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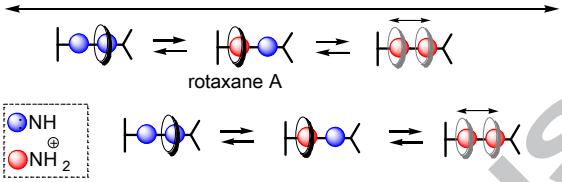

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Multi-state molecular shuttling of a pair of [2]rotaxane in response to weak and strong acid and base stimuli

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ABSTRACT

Type your Abstract text here This paper describes the base- and acid-mediated four-state (partially five-state) translational isomerization of a mixture of two [2]rotaxanes, each containing *N*-alkylamine and *N*-arylamine centers as binding sites for threaded crown ethers. Gradual changes in the molecular shuttling of each [2]rotaxane were achieved in response to both the amount and strength of the added acid or base.

Switchable rotaxanes that respond to external stimuli have received much attention.[1] A considerable number of bistable molecular systems have been developed and applied as molecular machines for nanoscience, including sensors,[2] actuators,[3] molecular memories,[4] and other devices.[1,5] Multi-state (more than three-state) molecular shuttles[6] have also been realized using rotaxane systems; they can be grouped into two types: multiple stimuli–responsive[7] and single stimulus–responsive[8] molecular shuttles, with the former being potentially applicable as sensing systems for a variety of chemical species and the latter as degree- or amplitude-controllable nanomachines. In a previous study, we developed an example of the latter system that functioned through acid/base-mediated three-state translational isomerization of a [2]rotaxane containing both *N*-alkylamine and *N*-arylamine centers as binding sites for a threaded crown ether unit.[9] Deprotonation (basic conditions) caused the aniline–crown ether interactions to dominate; under mono-protonated (neutral) conditions, the crown ether component predominantly recognized the alkylamine unit through cooperative binding of a proton; when both amino groups were protonated, both translational isomers were generated.

If two pairs of this type of [2]rotaxane were to be mixed, with the basicities of both *N*-alkylamines and *N*-arylamines in the two [2]rotaxanes being different, the protonation and deprotonation of the four different amines might be controllable in response to the amounts and strengths of added acids and bases, potentially providing a molecular shuttling system featuring five different states. In Fig. 1, the basicities of both the *N*-alkyl- and *N*-arylamines in the [2]rotaxane **1H$_0$** are higher than those in the

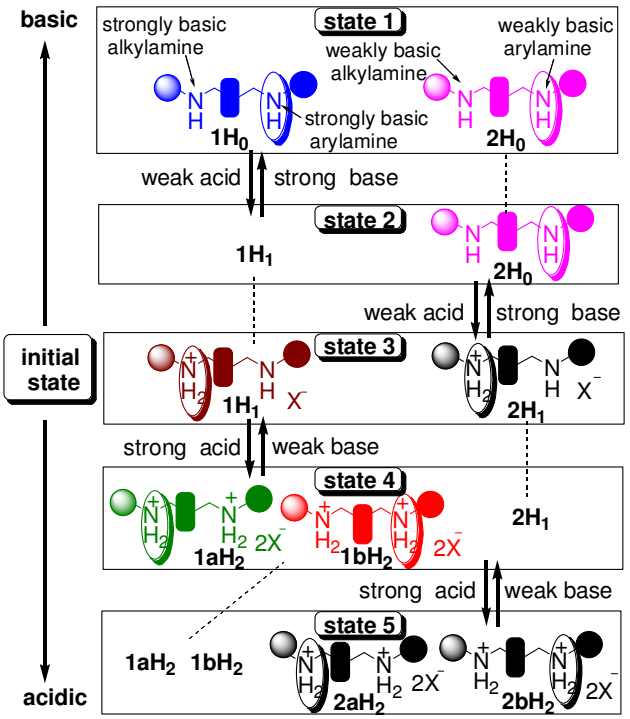

Figure 1. Cartoon representation of the conditions for five-state molecular shuttling using a pair of [2]rotaxanes **1H$_1$** and **2H$_2$** in their mono-ammonium forms.

[2]rotaxane **2H$_0$**. Upon the addition of an acid to a mixture of the [2]rotaxanes **1H$_0$** and **2H$_0$** (state 1), protonation would occur sequentially at the alkylamine unit in **1H$_0$** from **1H$_1$** (state 2), the alkylamine unit in **2H$_0$** (state 3), the arylamine unit in **1H$_1$** (state 4), and the arylamine unit in **2H$_1$** (state 5). In this Letter, we report our attempts to construct such a five-state system from a pair of [2]rotaxanes; we found, however, that we could detect at least four-state shuttling (a partial five-state system), without evidence for state 5.

Figure 2 outlines the concept of basicity regulation. The hydrogen bonding ability of the threaded crown ether regulates the acidities of the alkylammonium (the basicities of the alkylamine) units in the [2]rotaxanes **1H$_1$** and **2H$_1$** (**1H$_0$** and **2H$_0$**), because strong hydrogen bonding inhibits deprotonation of alkylammonium ions (Fig. 2a). We designed a more-basic [2]rotaxane **1H$_1$** (mono-ammonium form), which features a 24-membered crown ether ring with no fused benzene rings (24C8), and a less-basic [2]rotaxane **2H$_1$** (mono-ammonium form), which features a 25-membered crown ether ring presenting two fused benzene rings (DB25C8). These systems differ in that a 24-membered crown ether can provide stronger hydrogen bonds than those of a 25-membered crown ether,[10] and because oxygen atoms of dialkyl ether units are more basic than those of alkyl aryl ether units.[11] In contrast, to further control the basicities of the aniline moieties, the [2]rotaxanes **1H$_1$** and **2H$_1$** bear an electron-donating methoxy and an electron-withdrawing cyano group at the 4-position of their terminal aniline units, respectively (Fig. 2b). Fig. 3 displays the structures of the [2]rotaxanes **1H$_1$** and **2 H$_1$** in their mono-ammonium forms.

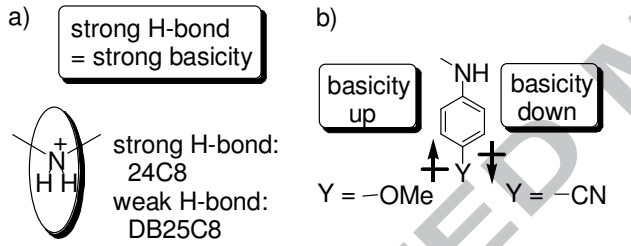

Figure 2. Regulation of the basicity of amino groups in [2]rotaxanes. (a) Regulation of the basicity of an alkylamine unit through control of its hydrogen bonding; (b) regulation of the basicity of an arylamine unit through substituent effects.

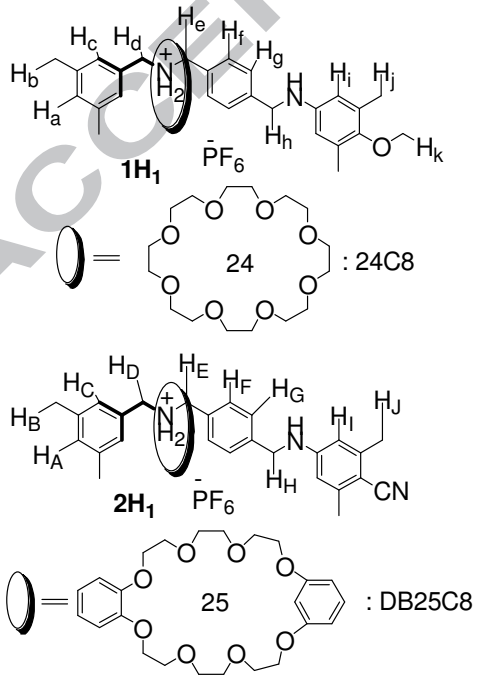

Figure 3. Structures of the [2]rotaxanes **1H$_1$** and **2H$_1$**.

To begin this study, we examined the deprotonation- and protonation-controlled molecular shuttling of the [2]rotaxanes **1H$_1$** and **2H$_1$** independently. The addition of Bu_4NOH (2.0 eq)[*12] as a base to a solution of **1H$_1$** in CD_3CN/CD_3OD (10:1) resulted in a ^1H NMR spectrum featuring a new set of signals for the deprotonated [2]rotaxane **1H$_0$**, in which the 24C8 unit encircles the arylamino group (Fig. S1a, ESI†). The signals of the benzylic protons H_d and H_e of **1H$_0$** appeared at significantly higher fields (3.65 and 3.74 ppm, respectively) relative to those of **1H$_1$** (4.39 and 4.48 ppm, respectively) because of (i) the loss of the deshielding effect of the 24C8 unit and (ii) deprotonation of the ammonium center. In addition, the signal for H_h moved to lower field (4.45 ppm), a likely result of the deshielding effect of the crown ether component. In the NOESY spectrum, we observed correlations between the signals of the crown ether protons and H_g, H_h, and H_i of the dumbbell-shaped component (Fig. S6b, ESI†).*[13] The reversibility of the interconversion between **1H$_0$** and **1H$_1$** was evidenced by adding AcOH as an acid after the addition of Bu_4NOH. Likewise, we confirmed the reversible interconversion between **2H$_1$** and **2H$_0$** through sequential additions of Bu_4NOH and TFA in the same manner as that described above (Fig. S2, ESI†). *[14]

The addition of TfOH to a solution of the [2]rotaxane **1H$_1$** in CD_3CN/CD_3OD (10:1) resulted in two sets of signals, for two translational isomers, appearing in the ^1H NMR spectrum; for example, a mixture of **1H$_1$** and TfOH (3 eq) afforded a 70:30 mixture of **1aH$_2$** and **1bH$_2$** (Fig. S1b, ESI†). We observed the signals for the protons H_d and H_e of **1aH$_2$** and for the proton H_h of **1bH$_2$** at high field (H_d and H_e of **1aH$_2$** at 4.38 and 4.56 ppm, respectively; H_h of **1bH$_2$** at 5.07 ppm), allowing us to identify these translational isomers. Moreover, the NOESY spectrum revealed correlations between the signals of the crown ether protons and protons H_c, H_d, H_e, and H_f of the dumbbell-shaped component in the major isomer **1aH$_2$** and between the crown ether protons and protons H_g and H_i in the minor isomer **1bH$_2$** (Fig. S7b, ESI†). Subsequent deprotonation of the arylammonium centers in **1aH$_2$** and **1bH$_2$** with Et_3N (4 eq) smoothly regenerated **1H$_1$**, with the 24C8 unit relocating to the original dialkylammonium station (Fig. S1b, ESI†).

Although we had expected the addition of TfOH to a solution of **2H$_1$** to generate protonated arylamine species, we did not detect any clear signals associated with the corresponding [2]rotaxane **2H$_2$** in the resulting ^1H NMR spectra until we had added 500 eq of TfOH (Fig. S3, ESI†). In variable temperature (VT) experiments, the ^1H NMR spectrum of a mixture of **2H$_1$** and TfOH (500 eq) at –50 °C afforded some sharp signals, including one at 4.92 ppm, which we assigned to the proton H_h of **2bH$_2$**, allowing us to identify a 85:15 mixture of **2aH$_2$** and **2bH$_2$** [Fig. S3(h), ESI†]. Because the ratio of **2aH$_2$** and **2bH$_2$** (85:15) was different from that of **1aH$_2$** and **1bH$_2$** (70:30), and because the signals were broad under the acidic conditions, we suspect that protonation of the arylamine unit of **2H$_1$** did not proceed completely, even though we had added 500 eq of TfOH. In consideration of the distribution of the [2]rotaxanes **2aH$_2$** and **2bH$_2$**, we calculated that approximately 50% of **2H$_1$** could be protonated under these conditions. Deprotonation of the arylammonium center in **2H$_2$** with an excess of $NaHCO_3$ smoothly regenerated **2H$_1$** (although some undefined signals appeared in the ^1H NMR spectrum) [Fig. S3(i), ESI†].

Having confirmed the deprotonation- and protonation-controlled molecular shuttling of each individual [2]rotaxane, we examined the multi-state molecular switching behavior of a system comprising a mixture of rotaxanes. The ^1H NMR spectrum of a solution of the [2]rotaxanes **1H$_1$** and **2H$_1$** (1:1, 3 mM) containing 1 eq of Bu_4NOH reflected the transformation of only the less-basic [2]rotaxane **2H$_1$** (i.e., without deprotonation of the [2]rotaxane **1H$_1$**), because the signals of **2H$_0$** were observed

instead of those of **2H$_1$**, while the signals of **1H$_1$** remained [Fig. 4(b), state 2].

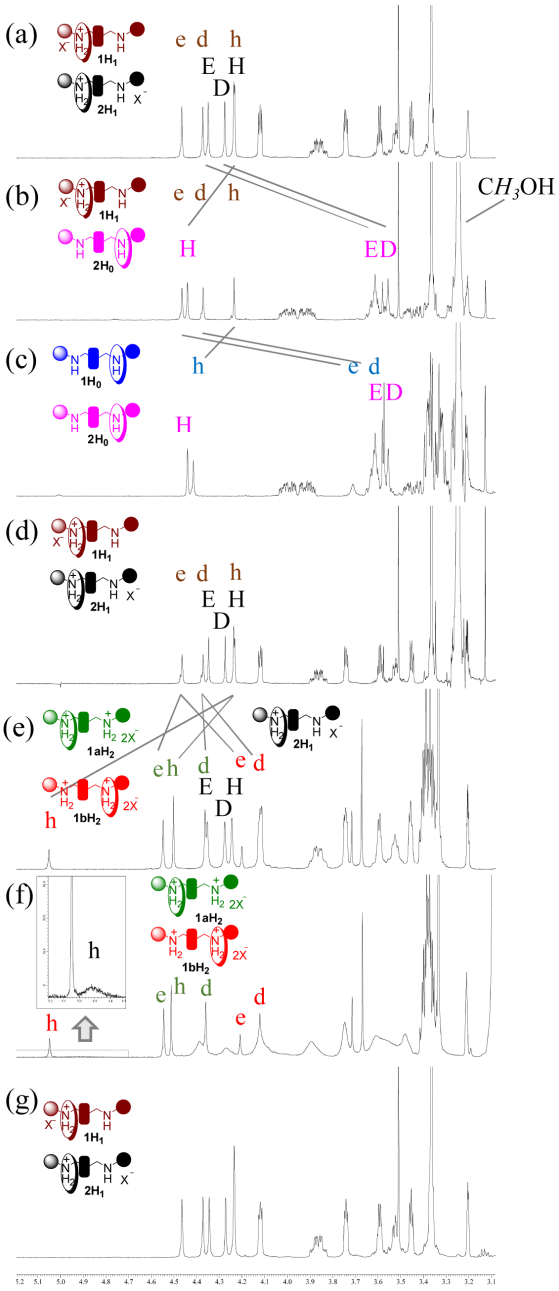

Figure 4. ^{1}H NMR spectra (600 MHz; CD_3CN/CD_3OD, 10:1) of a mixture of the [2]rotaxanes **1H$_1$** and **2H$_1$** under neutral, weakly basic, strongly basic, and acidic conditions. (a) Mixture of **1H$_1$** and **2H$_1$**; (b) the sample in (a) after the addition of Bu_4NOH (1.0 eq); (c) the sample in (b) after the addition of Bu_4NOH (1.2 eq); (d) the sample in (c) after the addition of AcOH (8.0 eq) and TfOH (1.8 eq); (e) the sample in (a) after the addition of TfOH (1.5 eq); (f) the sample in (e) after the addition of TfOH (10 eq); (g) the sample in (f) after the addition of Et_3N (12 eq). For atom labels, see Figs. 1 and 3.

Subsequently, deprotonation of [2]rotaxane **1H$_1$** was detected after the addition of a further 1.2 eq of Bu_4NOH [Fig. 4(c) (total 2.2 eq of Bu_4NOH), state 1]. Gradual protonation of the [2]rotaxanes of state 1 (**1H$_0$** and **2H$_0$**) was also possible; sequential addition of AcOH and TfOH to the system in state 1 resulted in the appearance of state 2 (AcOH: 1.2 eq) and state 3 [Fig. 4(d); AcOH: 9.2 eq; TfOH: 1.8 eq], again confirmed using NMR spectroscopy. The basicity of the alkylamine units in the [2]rotaxanes **1H$_0$** and **2H$_0$** was, therefore, completely regulated by the differences in the size and a number of fused benzene rings on their crown ether components.

Next, we monitored the protonation of the aniline moieties of these [2]rotaxanes. The aniline moiety of the [2]rotaxane **1H$_1$** was predominantly protonated until the addition of 1.5 eq of TfOH; ^{1}H NMR [CD_3CN/CD_3OD (10:1)] spectra of the mixture revealed the absence of the [2]rotaxane **1H$_1$**, but no significant change in the signals of **2H$_1$**. After we had added 1.5 eq of TfOH, the distribution of **1aH$_2$** and **1bH$_2$** was 69:31 [Fig. 4(e), state 4]. Addition of an excess of TfOH (10 eq) afforded the broad signals of the [2]rotaxane **2H$_1$** [Fig. 4(f)]. The broad signal at 4.92 ppm, which we assign to the proton H_h of **2bH$_2$**, was present; integration revealed a 90:10 ratio of **2aH$_2$** and **2bH$_2$** (partial state 5), suggesting that approximately 30% of the [2]rotaxane **2H$_1$** had undergone protonation. We confirmed the reversible interconversion of these species through the addition of Et_3N (13 eq) after the addition of TfOH (10 eq).

Having confirmed the possibility of performing these two reversible switching processes (the addition of a base followed by a weak acid, and the addition of an acid followed by a weak base), we combined them into one system to realize five-state switching. After the first switching process (from state 3 to state 1 and returning to state 3), we added TfOH (2.0 eq) to protonate the arylamino group of **1H$_1$** (from state 3 to state 4) and then further TfOH (7.6 eq) to switch the system from state 4 to partial state 5; finally, we added 9.0 eq of Et_3N to switch the mixture from partial state 5 to state 4, and then added 2.0 eq of Et_3N to switch it from state 4 to state 3 (Fig. S4, ESI†).

In conclusion, we have synthesized a pair of [2]rotaxanes, each featuring an alkylammonium center and an aryl amine unit as stations for a crown ether, with one of the pair featuring more-basic alkyl and aryl amino groups. The mixed [2]rotaxane system exhibited four (partially five) molecular shuttling patterns in response to the additions of weak and strong acids and bases. The crown ether units encircled the aryl amine moieties of both [2]rotaxanes under strongly basic conditions; under weakly basic conditions, the only the alkylamino group of the more-basic [2]rotaxane was protonated, allowing the 24C8 unit to reside at the alkylammonium station; under neutral conditions, the DB25C8 component also encircled the dialkylammonium station; under weakly acidic conditions, the more-basic arylamine unit was protonated selectively; finally under strongly acidic conditions, partial protonation of the less-basic arylamine also occurred, with all of the ammonium units behaving as stations. These shuttling processes can proceed reversibly under appropriate conditions.

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Supplementary Material

Supplementary material (full experimental details, additional spectra of NMR titration, and characterization data of compounds) associated with this article can be found, in the online version.

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14. TFA was used as an acid instead of AcOH in the case of [2]rotaxane $\mathbf{2H_1}$. The acidity or the effects of counter-anions might be important to relocate completely. For an example of the effects of counter-anions, see: Gibson, H. W.; Jones, J. W.; Zakharov, L. N.; Rheingold, A. L.; Slebodnick, C. *Chem. Eur. J.* **2011**, *17,* 3192–3206.