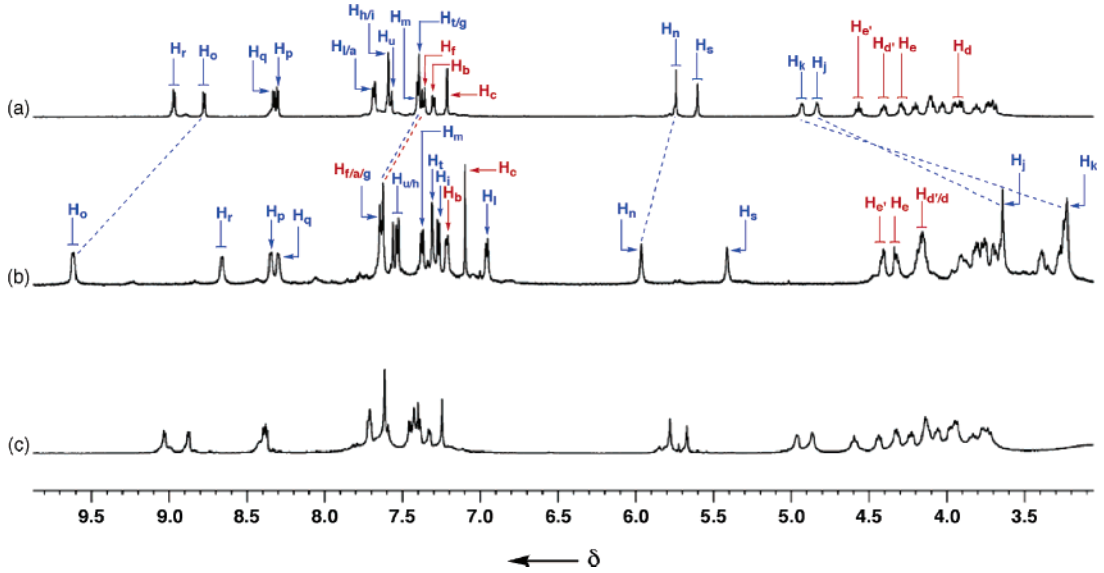


Figure 5. ^{1}H NMR spectra (600 MHz, in CD_3CN, 4.0 mM, and 298 K) recorded on [**8**H_3][PF_6]$_9$ before (a) and after (b) addition of 3.4 equiv of the phosphazene (*N*-*tert*-butyl-*N*′,*N*′,*N*″,*N*″,*N*‴,*N*‴-hexamethylphosphorimidic triamide) base. The original spectrum is regenerated (c) on addition of 3.4 equiv of trifluoroacetic acid.

For the molecular elevator [**8**H_3][PF_6]$_9$, the operation (Figure 5) is somehow similar to that of [**5**H_3][PF_6]$_9$. Upon addition of 3.4 equiv of the phosphazene base to [**8**H_3][PF_6]$_9$ in CD_3CN solution, complete deprotonation of $-NH_2^+-$ centers occurred (Figure 5b) and the tris-crown ether **7** migrated to the BIPY^{2+} recognition sites. The structure of this new hexacationic compound **8**$^{6+}$, in which the elevator is at the lower level, is confirmed by the chemical shifts observed (Figure 5b) in the ^{1}H NMR spectrum. Upfield shifts of the methylene protons H_j and H_k in [**8**H_3][PF_6]$_9$ from δ 4.92 and 4.83 ppm to δ 3.23 and 3.64 ppm, respectively, imply complete deprotonation of the three $-NH_2^+-$ centers. The resonances for the central aromatic core protons (H_g, H_h, and H_i) are shifted from δ 7.40, 7.60, and 7.60 ppm, respectively, to δ 7.60, 7.50, and 7.29 ppm, respectively, revealing, once more, the absence of any [$\pi-\pi$] stacking interactions upon addition of base. The *O*-methylene protons in the tris-crown ether **7** retain their diastereotopicities, indicating that the two components are interacting with each other. In addition, upfield shifts in the trifurcated protons H_s, H_t, and H_u in the vicinity of the three 3,5-di-*tert*-butylbenzyl stoppers and the *p*-xylyl protons, H_l and H_m, suggest that the tris-crown ether **7** interacts asymmetrically with the BIPY^{2+} recognition sites. It is important to note that the downfield shift of the H_o protons in the BIPY^{2+} units is much more pronounced for [**8**H_3][PF_6]$_9$ (from δ 8.70 to δ 9.60 ppm) than for [**5**H_3]-[PF_6]$_9$ (from δ 9.00 to 9.30 ppm). This observation can be explained by the better [$\pi-\pi$] stacking interactions involving naphtho rather than benzo aromatic units with the BIPY^{2+} recognition sites. Such [$\pi-\pi$] stacking enforces the [C—H···O] interactions and, therefore, affects the chemical shift of the H_o protons. On addition of TFA, the original spectrum (Figure 5c) is regenerated, demonstrating, once again, that the switching process is reversible.

The elevators' switching triggered by base and acid stimulation can also be clearly monitored by voltammetric experiments performed in MeCN solution, using the reduction processes of the bipyridinium units as a probe.[32] On deprotonation of [**5**H_3]$^{9+}$ and [**8**H_3]$^{9+}$ with 3.3 equiv of the phosphazene base P_1-*t*-Bu, two reversible three-electron reduction processes are still observed in cyclic voltammetric experiments, but they are displaced to more negative values (Table 1 and Figure 3). Such changes cannot be a result simply of deprotonation of the $-NH_2^+-$ centers, because the potential values for reduction of the BIPY^{2+} units in the rig component [**6**H_3]$^{9+}$ are identical to those in the corresponding deprotonated species, **6**$^{6+}$. Hence, the results obtained show[30] that, in the deprotonated molecular elevators **5**$^{6+}$ and **8**$^{6+}$, the BIPY^{2+} units in the three legs, although remaining equivalent and independent of one another, are surrounded by the electron donor DB24C8-type rings of the platform. The changes in reduction potential can be fully reversed by addition of a stoichiometric amount of TFA with respect to the previously added base. It is worthwhile to note that the negative shift of the potential for the reductions of the BIPY^{2+} units with respect to the rig component is larger for **8**$^{6+}$ than it is for **5**$^{6+}$. Such a larger shift, which indicates that the BIPY^{2+} units experience stronger electron donor—acceptor interactions in the former elevator than in the latter, is in agreement with the ^{1}H NMR spectroscopic data and is expected on the basis of the better π-electron donor ability of the dioxynaphthalene compared to the dioxybenzene units. This observation is an important one since the control of the intercomponent interactions allows the modulation of the energies associated with the elevators' molecular motions.

It is also important to consider the second reduction process of the BIPY^{2+} units. For the molecular elevators such a process is negatively shifted compared to the same process in the rig component, while it was not shifted in the [2]rotaxane [**1**H]$^{3+}$ (Scheme 1) studied previously.[22b] The lack of shift in the case of the [2]rotaxane was attributed to the shuttling of the DB24C8 ring away from the monoreduced bipyridinium unit, in keeping with the fact that one-electron reduction of the BIPY^{2+} unit disrupts the charge-transfer interactions with electron donors. In the present case, we have to conclude that the displacement of the platform away from the monoreduced bipyridinium units does not take place—at least on the time scale of the electro-

(32) The oxidation processes of the molecular elevators, being irreversible and poorly defined, are not useful for monitoring the switching of the systems.

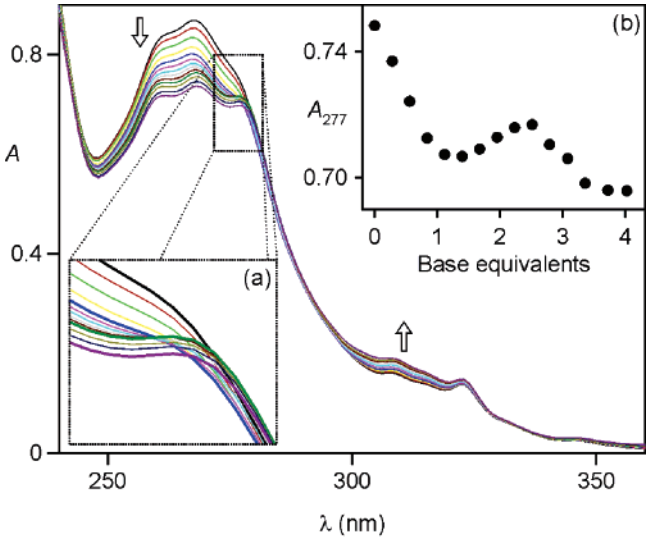


Figure 6. Absorption spectral changes observed upon titration at 298 K of a 4.0×10^{-6} mol L^{-1} MeCN solution of the molecular elevator $[\mathbf{8}H_3]^{9+}$ with the P_1-*t*-Bu base. Insets (a) and (b) show a magnification of the 272−282 nm region and the titration curve obtained from the absorbance changes at 277 nm, respectively.

chemical experiments—presumably because it is strongly activated owing to the structural complexity of the molecular elevators.

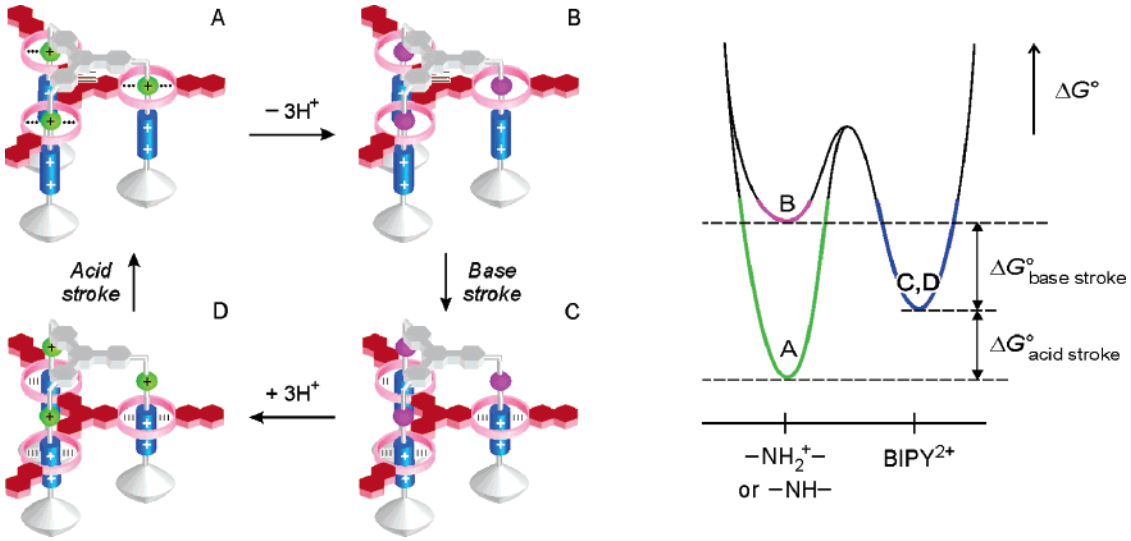
The chemically driven operation of $[\mathbf{5}H_3]^{9+}$ and $[\mathbf{8}H_3]^{9+}$ also leads to reversible changes in the absorption and fluorescence spectra (see Supporting Information). In particular, the elevators' motions can be monitored by observing the changes in absorbance at selected wavelengths, e.g., 310 nm, on successive additions of base and acid. The signal change, after some initial loss in the early cycles, reaches stability, indicating that the process can be repeated several times. This behavior is mirrored by the weak fluorescence band with λ_{max} around 380 nm, observed for both molecular elevators, that increases and, respectively, decreases in intensity on successive additions of stoichiometric amounts of base and acid.

More detailed information on the mechanism of the elevators' motions can be obtained by observing the changes in the voltammetric and spectroscopic properties of the compounds upon titration with the phosphazene base. On addition of the base, two new voltammetric waves are revealed at more negative potentials compared to the initial reduction waves (Figure 3a). On the basis of the above results, these new peaks have to be assigned to the reduction of $BIPY^{2+}$ units encircled by the crown ether rings of the platform component. The current intensity of the peaks, corresponding to the reduction of the complexed $BIPY^{2+}$ units, increases linearly on addition of 1, 2, and 3 equiv of base, at the expense of the intensity of the peaks corresponding to the reduction of the free $BIPY^{2+}$ units (Figure 3a). However, the distribution of the free and complexed $BIPY^{2+}$ units among the elevator molecules cannot be determined solely from these observations; in other words, it cannot be assessed whether the addition of 1 equiv of base forms exclusively the species with only one crown ether ring displaced, or a statistical distribution of species with none, one, two, or three rings displaced. We have therefore monitored the changes in the absorption spectra upon titration with base for both molecular elevators. Although the changes appear (Figure 6) to be complicated, a closer look reveals that the absorption curves can be grouped into three families exhibiting monotonic variations.

A plot of the absorbance values at a selected wavelength, e.g., at 277 nm (Figure 6), on titration of the molecular elevator with base shows the presence of three quite distinct steps, indicating that the three deprotonation processes are not equivalent. Molecular modeling (see Supporting Information) shows that the species in which two (or one) ring(s) surround (a) $-NH_2^+-$ center(s) and one (or two) rings surround(s) (a) $BIPY^{2+}$ unit(s) are sterically possible. Hence, for each molecular elevator, the platform operates by taking three distinct steps associated with each of the three deprotonation processes. In this regard, the molecular elevator is more reminiscent of a legged animal than it is of the passenger elevator.

It is interesting at this point to reflect upon the energies associated with the mechanical switching of these molecular machines (Scheme 4). The driving force for the motion of the platform from the upper to lower levels (base stroke) is provided

Scheme 4. Base−Acid-Controlled Mechanical Switching in the Molecular Elevators[a]



[a] The graph reports a simplified representation of the potential energy of the system as a function of the position of the platform relative to the rig for each co-conformation.

by the electron donor−acceptor interactions between the electron-donor units of the platform and the $BIPY^{2+}$ electron-acceptor units of the rig. The driving force for the motion of the platform from the lower to upper levels (acid stroke) is given by the larger stabilization energy offered to the platform's rings by the $-NH_2^+-$ centers compared to the $BIPY^{2+}$ units. The energies available for the relevant movements can be estimated[21] from the redox potential and thermodynamic constant values. The energy released in the base stroke amounts to ca. 21 and ca. 22 kcal mol^{-1} for $[\mathbf{5}H_3]^{9+}$ and $[\mathbf{8}H_3]^{9+}$, respectively, and that released in the acid stroke is estimated to be larger than 4 kcal mol^{-1} for both molecular elevators. The better electron-donating ability of the dioxynaphthalene units compared to the dioxybenzene units is responsible for the larger driving force associated with the base stroke for $[\mathbf{8}H_3]^{9+}$ but it is, of course, expected to lower the driving force for the acid stroke.

These large stabilization energies not only provide strong driving forces for the molecular motion, but also confer a high positional (co-conformational) integrity upon the elevators, giving rise to a clear-cut on/off behavior. Since molecular models show that the distance traveled by the platform is about 0.7 nm, we speculate that the elevators could potentially generate a maximum force of around 200 pN in the base stroke. Such force is more than 1 order of magnitude larger than the forces developed[4b] by natural linear motors like myosin[33] and kinesin.[34] In any instance, single-molecule experiments in which a load is applied to the molecular elevators, e.g., force spectroscopy experiments,[35] will have to be performed in order to investigate the operation mechanism of such artificial nanomotors and determine the amount of mechanical work that can be actually produced.

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Conclusions

The research described in this paper reveals how the concept of multivalency can be harnessed in the construction of mechanically interlocked molecular components beyond the realm of a relatively simple bistable [2]rotaxane. The two molecular elevators that have been investigated in detail in solution can be likened to a combination of three bistable [2]rotaxanes incorporated within one molecule in each case. Interestingly, when it comes to investigating how the rig and platform components move with respect to each other in these molecules under chemical stimuli, the recognition sites operate not in unison but rather one after the other. Coupled with the message that the force potentially generated during such movements is not insignificant, when compared with that generated by biological motors, we have gathered enough information and encouragement to look forward to the next challenge—that of pinning down molecular elevators on surfaces or marshalling them at interfaces.

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Supporting Information Available: Experimental procedures and further details; complete list of authors for refs 15c, 16f, 22b, and 26b. This material is available free of charge via the Internet at http://pubs.acs.org.

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