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This communication describes the base- and acid-induced five-state translational isomerization of a [3]rotaxane containing two pairs of *N*-arylamine and *N*-alkylamine centers as binding sites for two dibenzo[24]crown-8 components. Gradual molecular shuttling of this [3]rotaxane is achieved in response to both the amount and strength of the added acid or base.

Rotaxane systems driven by external stimuli have received much attention recently because of the ability to control their properties.[1] Changing the relative positions of the components of a rotaxane will transform its molecular shape, the positions of its functional groups, and its inter- and intramolecular interactions; accordingly, such systems constitute an effective and powerful strategy for the development of molecular switching machines, including sensors,[2] nanovalves,[3] actuators,[4] and other devices.[5,6]

The *sec*-ammonium ion–crown ether recognition pair has been used widely in acid–base-responsive molecular shuttles[7] because it allows fine control over the state of the hydrogen bonding donor ($^{+}NH_2$) through deprotonation and protonation. For example, in a previous study we prepared a three-state molecular shuttle containing such an ammonium ion–crown ether pair.[8] Multi-state (more than three-state) molecular shuttles[9] (outputting systems) have the potential to behave as high-performance nano-machines—for example, as molecular sensors that respond to the amount and/or strength of a stimulus; as nanovalves capable of multiple degrees of opening and shutting; and as amplitude-controllable actuators. Herein, we report the synthesis of a five-state – switchable [3]rotaxane featuring two sets of ammonium ion–crown ether recognition pairs and its multiple shuttling processes in response to the amounts and strength of acid and base stimuli.

Our previously reported three-state [2]rotaxane featured *N*-arylamine and *N*-alkylamine centers as binding sites for a threaded dibenzo[24]crown-8 (DB24C8) unit.[8] After the addition of a strong base, the crown ether component of this [2]rotaxane preferred to encircle the *N*-arylamine center; under neutral conditions, the crown ether component predominantly recognized the alkylammonium center; when both amino groups were protonated, both translational isomers were generated.

If two units of such a [2]rotaxane were present in a single molecule, we might expect to realize a system capable of exhibiting five different states of molecular shuttling, but only if it would allow control over the protonation and deprotonation of both amines centers (Fig. 1).[10] Accordingly, we designed a [3]rotaxane in which the two aryl N atoms are connected through the same aromatic core unit to allow multiple isomerism and selective switching of each of the two [2]rotaxane subunits. If this [3]rotaxane were to be deprotonated upon the addition of a base (from state 3 to state 1), hydrogen bonding and π-stacking of the aryl NH group–crown ether moiety in one of the [2]rotaxane subunits would increase the

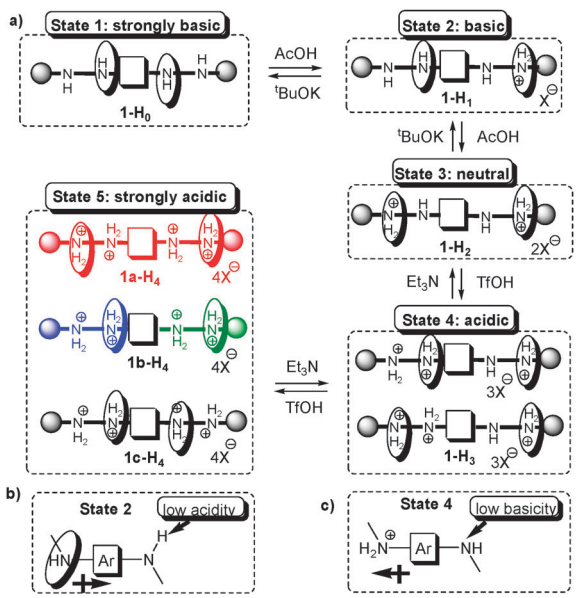

Fig. 1 (a) Cartoon representation of the conditions for five-state molecular shuttling and the effects of (b) hydrogen bonding and (c) protonation of the NH–Ar units on the electronic properties of the aromatic core.

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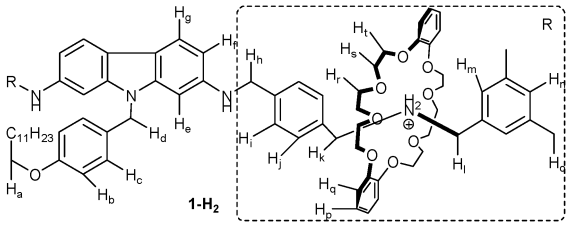

Fig. 2 Structure of the [3]rotaxane **1-H$_2$**.

electron density of the aromatic core, thereby potentially weakening the strength of the corresponding interactions in the other [2]rotaxane subunit (Fig. 1b, state 2). After arylammonium ion formation upon the addition of an acid (from state 3 to state 5), the first protonation might disturb the second, because of the strong electron-withdrawing properties of the first ammonium functionality; in other words, the form in which both aniline units are protonated might be destabilized (Fig. 1c, state 4). We chose a carbazole to form the aromatic core because we expected its flat, π-conjugated structure to influence the electronic behavior of the system in its deprotonated state (under basic conditions) and its protonated state (under acidic conditions). The designed [3]rotaxane **1-H$_2$** is shown in Fig. 2.

The addition of ^{t}BuOK (2.5 eq.) to a solution of **1-H$_2$** in CD_3CN–CD_3OD (10 : 1) resulted in a ^{1}H NMR spectrum revealing a new set of signals (Fig. 3b, from state 3 to state 1). These signals were consistent with the doubly deprotonated [3]rotaxane **1-H$_0$**, in which the two DB24C8 units encircle the two amino groups of the carbazole core. The signals of the benzylic protons H_k and H_l of **1-H$_0$** appeared at

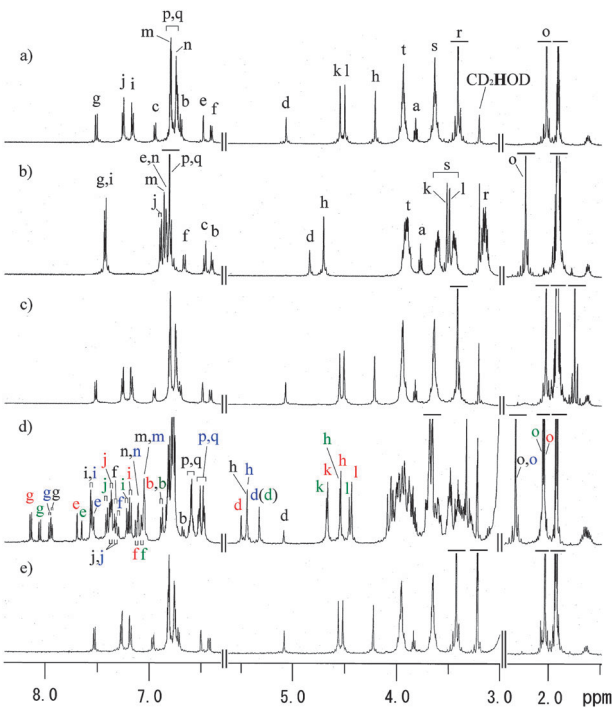

Fig. 3 ^{1}H NMR spectra (500 MHz; CD_3CN–CD_3OD, 10 : 1) of the [3]rotaxane **1-H$_2$** under neutral, basic, and acidic conditions. (a) **1-H$_2$**; (b) the sample in (a) after the addition of ^{t}BuOK (2.5 eq.); (c) the sample in (b) after the addition of AcOH (2.6 eq.); (d) the sample in (a) after the addition of TfOH (6 eq.); (e) the sample in (d) after the addition of Et_3N (15 eq.). For colour and atom labels, see Fig. 1 and 2.

significantly higher fields (3.54 and 3.52 ppm, respectively) relative to those of **1-H$_2$**, presumably because of the loss of the deshielding effects of the DB24C8 units and the deprotonation of the ammonium centers. In addition, the signal for H_h moved to a lower field (4.72 ppm), a likely result of the deshielding effect of the macrocyclic component. We also observed deshielding effects of the protons of the carbazole unit, resulting in downfield shifts of the signals of the aromatic protons (H_e: 6.86 ppm; H_f: 6.68 ppm) of **1-H$_0$**.

Next, we investigated whether the mono-protonated form **1-H$_1$** (state 2) might be produced selectively under weakly basic conditions, based on the electronic effects of hydrogen bonding of a DB24C8 unit to the aminocarbazole core (from state 1 to state 3). Accordingly, we monitored the ^{1}H NMR spectra of the mixture of the [3]rotaxane and ^{t}BuOK (2.5 eq.) after addition of variable amounts of AcOH (Fig. S1, ESI†). We observed signals for the mono-protonated species **1-H$_1$** (state 2) initially and then for the doubly protonated species **1-H$_2$** (state 3). The protonation of both dialkylamine units led to spontaneous switching of the DB24C8 units back to their original positions (*i.e.*, encircling the two dialkylammonium centers). Selective mono-protonation occurred until the addition of 1.5 eq. of AcOH; at this point, integration of the signals revealed an 18 : 64 : 18 mixture of **1-H$_0$**, **1-H$_1$**, and **1-H$_2$** (Fig. S1c, ESI†). Statistically, we would expect the ratio of isomers to be 25 : 50 : 25 under mono-protonation conditions in the absence of any electronic effects between the two sets of [2]rotaxane subunits. Finally, after the addition of 2.6 eq. of AcOH, only the original, doubly protonated species **1-H$_2$** was present (Fig. 3c); thus, we had confirmed the reversibility of the interconversion between **1-H$_0$** and **1-H$_2$** (from state 1 to state 3). We also confirmed the reversibility of the interconversion between **1-H$_0$** and **1-H$_2$** *via* **1-H$_1$** through four cycles of using Bu_4NOH as the base and AcOH as the acid (Fig. S2, ESI†), the difference between ^{t}BuOK and Bu_4NOH was not observed.

Next, we examined the protonation-controlled molecular shuttling of our [3]rotaxane (from state 3 to state 5). Although we expected that the addition of TfOH might generate some protonated arylamine species, we did not detect any clear signals associated with the corresponding ions in the resulting ^{1}H NMR spectra until we had added three equivalents of TfOH (Fig. S3, ESI†). The addition of four equivalents of TfOH to a solution of the [3]rotaxane was required to provide clear signals for the three translational isomers (Fig. 3d); finally a mixture of **1-H$_2$** and TfOH (375 eq.) afforded a 37 : 42 : 21 mixture of **1a-H$_4$**, **1b-H$_4$**, and **1c-H$_4$** (using H_g signals in the ^{1}H NMR spectrum). Subsequently, we investigated the effect of neutralization of the mixture of the [3]rotaxanes **1-H$_4$** on the translocation of the DB24C8 units after the addition of TfOH (6 eq.: a 32 : 51 : 17 mixture of **1a-H$_4$**, **1b-H$_4$**, and **1c-H$_4$**).[11] Deprotonation of the arylammonium centers in **1-H$_4$** with Et_3N (15 eq.) smoothly regenerated **1-H$_2$** (state 3), with the DB24C8 units relocating to their original sites (*i.e.*, those under neutral conditions): the dialkylammonium centers (Fig. 3e).

We used UV spectroscopy to determine the distribution of the components **1-H$_2$**, **1-H$_3$**, and **1-H$_4$** (states 3, 4, and 5, respectively) upon the gradual protonation of both arylamine moieties (Fig. S4, ESI†). The UV/vis spectra of the [3]rotaxane **1-H$_2$** recorded after the addition of TfOH reflected the transformation of the initial diaminocarbazole core (**1-H$_2$**) without associated crown ether moieties into

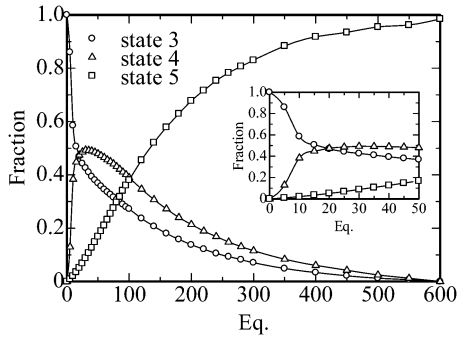

Fig. 4 Distribution of **1-H$_2$**, **1-H$_3$**, and **1-H$_4$** [20 μM in CH_3CN–CH_3OH (1 : 1)] in the presence of TfOH (0–600 eq.).

the singly protonated carbazole cores with and without crown ether moieties and then into the doubly protonated carbazole cores with and without associated crown ether moieties. Target factor analysis,[12] a chemometric technique, revealed the distributions of **1-H$_2$**, **1-H$_3$**, and **1-H$_4$** until all of the amino groups in the [3]rotaxane had become protonated. In Fig. 4, the content of the mono-protonated species (**1-H$_3$**) increased until the addition of approximately 30 equivalents of TfOH; at this stage, the distribution of **1-H$_2$** (state 3), **1-H$_3$** (state 4), and **1-H$_4$** (state 5) was 42 : 50 : 8. Thus, it appears as though the presence of the two amino groups on the same aromatic core allowed selective mono-protonation (50 : 8), as expected (Fig. 4; Fig. S4 and S8, ESI†).

UV spectra of a mixture of **1-H$_2$** and Et_3N after the addition of TfOH revealed that the interconversion of **1-H$_2$** and **1-H$_4$** was reversible; deprotonation of **1-H$_4$** with Et_3N smoothly regenerated **1-H$_2$** with the macrocyclic components located at the original positions about the ammonium centers, *via* the intermediate **1-H$_3$** (Fig. S5, ESI†). We could use UV spectroscopy to monitor these interconversions reversibly through repeated sequential additions of TfOH and Et_3N (Fig. S6, ESI†).

Having studied this system's two reversible switching processes (addition of a strong base followed by a weak acid; addition of a strong acid followed by a weak base), we combined them to perform five-state switching (Fig. S7, ESI†). First, we added Bu_4NOH (5 eq.) to deprotonate the dialkylammonium units of **1-H$_2$** (monitored using ^{1}H NMR spectroscopy); second, we added AcOH (5 eq.) to neutralize the mixture (monitored using ^{1}H NMR spectroscopy); third, we protonated the arylamino groups with TfOH after dilution of the mixture (monitored using UV spectroscopy); finally, we added Et_3N to the mixture (monitored using UV spectroscopy).

In conclusion, we have synthesized a symmetrical [3]rotaxane containing two [2]rotaxane subunits, each featuring a dialkylammonium center, an alkylaryl amine unit, and a DB24C8 unit, with a diaminocarbazole unit as a central aromatic core. This [3]rotaxane undergoes acid- and base-driven five-state molecular shuttling: under strongly basic conditions, the two DB24C8 units encircle the ArNH moieties; under weakly basic conditions, the dialkylamino groups are mono-protonated predominantly, with the DB24C8 units residing at both the dialkylammonium and ArNH centers; under neutral conditions, the macrocycles encircle the dialkylammonium centres; under weakly acidic conditions, mono-protonation of the arylamine units occurs selectively; finally under strongly acidic conditions, both the arylamine units become protonated, with all of the *sec*-ammonium groups acting as centers. The shuttling of the macrocyclic components could be performed reversibly through the addition of strong and weak bases and strong and weak acids.

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