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Shuttling Dynamics in an Acid–Base-Switchable [2]Rotaxane

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Molecular shuttles are an intriguing class of rotaxanes which constitute prototypes of mechanical molecular machines and motors. By using stopped-flow spectroscopic techniques in acetonitrile solution, we investigated the kinetics of the shuttling process of a dibenzo[24]crown-8 ether (DB24C8) macrocycle between two recognition sites or "stations"—a secondary ammonium ($-NH_2^+-$)/amine (–NH–) center and a 4,4′-bipyridinium (bipy^{2+}) unit—located on the dumbbell component in a [2]rotaxane. The affinity for DB24C8 decreases in the order $-NH_2^+- >$ bipy$^{2+} >$ –NH–. Hence, shuttling of the DB24C8 macrocycle can be obtained by deprotonation and reprotonation of the ammonium station, reactions which are easily accomplished by addition of base and acid to the solution. The rate constants were measured as a function of temperature in the range 277–303 K, and activation parameters for the shuttling motion in both directions were determined. The effect of different counterions on the shuttling rates was examined. The shuttling from the $-NH_2^+-$ to the bipy^{2+} station, induced by the deprotonation of the ammonium site, is considerably slower than the shuttling in the reverse direction, which is, in turn, activated by reprotonation of the amine site. The results show that the dynamics of the shuttling processes are related to the change in the intercomponent interactions and structural features of the two mutually interlocked molecular components. Our observations also indicate that the counterions of the cationic rotaxane constitute an important contribution to the activation barrier for shuttling.

Introduction

Molecular and supramolecular systems that can be switched between two or more stable states have attracted considerable attention, mainly because of their potential application in the field of information processing and storage.[1,2] Of particular interest are multicomponent switches wherein the switching process causes changes in the relative positions of the molecular components. The energy inputs needed for switching can typically be provided by 1) a chemical reaction, 2) an electrochemically induced redox process (thus consuming electrical energy), or 3) exploiting the energy of photons through a photochemical reaction. Such systems constitute simple prototypes of molecular machines and motors,[2,3] and can be viewed as artificial analogues—yet much less complex—of the motor proteins that operate in living organisms.[4]

Threaded and interlocked chemical species such as pseudorotaxanes, rotaxanes, and catenanes[5] have proven to be attractive entities for the development of artificial molecular machines and motors. [2]Rotaxanes are composed of a molecular axle surrounded by a macrocyclic ring of a suitable size. Stoppers are placed at the extremities of the axle to prevent the disassembly of the molecule: in other words, the two components are mechanically bound. In general, [2]rotaxanes enable the realization of both rotary and linear motions at the molecular level, since the macrocyclic component can both slide along the axle and rotate around it. In rotaxanes containing two different recognition sites on the axle, it is possible to switch the position of the macrocyclic ring between the two "stations" by an external energy input. Many systems of this kind, known as molecular shuttles,[6] have been developed both by us[2,7] and others.[2,8]

The investigated[9,10] [2]rotaxane **1**H^{3+} (Scheme 1) is made of a dibenzo[24]crown-8 ether (DB24C8), a π-electron-donor macrocycle, and a dumbbell component containing a secondary ammonium center ($-NH_2^+-$) and a 4,4′-bipyridinium (bipy^{2+}) unit. The stoppers are an anthracene moiety on one side—employed because its absorption, luminescence, and redox properties are useful for monitoring the state of the system—and a 3,5-di-*tert*-butylphenyl group on the other side. Since the [N$^+$–H···O] hydrogen-bonding interactions between the DB24C8 macrocycle and the ammonium center are much stronger than the charge-transfer (CT) interaction of the π-electron-donor macrocycle with the π-electron-acceptor bipy^{2+} unit, the stable co-conformation[11] of rotaxane **1**H^{3+} is that in which the macrocycle surrounds the ammonium station, denoted as **1 A**H^{3+} in Figure 1. Addition of a base (e.g., tributylamine)[12]

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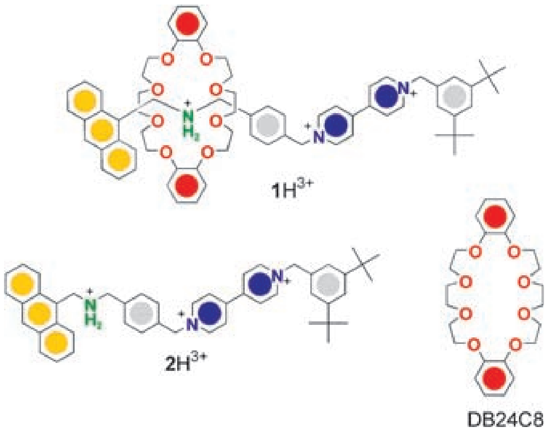

Scheme 1. Structures of the investigated [2]rotaxane **1**H^{3+} and of its molecular components, dumbbell 2H^{3+} and ring DB24C8.

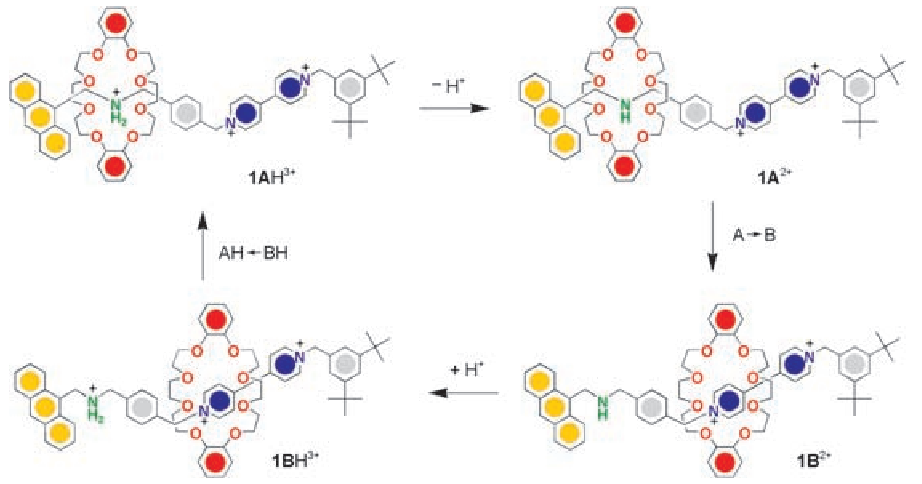

Figure 1. Schematic representation of the shuttling processes of the crown ether ring upon deprotonation and reprotonation of the ammonium site. Note that the A$\rightarrow$B process does not simply correspond to the reverse of the AH$\leftarrow$BH process, since the former motion concerns the shuttling of the ring from the *amine* to the bipyridinium station, whereas the latter concerns ring shuttling from the bipyridinium unit to the *ammonium* station.

converts the ammonium center into an amine function, to giving the transient state **1 A**$^{2+}$ that is transformed into the stable state **1 B**$^{2+}$ as a consequence of the displacement of the macrocycle onto the bipy^{2+} unit. The process can be reversed by addition of an acid (e.g., trifluoroacetic acid) and the initial state is restored via the transient state denoted as **1 B**H^{3+}. NMR, absorption, and luminescence spectroscopic experiments, together with electrochemical measurements, indicate[10] that the acid–base-controlled switching, which is fully reversible and relatively fast, exhibits a clear-cut on–off behavior. It should also be noted that, in the deprotonated rotaxane, the macrocyclic ring can be displaced from the bipy^{2+} station by destroying the CT interactions through one-electron reduction of the bipyridinium unit. The successful design and realization of this molecular shuttle was central to the recently reported[13] construction and operation of a molecular elevator.

Despite the large number of papers in the literature on artificial molecular machines, kinetic studies on the molecular motions in this kind of system are rare events. Examples include: 1) the rotation of molecular rings in catenane- and rotaxane-type Cu^{I} complexes,[14] 2) the Brownian shuttling process in rotaxanes as a function of the steric bulk of substituents placed on the axle (“speed-bumps”),[15] 3) the photoinduced switching of the macrocycle in molecular shuttles,[16] 4) the threading/dethreading of pseudorotaxanes,[17] 5) the slipping/deslipping processes in rotaxanes,[18] and 6) the influence of the environment on the electromechanical switching in donor–acceptor catenanes and rotaxanes.[19]

Herein, we describe the results of a stopped-flow spectroscopic investigation into the macrocycle’s shuttling process between the ammonium/amine and bipyridinium stations in the [2]rotaxane **1**H^{3+} (hexafluorophosphate salt), driven by the successive addition of base and acid. We measured the rate constants for the “forward” (A$\rightarrow$B) and “backward” (AH$\leftarrow$BH) shuttling motions (Figure 1) of the DB24C8 ring which occur, respectively, upon deprotonation and reprotonation of the ammonium/amine recognition site on the axle. Notably, the A$\rightarrow$B process does not simply correspond to the reverse of the AH$\leftarrow$BH process, since the former motion concerns the shuttling of the ring from the *amine* to the bipyridinium station, whereas the latter concerns ring shuttling from the bipyridinium unit to the *ammonium* station. The behavior of the rotaxane was compared with that of its dumbbell component, **2**H^{3+} (Scheme 1). All the experiments were carried out in acetonitrile solution as a function of temperature in the range 277–303 K. The activation parameters for the shuttling process in both directions were obtained. The effect of an excess of two different electrolytes (tosylate and hexafluorophosphate tetraalkylammonium salts) was also investigated at 293 K.

Experimental Section

Chemicals: The syntheses and characterization of compounds **1**H^{3+} and **2**H^{3+} as their hexafluorophosphate salts have been reported previously.[10] Tributylamine (Bu$_3$N, Fluka, $\geq$99.5 %) and trifluoroacetic acid (CF$_3$CO$_2$H, Merck, $>$99.8 %) were used as received. Tetraethylammonium tosylate (TEATsO) and tetrabutylammonium hexafluorophosphate (TBAPF$_6$) were both obtained from Fluka ($>$99 %) and were oven dried for two days before use. Acetonitrile solvent was purchased from Merck (Uvasol) and used without further purification.

Absorption and Emission Spectra: The measurements were carried out in air-equilibrated acetonitrile solutions at a concentration of 8.5×10^{-5} M and contained in quartz cells with a 1.0-cm path length. Some absorbance measurements were obtained with a 0.2-

cm-path-length cell. UV/Vis absorption and uncorrected luminescence spectra were recorded with a Perkin–Elmer Lambda 40 spectrophotometer and a Perkin–Elmer LS-50 spectrofluorimeter, respectively. Experimental errors: wavelength values, ±1 nm; molar absorption coefficients and fluorescence intensity values, ±5%.

Titration Experiments: Titrations were performed by adding small aliquots (typically 20 μL) of a concentrated (1.0×10^{-3} M) solution of either base or acid to 2 mL of a dilute (8.4×10^{-5} M) solution of the sample by using a microsyringe. UV/Vis absorption and luminescence changes were monitored during the titration. Whenever possible, excitation was performed at an isosbestic point, and corrections for inner-filter effects[20] were carried out if needed.

Stopped-Flow Experiments: Stopped-flow experiments were performed in air-equilibrated acetonitrile solutions with an Applied Photophysics SX 18-MV equipment. The standard flow tube had observation path lengths of 1.0 and 0.2 cm, and the driving ram for the mixing system was operated at the recommended pressure of 8.5 bar. Under these conditions the time required to fill the cell was 1.35 ms. A baseline correction was applied to take into account the dependence of the instrument response on pressure. In all the experiments, solutions of the sample were mixed with solutions containing a slight excess (1.3–1.5 equiv) of either base or acid to obtain, after mixing, a sample concentration in the range of $2–5\times10^{-5}$ M. The effect of the presence of 100 equiv of a salt (TEATsO or $TBAPF_6$) was also investigated at 293 K. The reactions were monitored by the increase (or decrease) of the absorption in the 240–390-nm region, calculated as $\Delta A = A_t - A_\infty$, where A_t is the absorbance at time t and A_∞ is the absorbance at the end of the process. In all the experiments, the cell block and drive syringes were thermostated by using a circulating constant-temperature bath maintained at the required temperature. The data were treated using the SPECFIT software.[21]

Results and Discussion

Acid–Base Switching

The redox properties and the absorption and luminescence spectra of the [2]rotaxane $\mathbf{1}H^{3+}$, and of the dumbbell component $\mathbf{2}H^{3+}$, as well as those of the corresponding deprotonated forms $\mathbf{1}^{2+}$ ($\mathbf{1}\,\mathbf{B}^{2+}$) and $\mathbf{2}^{2+}$, have been described previously.[10] ^{1}H NMR spectroscopic investigations and voltammetric experiments proved clearly that ring shuttling occurs upon deprotonation–reprotonation of $\mathbf{1}H^{3+}$. In this work we studied in detail the spectral changes that occur upon acid–base switching. The rotaxane possesses several chromophoric and luminophoric groups—namely, anthracene-, dioxybenzene-, and bipyridinium-type units—that can be used as a probe in this regard. In particular, the anthracene-type unit, which is incorporated in the dumbbell component, has intense and distinctive absorption and fluorescence spectra (see Supporting Information).[22] Hence, for the present system, steady-state and time-resolved absorption and fluorescence spectroscopic techniques are an optimal choice to investigate the protonation–deprotonation reactions and the structural rearrangements that can consequently take place.

Upon titration of the dumbbell component $\mathbf{2}H^{3+}$ with Bu_3N, small changes in the anthracene-structured band (300–400 nm) are observed, together with a decrease of the 254 nm band (see Supporting Information). Such changes are complete after addition of 1 equiv of base, which indicates that the deprotonated form $\mathbf{2}^{2+}$ is obtained. Deprotonation produces a decrease of the anthracene fluorescence intensity, presumably because a further quenching pathway—namely, reductive electron transfer from the amino group—becomes effective.[23] These modifications are completely reversed by addition of a stoichiometric amount (with respect to the previously added base) of CF_3CO_2H.

The deprotonation of $\mathbf{1}H^{3+}$ with 1 equiv of Bu_3N to give $\mathbf{1}^{2+}$ is accompanied by a blue shift of both the high-energy (256 nm) and low-energy (300–400 nm) anthracene bands (Figure 2). The latter bands also exhibit an intensity increase.

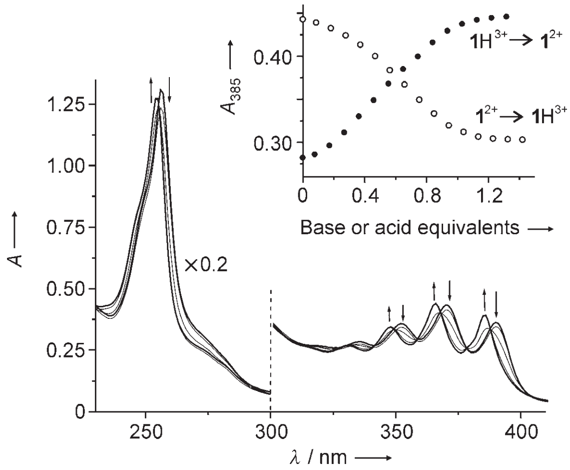

Figure 2. Absorption spectra of an acetonitrile solution of $\mathbf{1}H^{3+}$ (8.5×10^{-5} M, 2.5 mL) upon titration with Bu_3N (1.0×10^{-3} M) at room temperature. The inset shows the absorbance changes, monitored at 385 nm, upon addition of Bu_3N to $\mathbf{1}H^{3+}$ (●) and upon addition of CF_3CO_2H to $\mathbf{1}^{2+}$ (○).

This behavior indicates[24] a change in the perturbation of the anthracene chromophoric group along both of its symmetry axes and is consistent with the displacement of the aromatic moieties of DB24C8 from the anthracene unit. As for the dumbbell component, deprotonation leads to a quenching of the anthracene fluorescence intensity, and the changes caused by addition of base are completely reversed by subsequent addition of CF_3CO_2H.

It can be noticed (Figure 2) that, upon deprotonation, the intensity of the anthracene absorption band in the 250-nm region decreases for the dumbbell $\mathbf{2}H^{3+}$, while it moves to a higher energy and maintains approximately the same intensity for the rotaxane $\mathbf{1}H^{3+}$. Hence, the spectral changes observed after addition of tributylamine to the rotaxane cannot arise from proton removal from the ammonium site: they have to be assigned to a change in the interaction between the anthracene unit and DB24C8. The facts that 1) the presence of DB24C8 around the $-NH_2^+-$ station affects the anthracene absorption bands, and 2) the deprotonated $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$ species exhibit very similar absorption spectra indicate that the spectral changes of the anthracene unit upon deprotonation and reprotonation of the rotaxane are directly related, respectively, to the forward (A→B) and backward (AH←BH) shuttling processes of the DB24C8 ring.

Shuttling Kinetics

The kinetics of the shuttling process of DB24C8 between the ammonium/amine and the bipyridinium stations were studied by stopped-flow spectroscopic experiments in acetonitrile at various temperatures. The values of the rate constants for the base-induced A→B and acid-induced AH←BH shuttling processes are gathered together in Table 1.

Table 1. Rate constants for the base-induced forward (A→B) and the acid-induced backward (AH←BH) shuttling motions of rotaxane **1**H^{3+}/**1**$^{2+}$ in acetonitrile.

T [K]	$k_{A\rightarrow B}$ [s^{-1}]	$k_{AH\leftarrow BH}$ [s^{-1}]
277	0.42 ± 0.03	15 ± 2
283	0.55 ± 0.06	23 ± 1
293	0.72 ± 0.05	40 ± 3
303	1.2 ± 0.1	72 ± 6

Figure 3 shows the absorbance change at 386 nm as a function of the time after mixing Bu_3N and **1**H^{3+} (final concentration, 3.5×10^{-5} M), recorded at 277 and 303 K. Figure 4 shows the kinetic absorption trace at 254 nm after mixing CF_3CO_2H and **1**$^{2+}$ (final concentration, 2.4×10^{-5} M), again at both 277 and 303 K. The reprotonation of the amine site of **1**$^{2+}$ was realized in practice by mixing 1.5 equiv of CF_3CO_2H to a solution of rotaxane that had been previously deprotonated by addition of 1.3 equiv of Bu_3N.

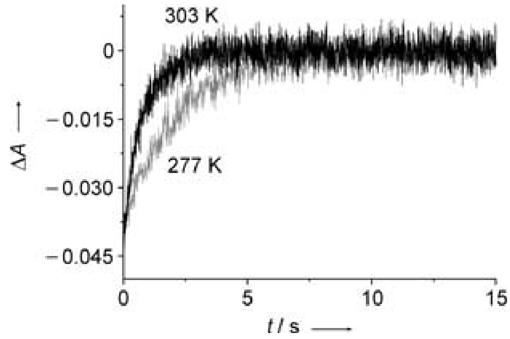

Figure 3. Stopped-flow kinetic traces, recorded at 277 and 303 K, for the absorbance change at 386 nm obtained upon deprotonation of the rotaxane by mixing **1**H^{3+} and 1.4 equiv of Bu_3N in acetonitrile. The concentration of the rotaxane after mixing was 3.5×10^{-5} M; path length = 1.0 cm.

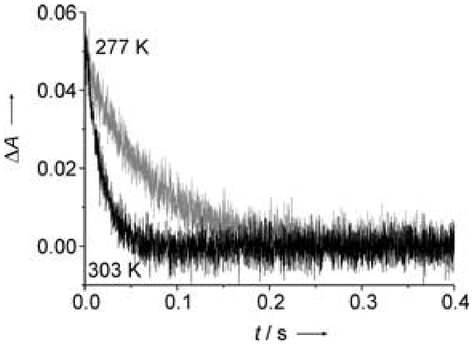

Figure 4. Stopped-flow kinetic traces, recorded at 277 and 303 K, for the absorbance change at 254 nm obtained upon reprotonation of the rotaxane by mixing **1**$^{2+}$ and 1.5 equiv of CF_3CO_2H in acetonitrile. The concentration of the rotaxane after mixing was 2.4×10^{-5} M; path length = 1.0 cm.

Notably, the spectral changes taking place as a function of time upon deprotonation of the dumbbell component **2**H^{3+} by Bu_3N could not be measured on the stopped-flow timescale. Similar results were obtained for the reprotonation of **2**$^{2+}$ by CF_3CO_2H. Such observations indicate that the acid–base equilibria are reached within the dead time of the equipment used (1.35 ms); in other words, the deprotonation of the ammonium site and the protonation of the amine site are too fast to be measured by the stopped-flow method ($k > 10^8$ $M^{-1}s^{-1}$). These results, which are not surprising since acid–base reactions are known to be very fast, are important because they ensure that the time-dependent spectral changes observed for the rotaxane are exclusively related to ring shuttling.

Fluorescence changes of the anthracene unit, associated with base- or acid-induced ring shuttling, were anticipated. In practice, no appreciable changes in the intensity of the anthracene fluorescence could be observed in the stopped-flow experiments upon mixing **1**H^{3+} with base, or **1**$^{2+}$ with acid. The same results were obtained for the dumbbell component. Since we found that protonation/deprotonation of the ammonium/amine site of the rotaxane (and of its dumbbell component) causes large changes in the anthracene fluorescence intensity (see above), such changes must occur within the stopped-flow dead time. The presence of time-dependent absorption changes, and the lack of time-dependent fluorescence changes, for the rotaxane suggests that the electronic interactions between the anthracene unit and the DB24C8 ring are more important when the former is in the ground state rather than in the first singlet excited state.

The stopped-flow traces were treated by a conventional kinetic analysis with the SPECFIT fitting program[21] to afford the values of the kinetic rate constants of shuttling (Table 1). The best fit was obtained for a first-order kinetic model, which confirmed that the process observed in the stopped-flow experiments is indeed the (intramolecular) ring-shuttling process, and is not related to the acid–base reactions, which would be expected to follow second-order kinetics. In each case, the fitting was performed for $t \geq 2$ ms and covered more than 90% of the reaction course. Note that the rate constant values are in agreement with those estimated[10] by digital simulation of the cyclic voltammetric patterns ($k_{A\rightarrow B} < 2.5$ s^{-1}).

Interestingly, for all the temperatures examined, the rate constant for the acid-induced AH←BH shuttling is much larger than that for the base-induced A→B shuttling (Table 1). Such an observation suggests that the forward and backward shuttling motions, which, as we have noted earlier, are not simply the reverse of one another (Figure 1), are governed by different factors. These differences will be better evidenced from the analysis of the activation parameters for the two shuttling processes.

Activation Parameters

The activation parameters for the base-induced forward (A→B) and acid-induced backward (AH←BH) shuttling processes of the DB24C8 ring, obtained from the temperature-dependence (Arrhenius and Eyring) plots of the rate constant values in the range 277–303 K, are reported in Table 2. The diagram of $\ln(k/T)$ versus $1/T$ and the corresponding linear fit, according to the Eyring equation for both shuttling processes, is shown in Figure 5.

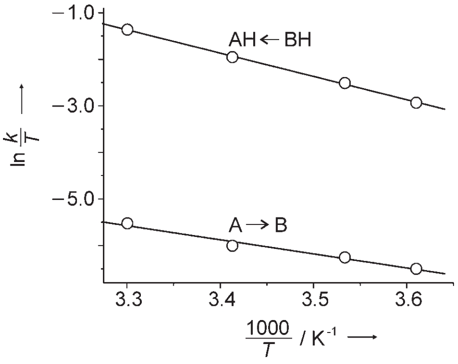

Figure 5. Eyring plots obtained for the base-induced A→B and acid-induced AH←BH shuttling processes in the temperature range 277–303 K in acetonitrile.

The Eyring equation, $\ln(k/T)=\ln(k_B/h)+\Delta S^{\ddagger}/R-\Delta H^{\ddagger}/RT$, where k_B, h, and R are the Boltzmann, Planck, and gas constants, respectively, enables us to determine the activation parameters (enthalpy, entropy, and free energy) of the shuttling motions. From the Arrhenius equation, $\ln k=\ln A-E_a/RT$, the values of the activation energy E_a and the pre-exponential (frequency) factor A can be obtained.

The activation barriers $\Delta G^{\ddagger}$ for both shuttling processes are similar to those observed for related rotaxanes such as those composed[25] of DB24C8 and a dumbbell whose main station is $-NH_2^+-$, and to that determined[26] in the case of a dumbbell with two identical stations threaded into a bis(*p*-phenylene)[34]crown-10. In the case of dumbbell components containing asymmetrically substituted monopyrrolotetrathiafulvalene (MPTTF) and 1,5-dioxynaphthalene (DNP) recognition sites for encirclement by cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$), the measured activation energies are comparable to those obtained in the present case, or higher if the dumbbell contains a "speed-bump" in the form of a thiomethyl group (SMe), for example, situated between the two stations.[27] The acid–base-switchable [2]rotaxane displays a general cycle of shuttling that is not too dissimilar from the one observed[19] for bistable redox-driven rotaxanes bearing TTF and DNP stations along a dumbbell, interlocked with $CBPQT^{4+}$. In these redox-driven switches and actuators, the transient states of the present work have been referred to in the literature[19] as metastable-state co-conformations (MSCCs). Whereas **1A**H^{3+} starts in a stable co-conformation and the sequential addition of acid followed by base produces the isomeric transient state **1B**H^{3+}, in the redox-driven rotaxanes, the sequential addition and removal of positive charges transforms the ground-state co-conformation (GSCC) into the MSCC. For redox-driven rotaxanes in the solution phase, the MSCC then relaxes thermally over a barrier ($\Delta G^{\ddagger}$ (298) ≈ 16 kcal mol^{-1}) to re-form the GSCC—a free energy barrier that is comparable with the backward shuttling process (AH←BH) for **1B**H^{3+} relaxing back to **1A**H^{3+}. The cycle of shuttling and the existence of transient or metastable states are probably required in any bistable molecule that has a chance to behave as a switch or actuator. It has already been proposed that bistability in redox-active rotaxanes is responsible for the memory effect in molecular-switch tunnel junctions.[28,29]

From the analysis of the parameters listed in Table 2 it can be noted that 1) $\Delta S^{\ddagger}$ is negative for both shuttling motions, and 2) the transition co-conformation for AH←BH shuttling is enthalpically more disfavored than that for A→B shuttling, but 3) it is much less disfavored from the entropic point of view. In fact, the reason for the much lower values of the rate constant for the A→B shuttling process compared to the AH←BH one seems to be of an entropic nature.

Activation Enthalpy

The potential energy curve relative to the ring-shuttling processes between the different stations on the dumbbell component depends on the mutual interplay between intercomponent hydrogen-bonding, hydrophobic, π–π stacking, charge-transfer, and other electrostatic interactions. Moreover, the counterions of the positively charged rotaxane species, as well as the solvent molecules, are likely to play an important role. Hence, an interpretation of the activation energy values in terms of changes in the supramolecular structure that occur in the shuttling motions is not straightforward. We can speculate, however, on what are likely to be the most important intercomponent interactions that must be broken to displace the ring from one station to the other during each shuttling process.

Table 2. Activation parameters for the base-induced forward (A→B) and the acid-induced backward (AH←BH) shuttling motions of rotaxane **1**H^{3+}/**1**$^{2+}$ (acetonitrile solution, temperature range 277–303 K).

Shuttling process	E_a [kcal mol^{-1}]	A[a] [s^{-1}]	$\Delta G^{\ddagger}$[b,c] [kcal mol^{-1}]	$\Delta H^{\ddagger}$[b] [kcal mol^{-1}]	$T\Delta S^{\ddagger}$[b,c] [kcal mol^{-1}]	$\Delta S^{\ddagger}$[b] [cal mol^{-1} K^{-1}]
A→B	6.5 ± 1.0	6.0×10^4	+17.3	+5.90	−11.4	−38.8
AH←BH	10.0 ± 1.0	1.3×10^9	+15.0	+9.48	−5.51	−18.8

[a] Estimated error < 20 %. [b] Estimated error < 10 %. [c] Calculated at 293 K.

When the **1**H^{3+} rotaxane is deprotonated upon addition of a base, the strong [N^+–H···O] hydrogen-bonding interactions are immediately (on the timescale of shuttling) cancelled. For the DB24C8 ring to reach the new thermodynamic minimum, which corresponds to its placement around the bipyridinium station, a residual [N–H···O] bond must be broken. The energy associated with this type of hydrogen bond (4–15 $kcal\,mol^{-1}$)[30] accounts for the $\Delta H^{\ddagger}$ value found for the A→B shuttling process. A minor contribution to $\Delta H^{\ddagger}$ can also be expected from the rupture of the π–π stacking interactions between the anthracene unit and the dioxybenzene-type moieties of DB24C8.

In the shuttling process induced by reprotonation of the $\mathbf{1}^{2+}$ rotaxane, the crown ether ring has to leave the bipyridinium station (and the corresponding energy minimum) and move toward the ammonium station, a situation which represents the new absolute energy minimum for the DB24C8 ring. Therefore, AH←BH shuttling requires the breaking of the CT interaction between DB24C8 and the bipyridinium station. The $\Delta H^{\ddagger}$ value for the A→B process is consistently smaller than that for the AH←BH process, an outcome which is expected on the basis of the relative affinity of the DB24C8 macrocycle for the –NH– and bipyridinium stations.

Activation Entropy

A discussion of the entropic effects on the rates of the shuttling processes is even more difficult, given the complexity of the system. In general, for an intramolecular rearrangement in solution the change (disruption or formation) of the solvent structure is expected to amount to an important contribution to the entropy of activation. In the present case, it should be recalled that 1) the rotaxane is a charged species, 2) counterions are present, and 3) the solvent is relatively polar. In addition, molecular models revealed that slipping of the ring through the central *p*-phenylene moiety increases the overall rigidity of the rotaxane. Therefore, one can reasonably expect nonnegligible activation entropy values associated with ring shuttling.[31] It has also been shown that entropic factors can be employed as elements of structural control in rotaxanes.[32]

We observed that the forward and backward shuttling processes exhibit both relatively large and negative $\Delta S^{\ddagger}$ values which, however, are remarkably different from each other (Table 2). These observations suggest that the forward and backward shuttling processes take place according to different, complex mechanisms.

A recent investigation showed[33] that, in an organic solvent such as acetone, 4,4′-bipyridinium dications form tight ion pairs with hexafluorophosphate anions, and that complexation of the bipyridinium unit by DB24C8 must be preceded by disruption of the pairs, that is, the complex is not ion-paired. Ion pairing has also been observed for alkylammonium ions in organic solvents,[34,35] although the association between the *N,N*-dibenzylammonium cation and the hexafluorophosphate anion was found to be insubstantial.[34] Hence, it is reasonable to assume that shuttling to and from the bipyridinium station, as well as shuttling toward the ammonium station, involve the breaking/restoring of ion pairs.[17b]

A speculation on the possible mechanisms for the A→B and AH←BH shuttling motions is reported in Figure 6.[36] The transition co-conformation for the A→B shuttling is likely to be similar to that shown in Figure 6a, wherein the two PF_6^- anions are detached from the bipyridinium station upon arrival of the ring. As a result of the structuring effect exerted on the polar solvent molecules by the "naked" hexafluorophosphate and bipyridinium ions, it is expected that the formation of such a transition co-conformation is accompanied by a large and negative entropy change. A smaller $\Delta S^{\ddagger}$ value may be expected for the AH←BH shuttling because, in the transition state (Figure 6b), one hexafluorophosphate anion is being removed from the ammonium station, but the 2:1 adduct between PF_6^- ions and the bipyridinium station is being restored.

The influence of the counterions on the shuttling rate constants was confirmed by kinetic experiments on the base- and acid-induced shuttling processes in the presence of 100 equiv of a tetraalkylammonium salt associated with either hexafluorophosphate or tosylate anions. The results of these experiments are gathered together in Table 3. We observed that,

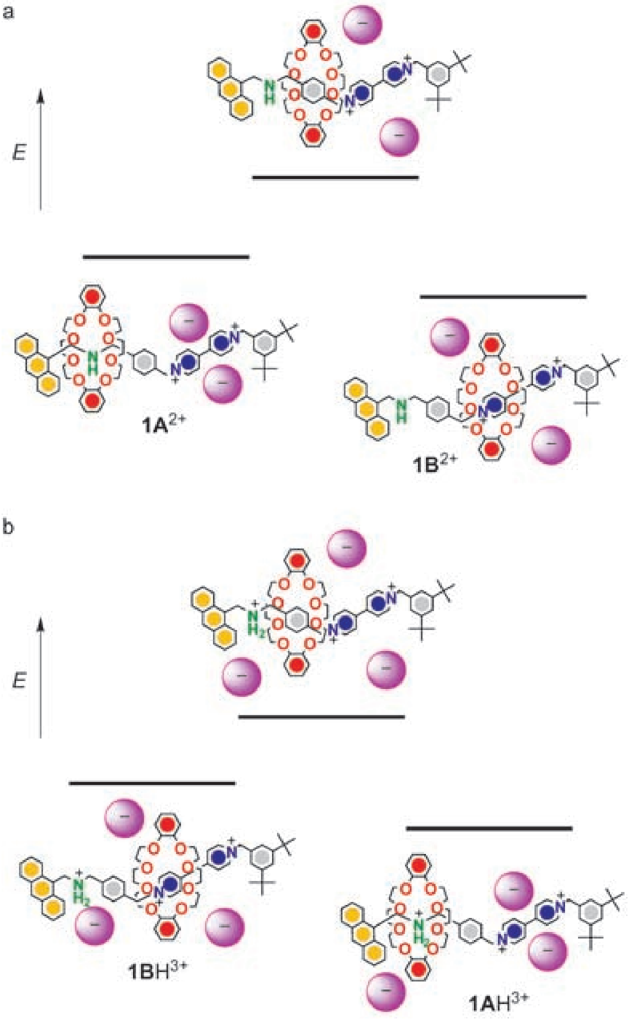

Figure 6. Schematic representation of the energy levels corresponding to the possible initial, transition, and final co-conformations for a) the forward A→B shuttling in $\mathbf{1}^{2+}$ and b) the backward AH←BH shuttling in **1**H^{3+}.

Table 3. Rate constants for the base-induced forward (A→B) and the acid-induced backward (AH←BH) shuttling motions of rotaxane $\mathbf{1}H^{3+}/\mathbf{1}^{2+}$ ($c = 1.85\times10^{-5}$ M) in the presence of 100 equiv of hexafluorophosphate or tosylate anions (acetonitrile solution, 293 K).

Conditions	$k_{A\rightarrow B}$ [s^{-1}]	$k_{AH\leftarrow BH}$ [s^{-1}]
No salt added	0.72 ± 0.05	40 ± 3
100 equiv PF_6^{-}[a]	0.62 ± 0.05	15 ± 1
100 equiv TsO^{-}[b]	1.4 ± 0.1	30 ± 2

[a] Tetrabutylammonium hexafluorophosphate. [b] Tetraethylammonium tosylate.

upon addition of an excess of PF_6^- ions, the rate constant values for both shuttling processes—and particularly for the AH←BH process—decrease. This observation is consistent with an increase in the concentration of ion pairs and a corresponding relative stabilization of the initial co-conformations of both shuttling processes with respect to the transition states (Figure 6). Interestingly, an excess of tosylate ions *accelerates* the forward A→B shuttling and *slows down* slightly the kinetics of the backward AH←BH motion. The particular behavior of tosylate compared to PF_6^- ions is most likely related to the ability of the former to donate hydrogen bonds.[17b,37,38] More specifically, tosylate ions may function as H-bond acceptors toward the –NH– group of $\mathbf{1}^{2+}$, thereby stabilizing the transition co-conformation shown in Figure 6a and accelerating the A→B shuttling. On the other hand, strong interactions between the ammonium station of $\mathbf{1}H^{3+}$ and a tosylate anion will lead to stabilization of the initial state for the AH←BH shuttling relative to the transition co-conformation (Figure 6b).

Conclusions

We have investigated the kinetics of the ring-shuttling processes in an acid–base-switchable [2]rotaxane in acetonitrile solution. The rotaxane is composed of a dumbbell component containing two different stations—a secondary ammonium unit and a bipyridinium unit—threaded through a DB24C8 crown ether ring. The ring exhibits more or less complete selectivity for the ammonium station; deprotonation of this station with a base triggers the motion of the ring to the bipyridinium unit, a process which is fully reversed upon addition of an acid that regenerates the ammonium site. The base- and acid-induced shuttling processes could be conveniently studied by stopped-flow spectroscopic techniques, whereas deprotonation/reprotonation of the ammonium/amine unit are too fast on the stopped-flow timescale. The results show that the base-induced forward shuttling is slower (seconds) than the acid-induced backward shuttling (tens of milliseconds). The values of the activation parameters suggest that the forward and backward shuttling motions occur by different, complex mechanisms. We also found that the nature and concentration of the counterions of the positively charged rotaxane affect the shuttling rate constants and most likely play a role in the shuttling processes. The two shuttling motions associated with the bistability of the acid–base-switchable rotaxane are observed to be qualitatively equivalent to the bistable character already observed for redox-driven switches used in molecular electronic devices and nanoelectromechanical systems.

Our experiments show that the dynamic processes taking place in artificial mechanically interlocked compounds, designed to work as molecular machines and motors, are crucial for guiding the development of bistable molecules for applications as switches and actuators. The study of such processes is useful not only for the future design of molecular devices, but also to foster the comprehension—albeit on a much lower level of complexity—of the operation mechanisms of functional biomolecules.

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Keywords: molecular devices · molecular dynamics · photochemistry · rotaxanes · supramolecular chemistry

[1] *Molecular Switches* (Ed.: B. L. Feringa), Wiley-VCH, Weinheim, **2001**.

[2] V. Balzani, A. Credi, M. Venturi, *Molecular Devices and Machines—A Journey into the Nano World*, Wiley-VCH, Weinheim, **2003**.

[3] a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem.* **2000**, *112*, 3484–3530; *Angew. Chem. Int. Ed.* **2000**, *39*, 3348–3391; b) *Molecular Machines* (Ed.: J. F. Stoddart), *Acc. Chem. Res. Special Issue* **2001**, 34(6); c) *Molecular Machines and Motors* (Ed.: J.-P. Sauvage), *Struct. Bonding Special Volume* **2001**, 99; d) C. J. Easton, S. F. Lincoln, L. Barr, H. Onagi, *Chem. Eur. J.* **2004**, *10*, 3120–3128; e) J.-P. Sauvage, *Chem. Commun.* **2005**, 1507–1510.

[4] a) *Molecular Motors* (Ed.: M. Schliwa), Wiley-VCH, Weinheim, **2003**; b) D. S. Goodsell, *Bionanotechnology: Lessons from Nature*, Wiley, Hoboken, **2004**.

[5] *Molecular Catenanes, Rotaxanes, and Knots* (Eds.: J.-P. Sauvage, C. O. Dietrich-Bucheker), Wiley-VCH, Weinheim, **1999**.

[6] P.-L. Anelli, N. Spencer, J. F. Stoddart, *J. Am. Chem. Soc.* **1991**, *113*, 5131–5133.

[7] For a recent example, see: H.-R. Tseng, S. A. Vignon, P. C. Celestre, J. Perkins, J. O. Jeppesen, A. Di Fabio, R. Ballardini, M. T. Gandolfi, M. Venturi, V. Balzani, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 155–172.

[8] For recent examples, see: a) A. Altieri, F. G. Gatti, E. R. Kay, D. A. Leigh, D. Martel, F. Paolucci, A. M. Z. Slawin, J. K. Y. Wong, *J. Am. Chem. Soc.* **2003**, *125*, 8644–8654; b) C. M. Keaveney, D. A. Leigh, *Angew. Chem.* **2004**, *116*, 1242–1244; *Angew. Chem. Int. Ed.* **2004**, *43*, 1222–1224; c) D. A. Leigh, E. M. Pérez, *Chem. Commun.* **2004**, 2262–2263.

[9] M.-V. Martínez-Díaz, N. Spencer, J. F. Stoddart, *Angew. Chem.* **1997**, *109*, 1991–1994; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1904–1907.

[10] P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. C. T. Fyfe, M. T. Gandolfi, M. Gómez-López, M.-V. Martínez-Díaz, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 11932–11942.

[11] M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, A. J. P. White, D. J. Williams, *Angew. Chem.* **1997**, *109*, 2158–2160; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2068–2070.

[12] Tributylamine is a suitable base to drive the switching process, because it is strong enough to deprotonate the $-NH_2^+-$ site while behaving

concurrently as a very weak (i.e., unreactive) nucleophile toward the bipyridinium unit.

[13] J. D. Badjic, V. Balzani, A. Credi, S. Silvi, J. F. Stoddart, *Science* **2004**, *303*, 1845 – 1849.

[14] I. Poleschak, J.-M. Kern, J.-P. Sauvage, *Chem. Commun.* **2004**, 474 – 476.

[15] a) J. O. Jeppesen, J. Perkins, J. Becher, J. F. Stoddart, *Angew. Chem.* **2001**, *113*, 1256 – 1261; *Angew. Chem. Int. Ed.* **2001**, *40*, 1216 – 1221; b) J. O. Jeppesen, J. Becher, J. F. Stoddart, *Org. Lett.* **2002**, *4*, 557 – 560; c) L. Frankfort, K. Sohlberg, *J. Mol. Struct. (Theochem)* **2003**, *621*, 253 – 260; d) J. O. Jeppesen, K. A. Nielsen, J. Perkins, S. A. Vignon, A. Di Fabio, R. Ballardini, M. T. Gandolfi, M. Venturi, V. Balzani, J. Becher, J. F. Stoddart, *Chem. Eur. J.* **2003**, *9*, 2982 – 3007.

[16] a) A. M. Brouwer, C. Frochot, F. G. Gatti, D. A. Leigh, L. Mottier, F. Paolucci, S. Roffia, G. W. H. Wurpel, *Science* **2001**, *291*, 2124 – 2128; b) A. M. Brouwer, S. M. Fazio, C. Frochot, F. G. Gatti, D. A. Leigh, J. K. Y. Wong, G. W. H. Wurpel, *Pure Appl. Chem.* **2003**, *75*, 1055 – 1060; c) V. Balzani, M. Clemente-Leon, A. Credi, B. Ferrer, M. Venturi, A. H. Flood, J. F. Stoddart, submitted.

[17] a) M. Venturi, S. Dumas, V. Balzani, J. Cao, J. F. Stoddart, *New J. Chem.* **2004**, *28*, 1032 – 1037; b) A. Credi, S. Dumas, S. Silvi, M. Venturi, A. Arduini, A. Pochini, A. Secchi, *J. Org. Chem.* **2004**, *69*, 5881 – 5887.

[18] a) P. R. Ashton, R. Ballardini, V. Balzani, M. Belohradsky, M. T. Gandolfi, D. Philp, L. Prodi, F. M. Raymo, M. V. Reddington, N. Spencer, J. F. Stoddart, M. Venturi, D. J. Williams, *J. Am. Chem. Soc.* **1996**, *118*, 4931 – 4951; b) M. Asakawa, P. R. Ashton, R. Ballardini, V. Balzani, M. Belohradsky, M. T. Gandolfi, O. Kocian, L. Prodi, F. M. Raymo, J. F. Stoddart, M. Venturi, *J. Am. Chem. Soc.* **1997**, *119*, 302 – 310; c) S.-H. Chiu, S. J. Rowan, S. J. Cantrill, P. T. Glink, R. L. Garrell, J. F. Stoddart, *Org. Lett.* **2000**, *2*, 3631 – 3634; d) X. Zhao, X.-K. Jiang, M. Shi, Y.-H. Yu, W. Xia, Z.-T. Li, *J. Org. Chem.* **2001**, *66*, 7035 – 7043; e) P. Linnartz, S. Bitter, C. A. Schalley, *Eur. J. Org. Chem.* **2003**, 4819 – 4829; f) J. D. Badjic, S. J. Cantrill, J. F. Stoddart, *J. Am. Chem. Soc.* **2004**, *126*, 2288 – 2289; g) S.-H. Chiu, K. S. Liao, J. K. Su, *Tetrahedron Lett.* **2004**, *45*, 213 – 216.

[19] a) T. J. Huang, H.-R. Tseng, L. Sha, W. Lu, B. Brough, A. H. Flood, B.-D. Yu, P. C. Celestre, J. P. Chang, J. F. Stoddart, C.-M. Ho, *Nano Lett.* **2004**, *4*, 2065 – 2071; b) A. H. Flood, A. J. Peters, S. A. Vignon, D. W. Steuerman, H.-R. Tseng, S. Kang, J. R. Heath, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 6558 – 6564; c) D. W. Steuerman, H.-R. Tseng, A. J. Peters, A. H. Flood, J. O. Jeppesen, K. A. Nielsen, J. F. Stoddart, J. R. Heath, *Angew. Chem.* **2004**, *116*, 6648 – 6653; *Angew. Chem. Int. Ed.* **2004**, *43*, 6486 – 6491; d) A. H. Flood, J. F. Stoddart, D. W. Steuerman, J. R. Heath, *Science* **2004**, *306*, 2055 – 2056.

[20] A. Credi, L. Prodi, *Spectrochim. Acta A* **1998**, *54*, 159 – 170.

[21] R. A. Binstead, *SPECFIT*, Spectrum Software Associates, Chapel Hill, NC, **1996**.

[22] The presence of CT interactions between the DB24C8 ring and the bipyridinium unit in the rotaxane is expected to cause the appearance of a broad, weak absorption band with a maximum between 400 and 450 nm. However, such a band could not be observed, most likely because it is covered by the intense absorption bands of the anthracene chromophore.

[23] A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.* **1997**, *97*, 1515 – 1566.

[24] I. B. Berlman, *Handbook of Fluorescence Spectra of Aromatic Molecules*, Academic, London, **1965**, p. 258.

[25] a) J. Cao, C. T. Fyfe, J. F. Stoddart, G. R. L. Cousins, P. T. Glink, *J. Org. Chem.* **2000**, *65*, 1937 – 1946; b) S.-H. Chiu, A. M. Elizarov, P. T. Glink, J. F. Stoddart, *Org. Lett.* **2002**, *4*, 3561 – 3564.

[26] M. Belohradsky, A. M. Elizarov, J. F. Stoddart, *Collect. Czech. Chem. Commun.* **2002**, *67*, 1719 – 1729.

[27] a) J. O. Jeppesen, S. A. Vignon, J. F. Stoddart, *Chem. Eur. J.* **2003**, *9*, 4611 – 4625; b) S. Kang, S. A. Vignon, H.-R. Tseng, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 2555 – 2564.

[28] Y. Collier, C. P. Collier, J. O. Jeppesen, K. A. Nielsen, E. Delonno, G. Ho, J. Perkins, H.-R. Tseng, T. Yamamoto, J. F. Stoddart, J. R. Heath, *ChemPhysChem* **2002**, *3*, 519 – 525.

[29] The same kind of bistability in redox-driven, two-station catenanes has also been exploited in molecular electronic devices; see: C. P. Collier, G. Mattersteig, E. W. Wong, Y. Luo, K. Beverly, J. Sampaio, F. M. Raymo, J. F. Stoddart, J. R. Heath, *Science* **2000**, *289*, 1172 – 1175. Operating as an actuator, the dual bistability exhibited by a palindromic [3]rotaxane, with two redox-driven units that act synchronously and cooperatively within a self-assembled monolayer, has been harnessed to bend micrometer-sized, gold-coated silicon cantilever beams, which could be considered as prototypes of nanoelectromechanical systems; see: T. J. Huang, B. Brough, C.-M. Ho, Y. Liu, A. H. Flood, P. Bonvallet, H.-R. Tseng, J. F. Stoddart, M. Baller, S. Magonov, *Appl. Phys. Lett.* **2004**, *85*, 5391 – 5393.

[30] G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, New York, **1997**, p. 303.

[31] A. Affeld, G. M. Hubner, C. Seel, C. A. Schalley, *Eur. J. Org. Chem.* **2001**, 2877 – 2890.

[32] a) A. Hanke, R. Metzler, *Chem. Phys. Lett.* **2002**, *359*, 22 – 26; b) G. Bottari, F. Dehez, D. A. Leigh, P. J. Nash, E. M. Pérez, J. K. Y. Wong, F. Zerbetto, *Angew. Chem.* **2003**, *115*, 6066 – 6069; *Angew. Chem. Int. Ed.* **2003**, *42*, 5886 – 5889.

[33] F. Huang, J. W. Jones, C. Slebodnick, H. W. Gibson, *J. Am. Chem. Soc.* **2003**, *125*, 14 458 – 14 464.

[34] J. W. Jones, H. W. Gibson, *J. Am. Chem. Soc.* **2003**, *125*, 7001 – 7004.

[35] a) S. Bartoli, S. Roelens, *J. Am. Chem. Soc.* **1999**, *121*, 11 908 – 11 909; b) S. Bartoli, S. Roelens, *J. Am. Chem. Soc.* **2002**, *124*, 8307 – 8315; c) M. Clemente-Leon, C. Pasquini, V. Hebbe-Viton, J. Lacour, A. Dalla Cort, A. Credi, *Eur. J. Org. Chem*, in press.

[36] The mechanism of the shuttling motion in two opposing directions, in keeping with the bistable character in acid–base-switchable rotaxanes, is similar to that observed for redox-driven bistable rotaxanes and catenanes (see ref. [19]). In redox-driven switches, the backward second shuttling motion, which corresponds qualitatively to the energy-level diagram in Figure 6 b, has been quantified. Although the barrier corresponding to the forward shuttling motion (Figure 6 a) has not been measured, we believe that it is considerably less than the 16 kcal mol^{-1} barrier observed for the backward shuttling motion.

[37] *Supramolecular Chemistry of Anions* (Eds.: A. Bianchi, K. Bowman-James, E. Garcia-Espana), Wiley-VCH, New York, **1997**, p. 461.

[38] a) S. Kubik, *J. Am. Chem. Soc.* **1999**, *121*, 5846 – 5855; b) S. Kubik, R. Goddard, *J. Org. Chem.* **1999**, *64*, 9475 – 9486; c) V. Böhmer, A. Dalla Cort, L. Mandolini, *J. Org. Chem.* **2001**, *66*, 1900 – 1902.

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