Halogen Bonding

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Iodide-Induced Shuttling of a Halogen- and Hydrogen-Bonding Two-Station Rotaxane**

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Abstract: *The first example of utilizing halogen-bonding anion recognition to facilitate molecular motion in an interlocked structure is described. A halogen-bonding and hydrogen-bonding bistable rotaxane is prepared and demonstrated to undergo shuttling of the macrocycle component from the hydrogen-bonding station to the halogen-bonding station upon iodide recognition. In contrast, chloride-anion binding reinforces the macrocycle to reside at the hydrogen-bonding station.*

The ability of mechanically interlocked molecules to undergo controlled molecular motion through changes in the relative positions of their constituent parts is receiving an ever increasing amount of interest because of the promise of molecular switches and machines as potential nanotechnological applications.[1] However, despite the recent advances in anion supramolecular chemistry,[2] there are still relatively few examples of such interlocked systems which are mediated by anions as an external stimulus.[3] Of these systems, only a small number have been shown to display selectivity between different coordinating anions.[3a,i,j] While during the past two decades hydrogen bonding (HB) has been widely exploited in anion-receptor design, halogen bonding (XB), the attractive highly directional interaction between an electron-deficient halogen atom and a Lewis base,[4] has only recently begun to be utilized for anion recognition. Of the relatively few examples of XB anion receptors reported to date,[5] it is noteworthy that all display promising, and, in some cases, significantly contrasting, anion-recognition behavior when compared to HB analogues. Moreover, anion-binding selectivity can also be modulated through the combination of halogen and hydrogen bonding in urea-based[5c] and rotaxane anion–host systems.[5g]

We report herein as a proof of concept the first example of using XB anion recognition to control the molecular motion of an interlocked structure. A halogen- and hydrogen-bonding two-station rotaxane is demonstrated to undergo the shuttling of the macrocyclic wheel component along the rotaxane's axle which is controlled by the nature of a coordinating halide anion (Figure 1). Covalently integrated into the interlocked structure's axle are two anion-recognition sites consisting of an iodotriazolium XB station and a protic triazolium HB station motif. Molecular motion of the isophthalamide-containing macrocycle to the XB station is driven by iodide recognition whereas chloride binding results in the macrocycle residing at the HB station. Additionally, the anion-binding properties of two new mono-station XB and HB rotaxanes further supports the observed halide-anion-induced shuttling behavior of the two-station-rotaxane system.

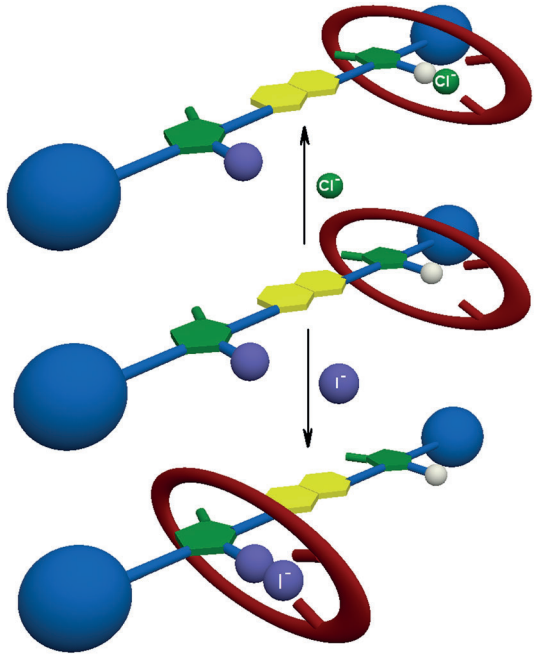

Figure 1. Schematic representation of the anion-induced shuttling behavior exhibited by the iodotriazolium and H-triazolium XB–HB two-station rotaxane.

Before preparing the target XB–HB two-station rotaxane, appropriately designed mono-station XB and HB rotaxanes were prepared to elucidate their respective halide-anion binding properties.

The HB and XB rotaxanes **1** and **2** (Figure 2) were synthesized using stepwise procedures described in the Supporting Information (Schemes S2 and S3).

Both rotaxanes **1·Cl** and **2·Cl** were characterized by ^{1}H, ^{13}C, and ^{1}H ROESY NMR spectroscopy, and high-resolution electrospray ionization mass spectrometry (ESI-MS). The characteristic upfield shifts of the signals attributable to the

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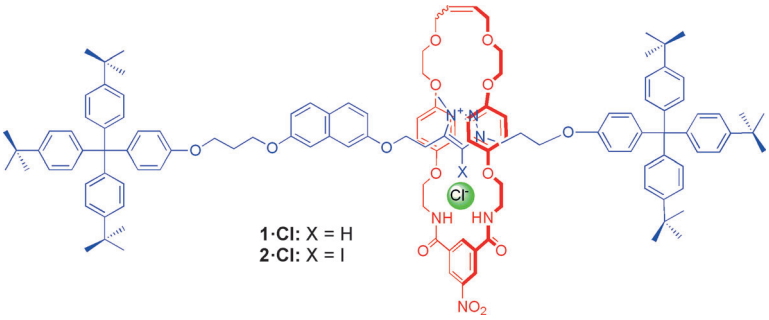


Figure 2. Structure of the mono-station rotaxanes **1·Cl** and **2·Cl**.

hydroquinone protons on the macrocycle as well as the multiple through-space correlations between signals arising from the axle and macrocycle protons in a 2D ^{1}H ROESY NMR spectrum confirm the interlocked nature of the rotaxanes (see Supporting Information). Repeated washings with aqueous NH_4PF_6 solution removed the chloride anion template to give the rotaxanes **1·PF$_6$** and **2·PF$_6$**.

The halide anion binding properties of the HB rotaxane **1·PF$_6$**, and the XB rotaxane **2·PF$_6$** were investigated using ^{1}H NMR spectroscopy titration experiments through the addition of aliquots of the tetrabutylammonium halide salt to solutions of the rotaxanes in a solvent mixture of CD_3OD/$CDCl_3$ (1:1 v/v).

In all cases the addition of the halide anions to **1·PF$_6$** and **2·PF$_6$** caused significant perturbations in the ^{1}H NMR spectra of the rotaxanes. Downfield shifts in the signals associated with the macrocycle isophthalamide, and, in the case of the HB rotaxane **1·PF$_6$**, the C-*H* proton of the triazolium heterocycle, were detected, indicating that the halide anion binds within the cavity of both rotaxanes. Additionally, a small upfield shift in the signals attributable to the hydroquinone and the *N*-methyl protons of the respective axle triazolium group was detected (Supporting Information).

Association constants were determined by WinEQNMR[6] analysis of the titration data using a 1:1 stoichiometric host–guest binding model (Table 1).

Whereas the HB rotaxane **1·PF$_6$** displays a preference for the smaller halide anions Cl^- and Br^-, the XB rotaxane **2·PF$_6$** exhibits the opposite selectivity trend with iodide being bound the most strongly, an observation also previously noted in a related XB rotaxane.[5g] This highlights the dramatic effect the integration of the iodine halogen atom into a rotaxane host cavity can have on the anion-recognition properties of the interlocked receptor system.

Table 1: Association constants K_a for **1·PF$_6$** and **2·PF$_6$** with different halides in $CDCl_3$/CD_3OD (1:1 v/v) at 295 K.

Receptor	Anion[a]	K_a [M^{-1}][b]
1·PF$_6$	Cl^-	536 (45)
	Br^-	496 (21)
	I^-	307 (25)
2·PF$_6$	Cl^-	462 (17)
	Br^-	710 (46)
	I^-	1098 (26)

[a] Anions were used as a tetrabutylammonium salt. [b] Calculated based on the internal phenyl protons. Error given in parentheses.

Encouraged by the contrasting halide-binding affinities of the HB and XB mono-station rotaxanes, the synthesis of a novel XB–HB two-station rotaxane was undertaken to investigate the exciting possibility of exploiting iodide–XB anion recognition to induce molecular shuttling from one station to another.

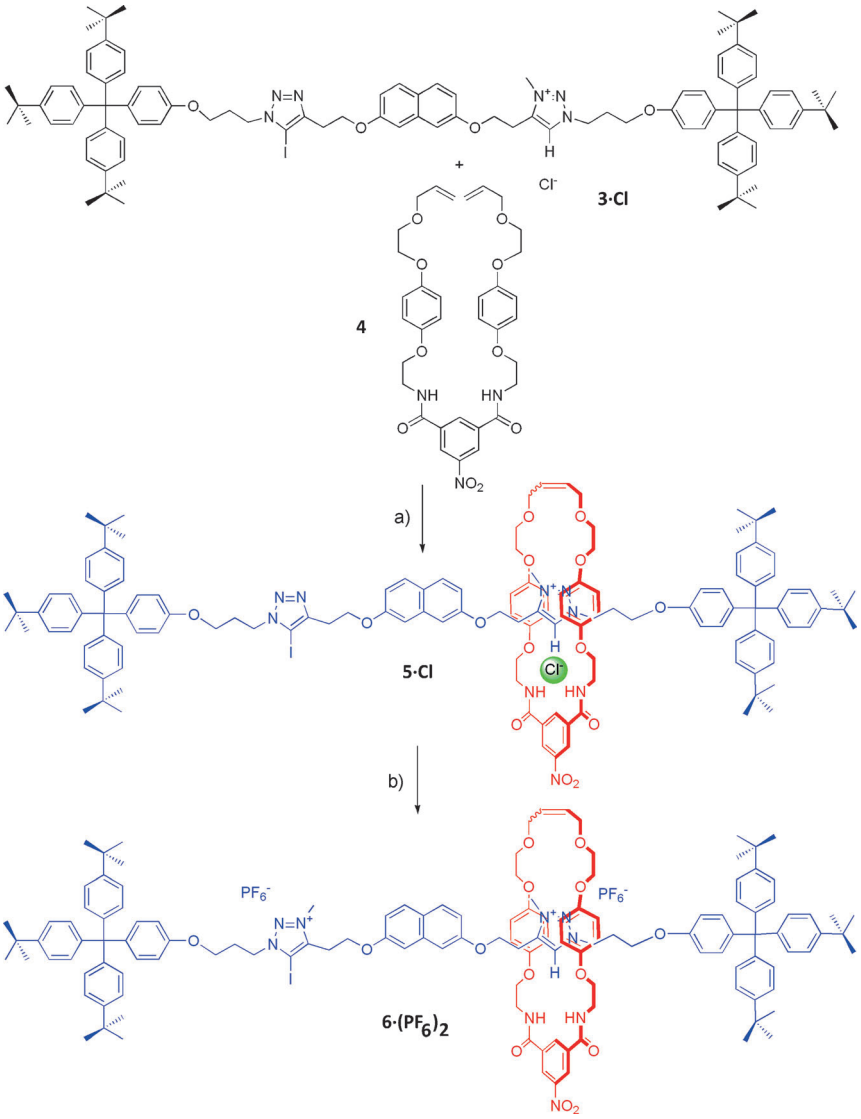
XB–HB two-station rotaxane **6·(PF$_6$)$_2$** (Scheme 1) was prepared by a multistep synthetic procedure in an overall yield of 3.5 % (Scheme S1 in the Supporting Information).

Reaction of an equimolar mixture of triazolium axle **3·Cl** and bis-vinyl-functionalized derivative **4**[7] with Grubbs′ II RCM (ring-closing metathesis) catalyst in CH_2Cl_2 solution followed by purification using preparative thin-layer chromatography gave the rotaxane **5·Cl** in 20 % yield. Methylation of the axle iodotriazole motif of the rotaxane **5·Cl** with an excess of trimethyloxonium tetrafluoroborate and subsequent anion exchange with aqueous saturated NH_4PF_6 afforded the target XB–HB two-station rotaxane **6·(PF$_6$)$_2$** (Scheme 1). Both rotaxanes were characterized by ^{1}H, ^{13}C, and ^{1}H 2D ROESY NMR spectroscopy, and high-resolution ESI-MS (Supporting Information).

A comparison of the ^{1}H NMR spectra in $CDCl_3$ of the rotaxane **5·Cl** with the axle **3·Cl** and macrocycle is shown in the Supporting Information. Diagnostic upfield shifts of the signals attributable to the macrocycle hydroquinone protons are detected for **5·Cl** which is indicative of aromatic donor–acceptor charge-transfer interactions between the electron-rich hydroquinone groups of the macrocycle and the electron-deficient triazolium heterocycle of the axle. Resonance signals attributable to isophthalamide protons H_a and the amide protons H_e also undergo significant downfield shifts, which is characteristic of chloride-anion binding in the macrocyclic cavity by hydrogen bonding to the respective protons.

The mechanically bonded nature of the rotaxanes was further supported by the appearance of multiple through-space correlations between signals arising from the respective axle and macrocycle protons found in 2D ^{1}H ROESY NMR spectra (see Supporting Information). The main difference between the rotaxanes is the presence in rotaxane **6·(PF$_6$)$_2$** of two singlets at $\delta = 4.37$ and $\delta = 4.01$ ppm (1:1 $CDCl_3$/CD_3OD) corresponding to the *N*-methyl group (N-CH_3) of the iodotriazolium and H-triazolium axle heterocycles, respectively.

Importantly, the 2D ^{1}H ROESY NMR spectrum of rotaxane **6·(PF$_6$)$_2$** revealed only through-space correlations with the HB-triazolium station. The most important interactions correspond to the hydroquinone (f) and the CH=CH (g) protons of the macrocycle with the N-CH_3 (d) protons of the H-triazolium (see Supporting Information). This confirms that the isophthalamide macrocycle component of rotaxane **6·(PF$_6$)$_2$** resides exclusively at the HB-triazolium station.[8]



Scheme 1. Synthesis of the rotaxane **6·(PF$_6$)$_2$**. Reagents and conditions: a) Grubbs' II catalyst (10 wt%), CH_2Cl_2, room temperature, 16 hours, 25%; b) $(Me)_3OBF_4$, CH_2Cl_2, room temperature, 16 hours; wash with saturated NH_4PF_6 (aq.), 88%.

The addition of one equivalent of Cl^- anions to a solution of the two-station rotaxane·**6·(PF$_6$)$_2$** in $CDCl_3/CD_3OD$ (1:1 v/v) induced similar changes in the HB-triazolium station to those detected upon Cl^- anion addition to the HB rotaxane **1·PF$_6$**, specifically downfield shifts in the resonance signals arising from the macrocycle isophthalamide protons and in the C-*H* signal of the HB-triazolium ring. Additionally, an upfield shift of the signals for the N-CH_3 protons of the HB-triazolium ring was detected whereas the corresponding N-CH_3 axle protons of the XB-triazolium motif were unperturbed. This difference indicates that the macrocycle remains at the HB-triazolium station upon chloride-anion binding. 2D ^{1}H ROESY NMR experiments confirmed the appearance of through-space correlations solely between signals for the macrocycle and the N-CH_3 protons of the HB-triazolium station of the axle after the addition of chloride. These observations all suggest that chloride binding takes place exclusively within the rotaxane interlocked cavity of the macrocycle and the axle HB-triazolium recognition site (see Supporting Information).

The addition of iodide anions to **6·(PF$_6$)$_2$** resulted in the characteristic downfield shift of resonance signals arising from the macrocycle isophthalamide protons. Significant perturbations were also found in the chemical shift of the two different XB and HB *N*-methyl triazolium protons present in the rotaxane **6·(PF$_6$)$_2$**. The protons of the *N*-methyl group attributed to the iodotriazolium (e) displayed the characteristic upfield shift detected in the mono-station rotaxanes **1·PF$_6$** and **2·PF$_6$** when halide complexation takes place, while the N-CH_3 protons attributed to the HB-triazolium ring (d) shifted downfield (Figure 3).

The contrasting chemical shift perturbations of the two signals corresponding to the N-CH_3 triazolium protons suggest the macrocycle has moved from the HB-triazolium station to the XB-triazolium station upon iodide recognition.

Further evidence for iodide-induced shuttling of the macrocycle to the XB-triazolium station is provided by the 2D ^{1}H ROESY NMR spectrum (see Supporting Information) displaying the appearance of new correlations between resonance signals arising from the macrocycle and the iodotriazolium N-CH_3 protons.

To estimate the percentage occupancy of the macrocycle at the respective XB-iodotriazolium and HB-triazolium axle stations of rotaxane **6·(PF$_6$)$_2$** upon increasing amounts of iodide addition, the dimethylated two-station axle **7·(PF$_6$)$_2$** (Figure 4) was prepared. The ^{1}H NMR chemical shift of the signals arising from the N-CH_3 protons of the HB-triazolium and XB-iodotriazolium heterocycles of **7·(PF$_6$)$_2$** were compared with the chemical-shift values of the HB rotaxane **1·PF$_6$** and with the XB rotaxane **2·PF$_6$** after the addition of iodide anions.

Resonance signals for the N-CH_3 protons of the two-station axle **7·(PF$_6$)$_2$** (in the absence of macrocycle) appear at $\delta = 4.27$ ppm for the XB-iodotriazolium station and $\delta = 4.17$ ppm for the HB-triazolium station. The chemical shift of the N-CH_3 protons of the HB rotaxane **1·PF$_6$** are found at $\delta = 4.01$ ppm, indicating that the presence of the macrocycle induced an upfield shift of $\Delta\delta = -0.16$ ppm in the N-CH_3 protons of the HB station. Furthermore, after the addition of an excess of iodide anions, the signals arising from the N-

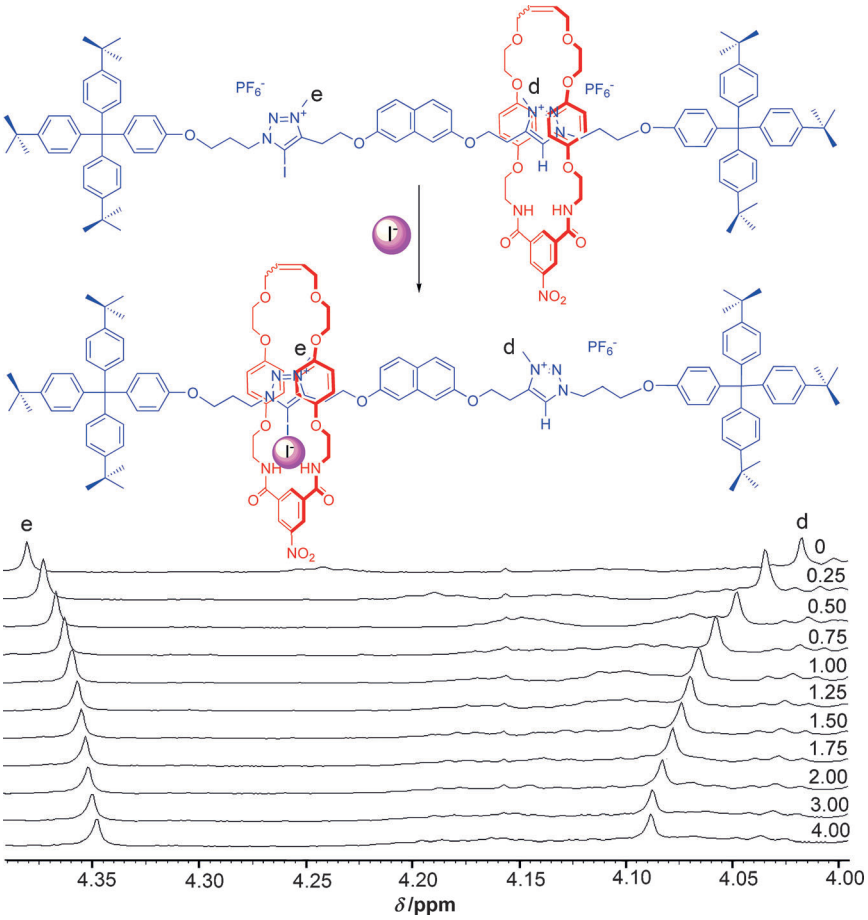


Figure 3. Top: Representation of the shuttling of the macrocyclic ring in **6·(PF$_6$)$_2$** upon addition of iodide ions. Bottom: Corresponding ^{1}H NMR spectra showing changes in the resonance signals arising from rotaxane **6·(PF$_6$)$_2$** protons in $CDCl_3/CD_3OD$ (1:1 v/v) at 295 K upon addition of up to 4 equivalents of iodide anions. Numbers on right-hand side indicate total number of equivalents of iodide ions in solution.

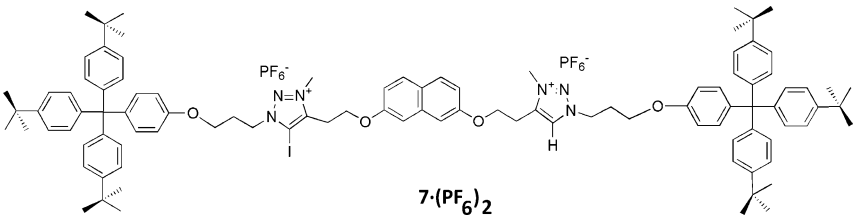


Figure 4. Structure of the two-station axle **7·(PF$_6$)$_2$**.

signals arising from the N-CH_3 protons of the HB-triazolium group, reaching a maximum of $\Delta\delta = 0.086$ ppm after 4 equivalents. Thus, from the ratio of the HB-triazolium chemical-shift $\Delta\delta$ values (0.086/0.16), it was estimated that 54% of the macrocycle had moved away from the HB station. Concomitantly, the signals attributable to the N-CH_3 protons of the XB-iodotriazolium motif were shifted upfield ($\Delta\delta = -0.022$ ppm). This upfield shift also indicates from the ratio of the XB-iodotriazolium chemical-shift $\Delta\delta$ values (0.022/0.04) that the macrocycle occupies the XB station with a percentage of similar magnitude. Thus, the addition of up to 4 equivalents of iodide to the two-station rotaxane **6·(PF$_6$)$_2$** promotes a change in the ratio of the occupancy of the macrocycle at the XB and HB stations from 0/100 to 54/46.[9] A representation of the percentage occupancy of the macrocycle at each station on addition of increasing amounts of iodide anions is given in Figure 5.

Finally the reversibility of the shuttling process was demonstrated by the addition of $AgPF_6$ to a mixture of **6·(PF$_6$)$_2$** in the presence of 4 equivalents of iodide in $CDCl_3/CD_3OD$ (1:1 v/v). The ^{1}H NMR spectrum after the addition of the silver salt was identical to the rotaxane's original ^{1}H NMR spectrum.

In conclusion, by exploiting the contrasting halide anion binding affinities of two new mono-station HB-triazolium and XB-iodotriazolium rotaxanes, a novel XB–HB two-station rotaxane was demonstrated to undergo molecular motion of the isophthalamide-containing macrocycle wheel component from the HB- to the XB-triazolium station. This motion was in response to iodide-anion recognition, whereas chloride binding just reinforced the macrocycle residing at the HB station. To our knowledge, this is the first example of using XB in a solution-phase molecular recognition process to control molecular motion and as such highlights the exciting potential XB has in dynamic molecular mechanically bonded nanotechnological applications.

CH_3 protons of the XB rotaxane **2·PF$_6$** were shifted upfield by $\Delta\delta = -0.04$ ppm with respect to the N-CH_3 protons of the XB-iodotriazolium station of axle **7·(PF$_6$)$_2$**.

The chemical shift of the N-CH_3 protons of the HB-triazolium motif in the two-station rotaxane **6·(PF$_6$)$_2$** appears at an identical chemical-shift value ($\delta = 4.01$ ppm) to that of the HB-rotaxane **1·PF$_6$**, which indicates that the occupancy of the macrocycle at the HB-triazolium station is 100%. This result is in agreement with the data obtained previously by 2D ^{1}H NMR ROESY experiments. The addition of increasing equivalents of iodide anions to the two-station rotaxane **6·(PF$_6$)$_2$** induced a progressive downfield shift in resonance

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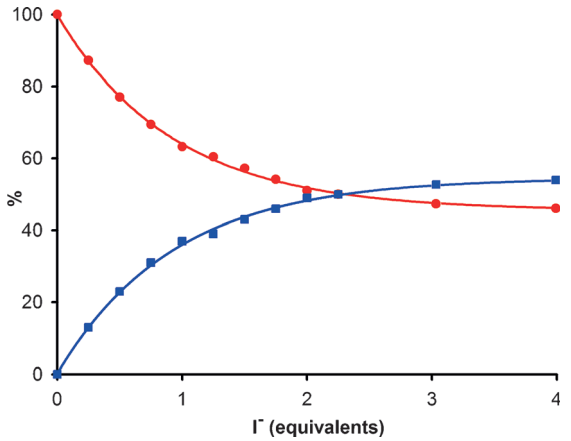

Figure 5. Percentage occupancy (%) of the macrocycle of **6·(PF$_6$)$_2$** at the HB station (red line) and at the XB station (blue line). Percentages were calculated from the relative chemical-shift values of the N-CH$_3$ protons of the rotaxane's axle HB-triazolium and XB-iodotriazolium motifs upon addition of iodide anions in CDCl$_3$/CD$_3$OD (1:1 v/v) at 295 K.

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[8] The presence of the macrocycle at the HB station may be attributed to a favorable hydrogen-bonding interaction between the C-H proton of the axle HB-triazolium motif and an amide carbonyl oxygen group of the macrocycle. A solid state structure of a catenane hexafluorophosphate salt reveals intramolecular hydrogen bonding between carbonyl oxygen and amide protons of opposing macrocycles with the carbonyl oxygen of the macrocycles displaying a syn-anti amide conformation; see L. M. Hancock, L. C. Gilday, N. L. Kilah, C. J. Serpell, P. D. Beer, *Chem. Commun.* **2011**, *47*, 1725.

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