

Anion and pH dependent molecular motion by a halogen bonding [2]rotaxane

 Harry A. Klein,^a Heike Kuhn^a and Paul D. Beer^{*a}

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A bistable [2]rotaxane containing a halogen bonding benzimidazole-iodotriazole station directly conjugated to a naphthalimide station axle component is demonstrated to undergo macrocycle shuttling translocation only upon both protonation and chloride anion recognition. A naked-eye detectable colour response results from the co-conformational change of the host structure.

Highlighted by the 2016 Nobel Prize in Chemistry, the potential for mechanically interlocked molecules (MIMs) to act as molecular-scale switchable devices, even machines, arises from their ability to undergo reversible molecular motion through changes in the relative positions of their constituent parts.¹ A variety of external stimuli have been exploited to control this process, with examples including light,^{1–3} redox,^{4,5} pH,^{6,7} and cation binding.⁸ MIMs displaying anion induced motion however are rare,^{9–12} especially utilising halogen bonding-anion interactions.^{13,14} Recent examples have incorporated photoactive reporter groups into [2]rotaxane frameworks, with anion recognition inducing changes in the ground or excited state emission of the reporter group as a consequence of macrocycle translocation.^{14–17}

Benzimidazole species have been utilised extensively as anion receptors, typically in conjunction with proximal hydrogen bond donors.^{18–21} Surprisingly, despite the emergence of solution phase halogen bonding as a tool for building potent anion receptors, to our knowledge no examples exist combining this interaction with 2-substituted benzimidazole derivatives.²² The incorporation of a 2-substituted benzimidazole axle into [2]rotaxanes has been reported by Loeb,^{23–26} with a recent example exploiting the facile protonation of this motif to control shuttling rate of the macrocycle along the axle.²⁷

Herein, we report a novel halogen bonding benzimidazole-iodotriazole motif which is incorporated into a photoactive

naphthalimide-based axle component of a bistable [2]rotaxane. Crucially, protonation of the benzimidazole moiety along with addition of a coordinating anion such as chloride is shown to facilitate macrocycle translocation from the naphthalimide station to the benzimidazolium-iodotriazole station. Interestingly, both of these stimuli are found to be necessary to induce the co-conformational change of the MIM host structure which results in a naked-eye detectable colour response (Fig. 1).

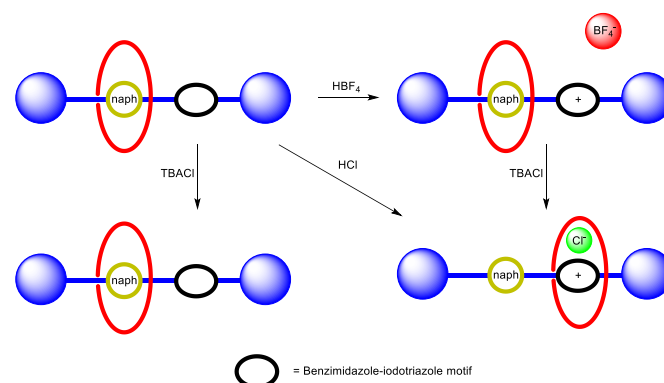
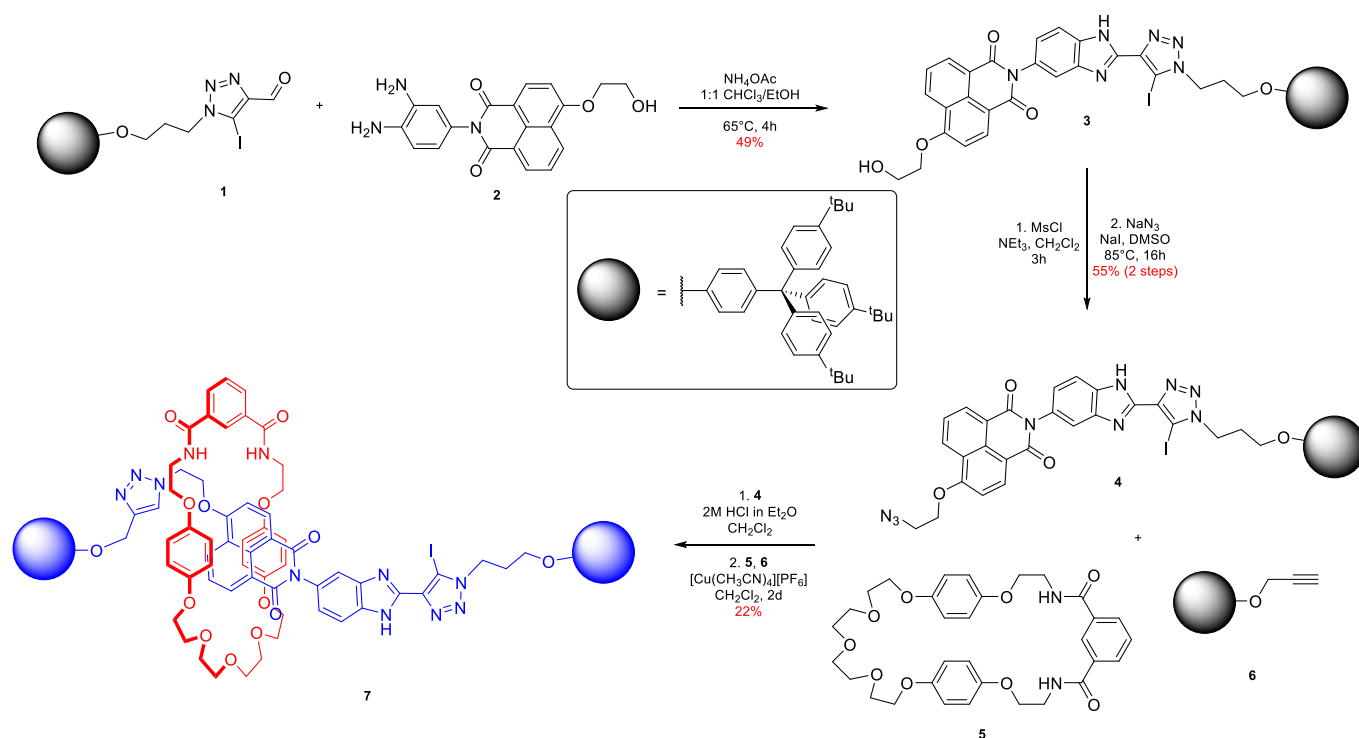


Fig. 1 Schematic outline of molecular switching exhibited by [2]rotaxane in this work. Both protonation and chloride addition are required to induce macrocycle translocation.

The protocol for rotaxane preparation was to separately synthesise the half-axle precursors: a naphthalimide-based benzimidazole-iodotriazole stoppered azide and a stoppered alkyne. Through protonation of the benzimidazole azide site and subsequent addition of an isophthalamide macrocycle, it was envisaged that the target [2]rotaxane would be formed via a chloride anion template CuAAC stoppering reaction.

Formation of the novel naphthalimide containing benzimidazole-iodotriazolium azide axle precursor, **4**, first required the preparation of iodotriazole aldehyde **1** and naphthalimide diamine **2**, the syntheses of which are described in the ESI. Addition of **1** and **2** to a CHCl₃/CH₃OH solution containing NH₄OAc resulted in the formation of benzimidazole-iodotriazole alcohol **3** in good yield (Scheme 1). This was

^a Chemistry Research Laboratory, Department of Chemistry, University of Oxford, Mansfield Road, Oxford, OX1 3TA, UK. E-mail: paul.beer@chem.ox.ac.uk. Electronic Supplementary Information (ESI) available: Synthesis, structural characterisation, additional figures. See DOI: 10.1039/x0xx00000x

Scheme 1 Synthesis of [2]rotaxane **7** via a chloride anion template CuAAC stoppering method.

converted to the corresponding azide **4** via the mesylate intermediate.

[2]Rotaxane **7** was prepared via a chloride anion template stoppering approach. Azide **4** was dissolved in CH_2Cl_2 and protonated using 2M HCl, forming the benzimidazolium-iodotriazole intermediate, and subsequently macrocycle **5**, $[\text{Cu}(\text{CH}_3\text{CN})_4][\text{PF}_6]$ and stopper alkyne **6** were added. After two days, [2]rotaxane **7** was isolated in 22% yield after purification by preparative TLC and performing an aqueous wash upon the resulting solid. Full characterisation data of rotaxane **7**, including ^1H , ^{13}C , ^1H - ^1H ROESY NMR spectroscopy and high resolution mass spectrometry, can be found in the ESI.

Protonation of rotaxane **7** was achieved using both a coordinating and a non-coordinating counter anion. Washing a CHCl_3 solution of **7** with 3M $\text{HCl}_{(\text{aq})}$ afforded rotaxane **7·HCl**, whilst addition of HBF_4 gave **7·HBF₄** (Fig. 2a). Interestingly, these rotaxanes exhibited contrasting colour solution phase appearances. Whilst neutral rotaxane **7** was yellow in solution, attributed to charge transfer between the macrocycle component's electron rich hydroquinone groups and the axle electron deficient naphthalimide motif of the rotaxane, protonation with HCl caused an immediate loss of colour. This was not the case upon protonation with HBF_4 , with the solution

remaining yellow. This was supported by the UV-vis absorbance data; the spectrum of **7·HBF₄** appeared very similar to **7**, whereas **7·HCl** displayed a significant shift in the region $\lambda > 340$ nm, with the loss of the broad absorbance band at 380 nm explaining the colour change (Fig. 2b).

Comparison of the ^1H NMR spectra of neutral rotaxane **7** with **7·HCl** revealed key changes (Fig. 3). Downfield chemical shifts were exhibited by the macrocyclic component aryl and hydroquinone protons suggesting a loss of shielding π -stacking interactions with the axle naphthalimide motif, and in particular in the case of macrocycle isophthalamide proton H_3 as a result of chloride association. Perturbations were also observed in the chemical shifts of the axle naphthalimide-based protons, along with a sharpening of the corresponding resonances. Further changes included a desymmetrisation of stopper proton environments.

Comparison of the ^1H - ^1H ROESY NMR spectra of each compound suggested that the observed change in colour and ^1H NMR was a result of MIM co-conformational difference. (see ESI for spectra). In the spectrum of rotaxane **7**, numerous cross-peaks were observed between the hydroquinone macrocycle protons and the axle naphthalimide region, as well as between the internal isophthalamide macrocycle phenyl proton and the

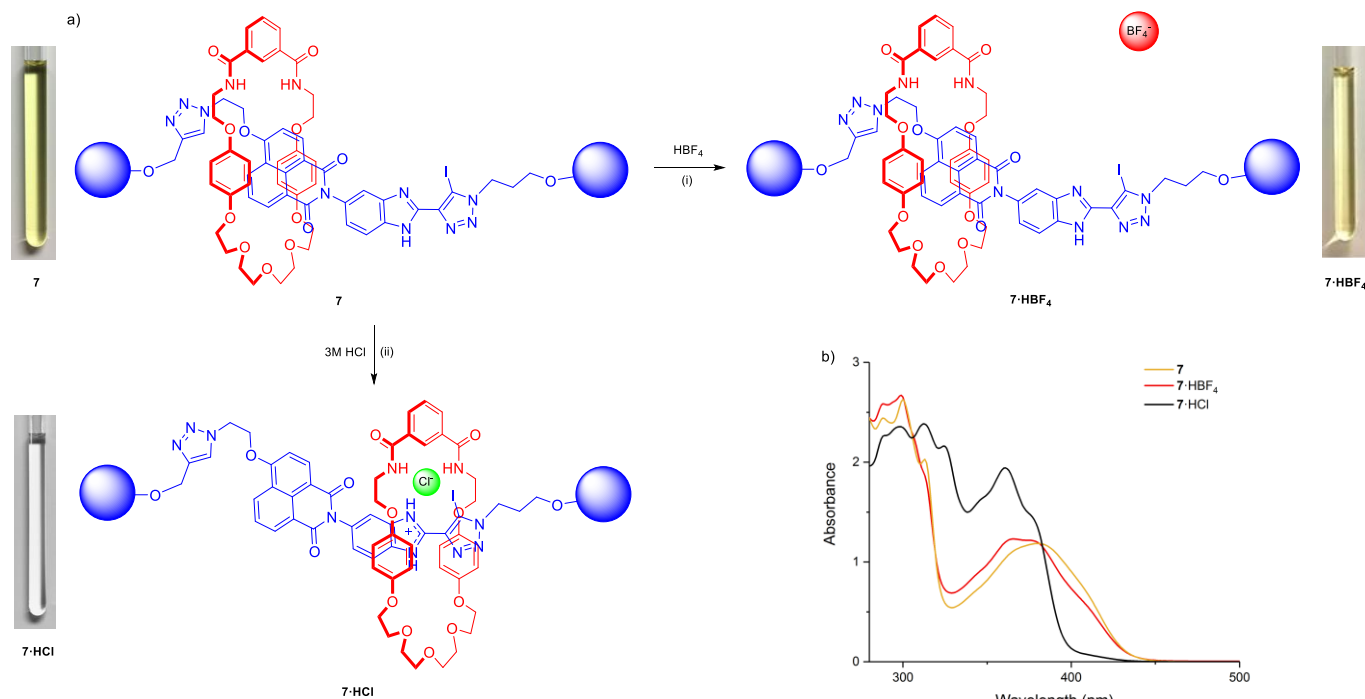


Fig. 2 a) Protonation of [2]rotaxane **7** with (i) HBF_4 , causing modest colour change, and (ii) HCl , inducing loss of colour, indicative of macrocycle translocation. b) UV-vis spectra of each rotaxane in CHCl_3 . Significant spectral change upon HCl addition compared to HBF_4 addition suggests observed colour changing behaviour (1×10^{-4} M, 298 K).

axle proto-triazole and adjacent alkyl protons. However, upon HCl addition these disappeared; the only observable cross-peaks were between the hydroquinone macrocycle protons and the benzimidazolium aromatic region. This suggests macrocycle translocation from the naphthalimide to the benzimidazolium-iodotriazole station had occurred, with the corresponding naked-eye colour change from yellow to colourless a consequence of the absence of the macrocycle hydroquinone donor-axle naphthalimide acceptor charge transfer interaction.

To further confirm that these observations were a result of co-conformational rotaxane differences, and not purely an artefact of chloride addition, free axle **8** was prepared following a CuAAC reaction between azide **4** and alkyne **6** (full synthetic details and characterisation in ESI). Protonation with HCl , to generate **8·HCl** resulted in no detectable changes either by naked-eye or by UV-vis spectroscopy (Fig. S2-1). In addition, the ^1H NMR spectrum of **8·HCl** was almost identical to that of **8**, unlike the extensive differences observed between the spectra of rotaxanes **7** and **7·HCl**. This provides further evidence that the spectroscopic response exhibited by rotaxane **7** upon HCl addition is a consequence of macrocycle translocation.

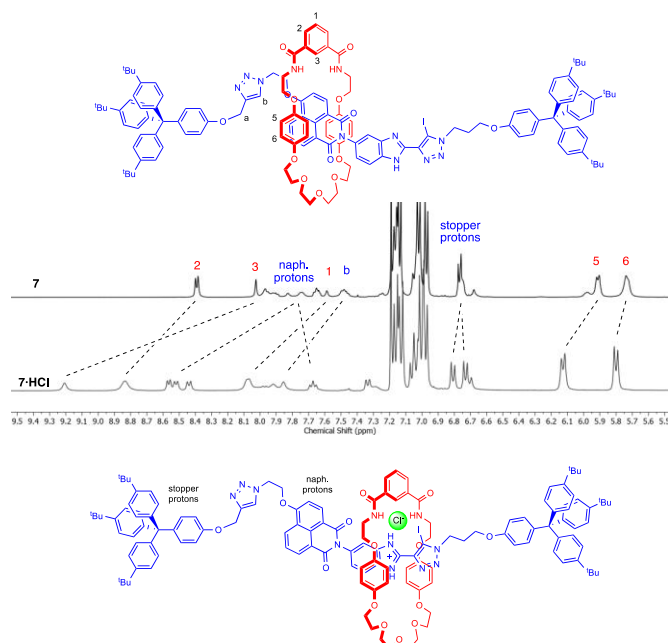


Fig. 3 ^1H NMR spectra of [2]rotaxanes **7** and **7·HCl** (CDCl_3 , 298 K, 500 MHz), with key changes in proton resonances shown (numbering matches ROESY spectra in ESI).

In order to probe the importance of the coordinating nature of the counter anion to induce macrocycle translocation, a qualitative UV-vis spectroscopic anion titration experiment with **7**·HBF₄ was performed. Upon addition of 50 equivalents of TBACl a dramatic change in absorbance was observed, with the spectrum closely resembling that of **7**·HCl (Fig. 4a). This was accompanied by a naked-eye colour change of the sample from yellow to colourless, suggesting movement of the macrocycle to the benzimidazolium-iodotriazole station. Furthermore, there was a noticeable increase in the fluorescence emission maxima of the rotaxane upon chloride addition, postulated to be a consequence of the removal of macrocycle-based PET quenching of the naphthalimide station after translocation (Fig. 4b). Interestingly, no change in optical properties were observed upon chloride addition to a sample of neutral rotaxane **7**, suggesting the necessity of protonation, as well as the presence of a coordinating anion, to facilitate macrocycle translocation. As a control, axle **8** was protonated with HBF₄ to produce **8**·HBF₄. Chloride addition to this sample did not produce any observable change in the visible region ($\lambda > 340$ nm) of the UV-vis spectrum (Fig. S2-2), suggesting that the changes exhibited upon Cl⁻ addition to rotaxane **7**·HBF₄ were indeed a consequence of macrocycle translocation.

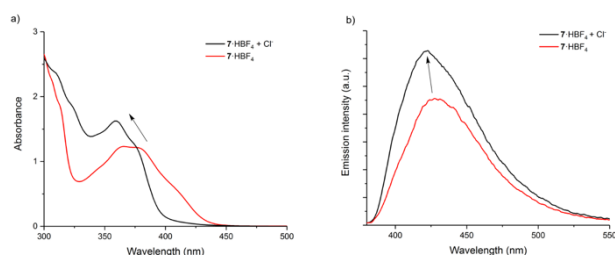


Fig. 4 Spectroscopic changes upon addition of 50 equivalents of chloride to **7**·HBF₄ in CHCl₃. a) UV-vis spectra, b) fluorescence emission spectra (1x10⁻⁴ M, 298 K).

In summary, a novel halogen bonding benzimidazole-iodotriazole motif has been integrated into a naphthalimide-containing axle component of a bistable [2]rotaxane **7**, which was constructed via a chloride anion template stopping methodology. Importantly, the two station rotaxane was found to exhibit macrocycle molecular shuttling motion dependent upon both the protonation state of the MIM host structure and the nature of the counter anion. In the neutral state, **7**, the macrocycle was found to reside at the naphthalimide station; neither addition of chloride nor protonation with HBF₄ caused any observable spectroscopic changes. Only upon addition of aqueous HCl solution, or chloride to **7**·HBF₄, did co-conformational modulation occur. The macrocycle translocated to the axle benzimidazolium-iodotriazole station which was observed via a naked-eye detectable colour change of the solution. The need for both protonation and chloride external stimuli to facilitate MIM macrocycle translocation is akin to the behaviour of a molecular Boolean AND logic gate²⁸ and thus has potential uses in switchable nanotechnological device applications.

Conflicts of interest

There are no conflicts to declare.

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