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PAPER

A ferrocene functionalized rotaxane host system capable of the electrochemical recognition of chloride†

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A ferrocene appended rotaxane is prepared by chloride anion templation and ring closing metathesis. Upon removal of the chloride template, the rotaxane is demonstrated to be selective for chloride over more basic oxoanions by ^{1}H NMR spectroscopy and electrochemistry, in marked contrast to an acyclic analogue - the first example of a solution based redox-active interlocked host system capable of the electrochemical recognition of anions.

Introduction

Rotaxanes, interlocked molecules comprising of a macrocyclic component locked onto an axle by bulky stopper groups, have been at the forefront of research into molecular machine-like nanotechnological applications due to the possibilities of shuttling and/or pirouetting of their components.[1] However, these molecules also possess unique topologically constrained cavities which may be exploited to selectively bind guest species for future chemical sensory purposes.[2] Despite this intriguing possibility, only a few examples of designed rotaxane host systems that bind charged species in their cavities have been reported to date.[3,4] Due to the challenges of recognising anions (such as their low charge densities, various geometries, high hydration energies and pH dependence),[5] rotaxane cavities are promising candidates for anion binding. Our group has previously synthesised a range of solution and surface confined rotaxanes by rational use of anion templation, and have demonstrated such interlocked host systems to selectively bind anions in highly competitive solvent mixtures.[4a–i]

To achieve selective *sensing* of guests in such rotaxane hosts, appropriate reporter group functionality needs to be incorporated into the interlocked molecular framework to provide a response (either optical or electrochemical). Relatively few examples have been designed and constructed to exhibit such sensory behaviour[3a,c–d,4b,d,j] and only one electrochemically senses anions, when confined to a surface.[4d] With the aim to selectively sensing chloride electrochemically in solution, our attention has turned towards attaching the redox-active ferrocene group to a rotaxane (see Fig. 1). Ferrocene has been demonstrated to be suitable for the detection of anions in a wide range of acyclic and macrocyclic receptors.[6] However, its appearances in rotaxanes as a stopper[7] or as part of the macrocyclic component[4d,8] are rare compared to the numerous examples of non-interlocked ferrocene anion receptors.

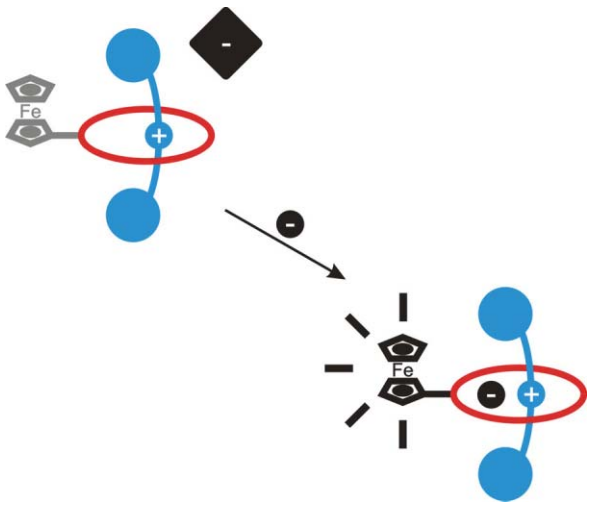

Fig. 1 Schematic representation of the use of a ferrocene-appended rotaxane to electrochemically sense anions.

In this paper we report the synthesis of the first redox-active rotaxane capable of electrochemically recognising anionic guest species, with a notably different electrochemical response to chloride compared to oxoanions being observed.

Results and discussion

Design, synthesis and characterization

To achieve the electrochemical recognition of an anion by a rotaxane, installation of an appropriate reporter group to a rotaxane capable of binding anions is required. Integration of a redox-active ferrocene moiety into such a rotaxane anion host system could be accomplished *via* a direct C–C bond to the isophthalamide

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group of an anion binding rotaxane's macrocyclic component as illustrated in Fig. 2. The chloride salt of rotaxane $\mathbf{1}^{+}PF_6^{-}$ could be prepared by a ring closing metathesis (RCM) reaction of an appropriately functionalized bis-vinyl appended macrocyclic precursor and methyl pyridinium chloride axle, the two rotaxane precursor components self-assembling in solution by a combination of anion templation, π–π stacking and hydrogen bonding.[4a,c] Following anion exchange rotaxane $\mathbf{1}^{+}PF_6^{-}$ contains a cavity that is anticipated to be selective for chloride,[4a,c,e,i] while the presence of a proximal ferrocene would enable reporting of an anion binding event by the rotaxane *via* cathodic shifts in the Fc/Fc^{+} redox couple.[9]

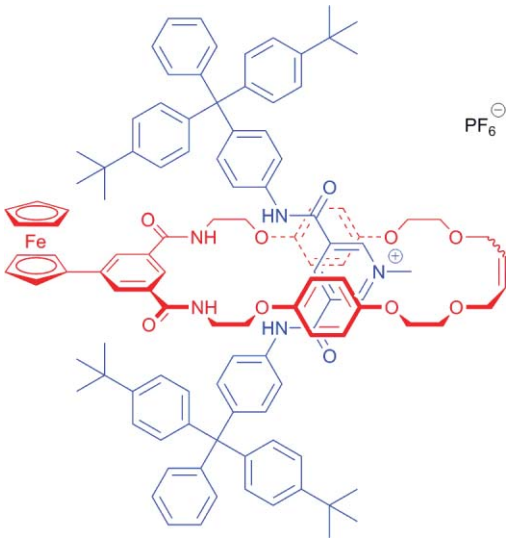
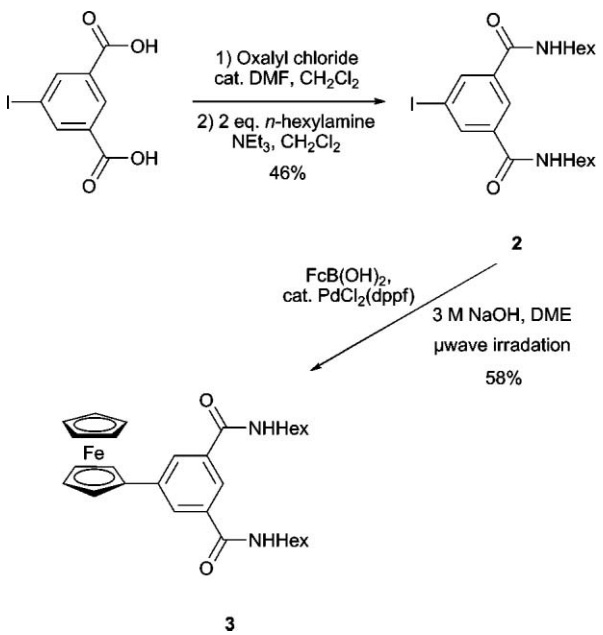


Fig. 2 Target rotaxane $\mathbf{1}^{+}PF_6^{-}$.

Initial synthetic investigations were therefore undertaken to find appropriate conditions for the direct appendage of ferrocene to an isophthalamide motif by attempting the synthesis of acyclic model system **3** (Scheme 1). The attachment of ferrocene was



Scheme 1 Synthesis of model **3**.

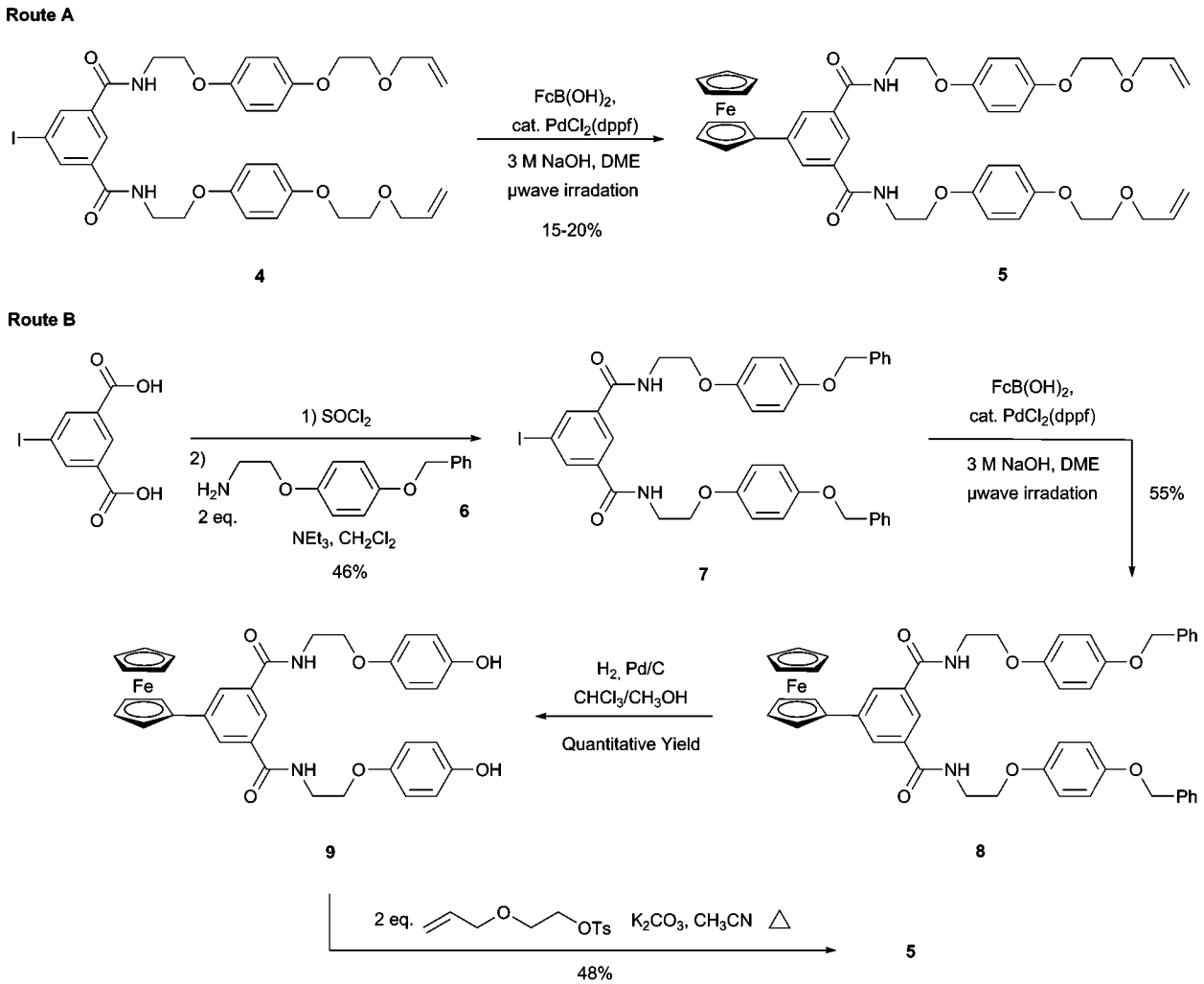
achieved by following a literature procedure for the Suzuki coupling of ferroceneboronic acid with iodo-arene compounds,[10] but using microwave irradiation for 30 min rather than refluxing for several days. Preparing iodo compound **2** and submitting it to these reaction conditions, followed by workup and column chromatography, allowed isolation of target compound **3** in a respectable yield of 58%. Model **3** was subsequently characterized by ^{1}H and ^{13}C NMR spectroscopy and high resolution mass spectrometry.

Having successfully demonstrated that it was possible to couple ferrocene to an isophthalamide motif, synthesis of target rotaxane $\mathbf{1}^{+}PF_6^{-}$ was carried out as shown in Schemes 2 and 3. Preparation of macrocycle precursor **5** was originally attempted by preparing compound **4**[5c] and exposing this to the same Suzuki conditions as for compound **2** (Route A in Scheme 2). Disappointingly, a repeatedly low yield (15–20%) for the formation of **5** was observed after workup and silica gel chromotography. In the belief that the presence of the terminal vinyl groups were interfering with the Suzuki coupling, an alternative route to **5** was pursued (Route B in Scheme 2). Pleasingly, the Suzuki coupling of compound **7** to form **8**, occurred in a significantly higher yield of 55%. Removal of the benzyl protecting groups was achieved quantitatively by hydrogenation to yield **9** which was alkylated to produce the desired bis-vinyl appended precursor **5**.

Rotaxane $\mathbf{1}^{+}Cl^{-}$ was prepared by RCM reaction of equimolar amounts of **5** and methyl pyridinium chloride axle $\mathbf{10}^{+}Cl^{-}$[4a] in dichloromethane solution, in the presence of 10% (by wt) Grubbs' 2nd generation catalyst. The rotaxane was isolated in 25% yield after careful separation from other components in the reaction mixture by silica gel preparatory thin layer chromatography. Subsequent removal of the chloride ion template *via* anion exchange by washing with NH_4PF_6 furnished the desired rotaxane salt $\mathbf{1}^{+}PF_6^{-}$ (Scheme 3).

Both salts were characterized by ^{1}H (1D and 2D) and ^{13}C (and in the case of $\mathbf{1}^{+}PF_6^{-}$ by ^{19}F and ^{31}P) NMR spectroscopy and high resolution mass spectrometry.

Comparison of the ^{1}H NMR spectra of the rotaxane $\mathbf{1}^{+}Cl^{-}$ with macrocycle precursor **5** and axle $\mathbf{10}^{+}Cl^{-}$ provides evidence of the interlocked nature of the rotaxane (Fig. 3). The success of the RCM reaction is indicated by the loss of peak *o* and the sharpening of multiplet *n* to a pseudo-singlet, these signals arising from the vinylic protons of the macrocycle precursor, with *o* lost as ethene, the by-product of the reaction. The spectra indicate three regions of interactions between the macrocyclic and axle components of the rotaxane. The first, the isophthalamide clefts, where strong upfield shifts in the axle signals *r* and *s* and downfield shifts in the macrocycle signals *e* and *f*, due to competitive hydrogen bond interactions between these protons and the chloride anion template, are observed. Second, the hydroquinone protons *i* and *j* have split and moved upfield, indicative of π–π stacking with the electron poor pyridinium unit. Finally, there is a large downfield shift in N-methyl peak *p*, indicating hydrogen bonding to the polyether oxygens of the macrocyclic component. Upon exchange to the hexafluorophosphate salt, there are upfield shifts of the isophthalamide cavity protons *e*, *f*, *r* and *s*, due to the removal of the chloride anion template. However, the hydroquinone protons *i* and *j* remain split and upfield compared to macrocycle precursor **5**, indicating the π–π stacking between two components, and that the rotaxane species remains interlocked.



Scheme 2 Synthetic routes to macrocyclic precursor **5**.

The cationic fragment $\mathbf{1}^+$ is to be found at $m/z \sim 1801.86$ in high resolution electrospray mass spectra of both rotaxane salts. Conclusive evidence of the interlocked nature of the rotaxane chloride and hexafluorophophate salts was provided by the observation of numerous through space interactions between macrocycle and axle components in 2D ROESY ^{1}H NMR spectra (see Fig. 4).

Anion recognition studies

^{1}H NMR Titrations. The anion binding properties of rotaxane $\mathbf{1}^+PF_6^-$ and, for comparison, acyclic ferrocene isophthalamide derivative **3** were investigated by ^{1}H NMR titration experiments.‡ NMR samples of the two compounds were prepared, to which aliquots of tetrabutylammonium (TBA) salts of various anions were added. The chemical shifts of peaks arising from protons in the isophthalamide groups were monitored. In all cases the anion binding event was observed to be fast on the NMR timescale allowing for the calculation of association constants by the computer program winEQNMR2,[11] with data fitting to a 1 : 1 binding model (see Table 1).

Table 1 1 : 1 Association constants, K, of model **3** and rotaxane $\mathbf{1}^+PF_6^-$[a]

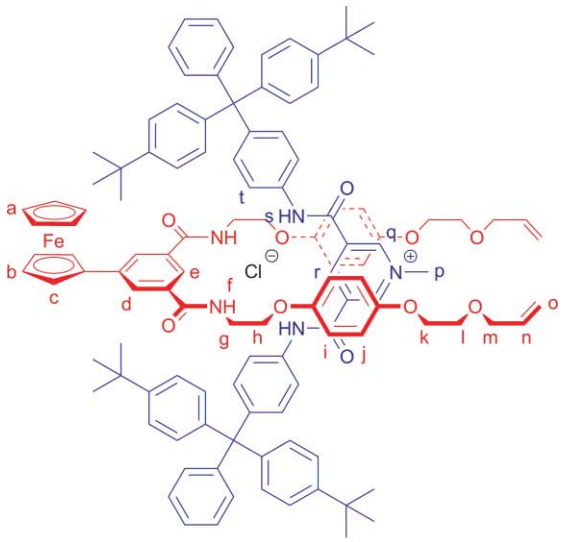
Anion	Model **3**[b]	Rotaxane $\mathbf{1}^+PF_6^-$[c]
Cl^-	170	4200[d]
$H_2PO_4^-$	100	640
BzO^-	450	640
HSO_4^-	40	1560

[a] Anions added as TBA salts. $T = 293$ K. Errors < 10%. [b] Solvent: CD_3CN, peak monitored: amide. [c] Solvent: 1 : 1 $CDCl_3$:CD_3OD, peak monitored: cleft pyridinium. [d] $K > 10^4$ M^{-1} in CD_3CN.

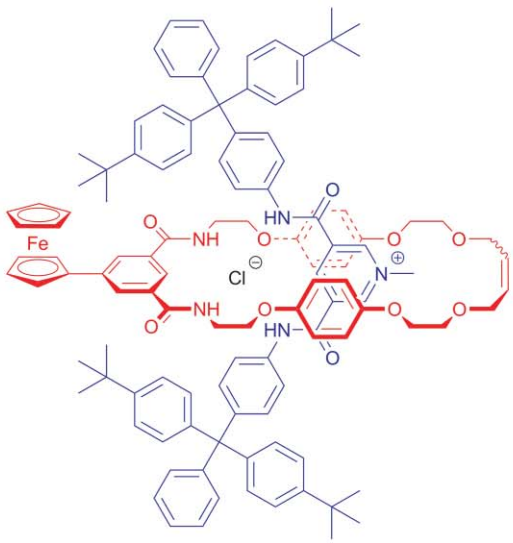
With model **3**, the anions are bound weakly in CD_3CN and generally in the order of their basicity, *i.e.* benzoate > dihydrogen phosphate > hydrogen sulfate. Chloride is bound slightly more strongly than dihydrogen phosphate and hydrogen sulfate anions because of the size-fit complementarity with the isophthalamide cleft by the spherical monoatomic halide anion.[12]

An initial ^{1}H NMR titration was undertaken with rotaxane $\mathbf{1}^+PF_6^-$ and TBACl in CD_3CN. Exceptionally strong 1 : 1 binding

‡ While perhaps being more appropriate for comparison to rotaxane $\mathbf{1}^+PF_6^-$ than acyclic model **3**, the macrocyclic component of the rotaxane proved very difficult to isolate pure in sufficient quantities for anion recognition studies. In addition, it was also found to have low solubility in acetonitrile, the solvent used in the electrochemistry investigations.



Grubbs' II
(10% by wt)
CH_2Cl_2
25%



0.1 M NH_4PF_6(aq)
$CHCl_3$
78%

$1^+PF_6^-$

Scheme 3 Synthesis of rotaxane $\mathbf{1}^+X^-$ ($X^- = Cl^-, PF_6^-$).

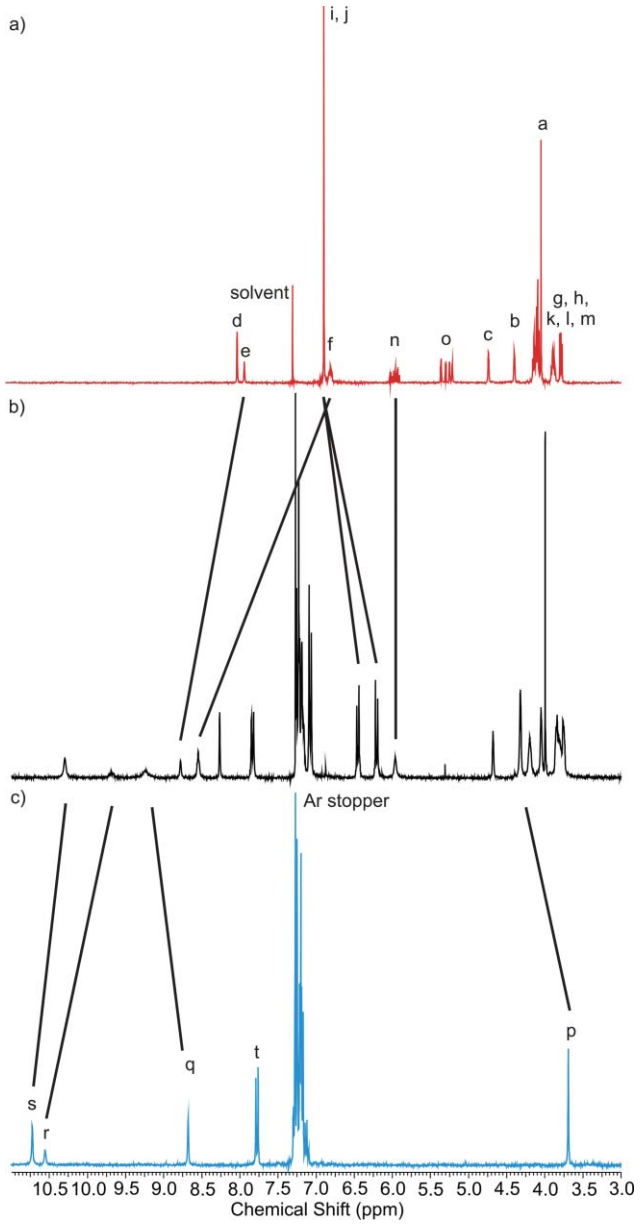


Fig. 3 Partial ^{1}H NMR spectra of a) macrocycle precursor **5**, b) rotaxane $\mathbf{1}^+Cl^-$ and c) axle $\mathbf{10}^+Cl^-$ Solvent: $CDCl_3$. See Scheme 3 for proton labels.

was observed ($K > 10^4$ M^{-1}). This is not unexpected: the rotaxane is positively charged, while the model is neutral. To allow for meaningful comparison of association constants of different anions with the rotaxane, the highly competitive solvent system 1 : 1 $CDCl_3$:CD_3OD was therefore used in subsequent titrations. There is a marked difference in selectivity of binding of the anion by rotaxane $\mathbf{1}^+PF_6^-$ in comparison to model **3**. Most notably chloride - the least basic of the anions - is now bound the most strongly. Evidence of the origin of this is provided in the appearance of the titration curves (see Fig. 5). For chloride, the cleft proton of the pyridinium isophthalamide (proton *r* in Scheme 3) moves downfield upon addition of the anion, whereas for the oxoanions, this proton moves upfield. This is indicative of an alternative binding mode for these anions - presumably they are too large to penetrate into the cavity of the rotaxane and associate peripherally instead.

Electrochemical anion sensory studies. In order to evaluate the electrochemical sensory properties of model **3** and rotaxane $\mathbf{1}^+PF_6^-$, cyclic and square wave voltammograms were recorded in 0.1 M $TBAPF_6$ CH_3CN solution.

Model **3** exhibits a quasi-reversible oxidation for the Fc/Fc^+ redox couple with $E_{1/2} = +85$ mV (compared to $E_{1/2(\text{ferrocene})} = 0$ V).

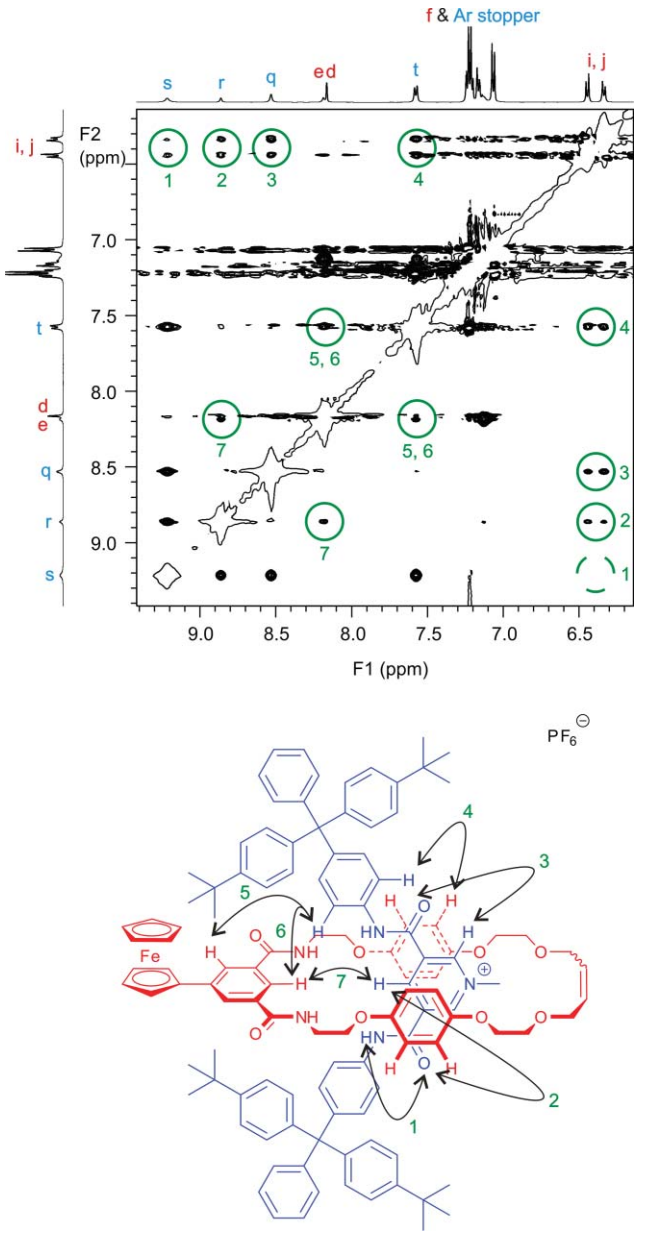


Fig. 4 Section of ^{1}H ROESY NMR spectrum of rotaxane $\mathbf{1}^+PF_6^-$ with through space intercomponent interactions highlighted. See Scheme 3 for proton labels.

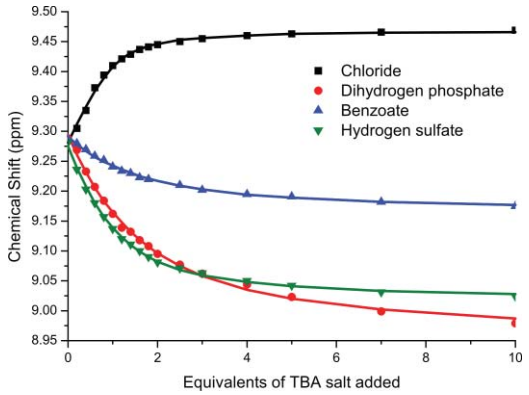


Fig. 5 Plot of chemical shift of pyridinium cleft proton of rotaxane $\mathbf{1}^+PF_6^-$ *versus* equivalents of TBA salt added.

Table 2 Shift in Fc/Fc$^+$ redox couple of model **3** upon addition of anions[a]

Anion	$\Delta E_{1/2}$/mV
Cl^-	–20
$H_2PO_4^-$	–80[b]
BzO^-	–10[b]
HSO_4^-	–10

[a] Anions added as TBA salts. Electrolyte: 0.1 M $TBAPF_6$ in CH_3CN. Reference electrode: Ag/AgCl. Working electrode: Glassy Carbon. Auxiliary electrode: Platinum. 10 equivalents of anions added. Values reported to nearest 5 mV. T = 293 K. [b] Shift of oxidation peak, ΔE_{pa}, due to loss of reversibility.

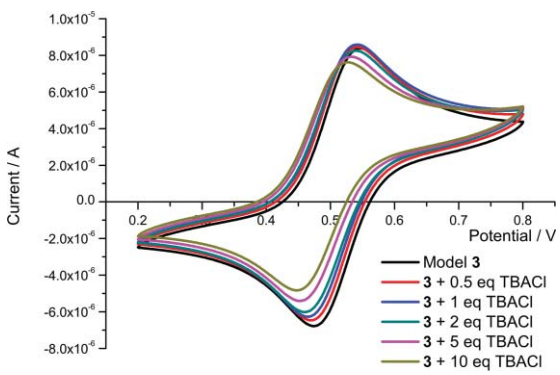


Fig. 6 CVs of model **3** in 0.1 M $TBAPF_6/CH_3CN$ upon the addition of aliquots of TBACl (Potential compared to Ag/AgCl reference).

Upon progressive addition of stoichiometric equivalents of anions cathodic shifts of the waves were observed: the maximum observed shifts in the redox wave being summarised in Table 2. These cathodic shifts can be attributed to the binding of the anion by the isophthalamide cleft protons, facilitating oxidation of ferrocene to ferrocenium. As chloride is added, a stepwise shifting of the quasi-reversible redox wave is observed, to a value of –20 mV upon addition of 10 equivalents of TBACl (see Fig. 6). In contrast, with dihydrogen phosphate and benzoate there is a loss of reversibility upon the addition of only small amounts of anion (1–2 equivalents). The disappearance of the reduction wave indicates either that the complexed anion-ferrocenium cation interaction is disfavouring reduction back to ferrocene or that an EC mechanism is in operation. Upon the addition of hydrogen sulfate the redox wave remains reversible throughout but only a modest cathodic shift is observed.

Rotaxane $\mathbf{1}^+PF_6^-$ also displays a quasi-reversible Fc/Fc$^+$ redox couple, but with $E_{1/2}$ = +115 mV (compared to $E_{1/2(\text{ferrocene})}$ = 0 V). The more anodic potential for the rotaxane compared to acyclic model system **3** is expected as the rotaxane is positively charged which disfavours oxidation of the ferrocene moiety. Like the model, upon addition of chloride and hydrogen sulfate to samples of rotaxane, the redox couple remains quasi-reversible, while the addition of approximately 2 equivalents of dihydrogen phosphate or benzoate causes a loss of reversibility in the redox wave (see Fig. 7 for CVs of chloride and dihydrogen phosphate titrations). Not only is the magnitude of cathodic shift for chloride larger than any of the oxoanions at equimolar concentrations of rotaxane host

Table 3 Shift in Fc/Fc^+ redox couple of rotaxane $\mathbf{1}^+PF_6^-$ upon addition of anions[a]

	$\Delta E_{1/2}$/mV	
Anion	After 1 eq. of anion	After 10 eq. of anion
Cl^-	−20	−20
$H_2PO_4^-$	−10	−100[b]
BzO^-	−15	−25[b]
HSO_4^-	−15	−40

[a] Anions added as TBA salts. Electrolyte: 0.1 M $TBAPF_6$ in CH_3CN. Reference electrode: Ag/AgCl. Working electrode: Glassy Carbon. Auxiliary electrode: Platinum. Values reported to nearest 5 mV. $T = 293$ K. [b] Shift of oxidation peak, ΔE_{pa}, due to loss of reversibility.

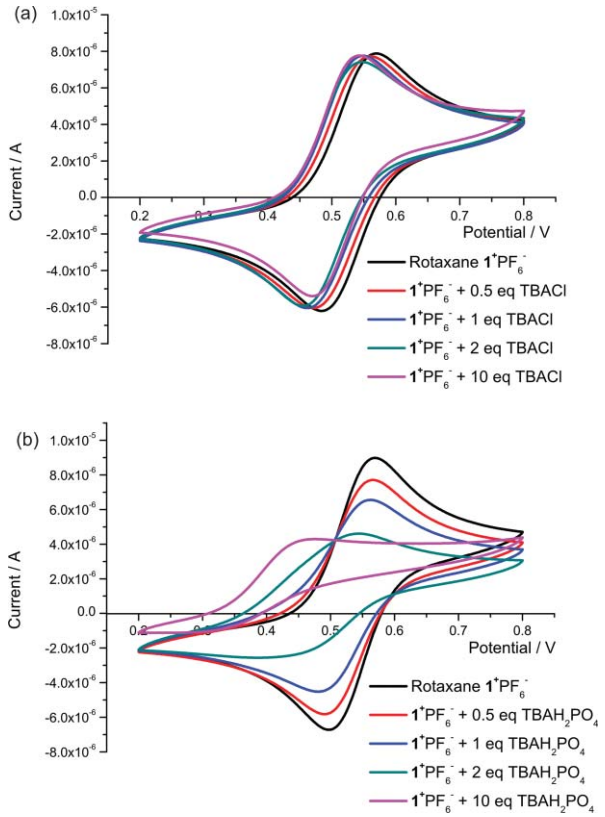


Fig. 7 Selected CVs of rotaxane $\mathbf{1}^+PF_6^-$ in 0.1 M $TBAPF_6/CH_3CN$ upon the addition of aliquots of (a) TBACl and (b) $TBAH_2PO_4$ (Potential compared to Ag/AgCl reference).

and anion guest, but the cathodic shift of 20 mV is observed at 1 equivalent of added chloride anion with negligible further shift (< 5 mV) observed upon addition of further equivalents (see Table 3). These observations support the theory that only chloride is able to bind strongly within the interlocked cavity, with its presence being communicated to ferrocene presumably *via* a through-bond mechanism.[13] With the oxoanions, there is a continued cathodic shift in the redox wave upon the addition of further equivalents of anion.§ Taking into account the ^1H NMR anion binding results, which suggest the oxoanion association occurs on the periphery of the rotaxane structure, it is hypothesised that a through-space communication mechanism is in operation between the rotaxane's ferrocene redox centre and the oxoanion.[13]

§ Attempts at electrochemical anion recognition competition experiments (*e.g.* addition of chloride to rotaxane $\mathbf{1}^+PF_6^-$ in the presence of excess equivalents of oxoanions) were undertaken but proved inconclusive due to irreversible electrochemical behaviour.

Conclusions

A redox-active ferrocene functionalized rotaxane host system has been prepared by chloride anion templation. Upon exchange of the chloride anion template for the non-coordinating hexafluorophosphate anion ^1H NMR anion titration investigations reveal that chloride is bound selectively over more basic oxoanions by the rotaxane: this is due to a complementary size match of the interlocked cavity for the monoatomic chloride anion, whereas oxoanions are too large to penetrate the cavity and associate peripherally. It has also been demonstrated that the rotaxane displays electrochemical recognition for chloride as evidenced by a maximum cathodic shift response of the Fc/Fc^+ redox couple being observed at equimolar concentrations of rotaxane host and halide anion guest, whereas excess equivalents are required for oxoanions. The incorporation of redox-active groups into interlocked host design is continuing in our laboratories.

Experimental

General

Commercially available solvents and chemicals were used without further purification unless stated. Where dry solvents were used, they were degassed with nitrogen, dried by passing through a MBraun MPSP-800 column and then used immediately. Deionised water was used in all cases. Triethylamine was distilled from and stored over potassium hydroxide. Thionyl chloride was distilled from triphenyl phosphate. Grubbs' 2nd generation catalyst was stored in a desiccator. Microwave reactions were carried out using a Biotage Initiator 2.0 microwave

NMR spectra were recorded on Varian Mercury 300, Varian Unity Plus 500 and Bruker AVII 500 (with ^{13}C Cryoprobe) spectrometers. Electrospray mass spectra were carried out on Micromass LCT and Bruker micrOTOF spectrometers. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected.

Synthesis

5-Iodoisophthalic acid,[14] iodo-arene precursor **4**,[4c] amine **6**,[15] 2-(allyloxy)ethyl 4-methylbenzenesulfonate[16] and chloride axle $\mathbf{10}^+Cl^-$[4a] were prepared by literature procedure.

***N*¹, *N*³-Dihexyl-5-iodoisophthalamide (2).** To a solution of 5-iodoisophthalic acid (2.00 g, 6.85 mmol) dissolved in dry CH_2Cl_2 (100 mL), oxalyl chloride (1.74 g, 1.16 mL, 13.7 mmol) and dry DMF (a drop, catalytic amount) were added, after which the solution was stirred under a nitrogen atmosphere until all solid had gone into solution. The solution was then concentrated to leave an orange oily film. This was redissolved in dry CH_2Cl_2 (100 mL), cooled to 0 °C, and NEt_3 (5 mL, excess) and n-hexylamine (1.39 g, 1.81 mL, 13.7 mmol) were added. This reaction mixture was stirred for 16 h. The resulting organic solution was washed with 1 M $HCl_{(aq)}$ solution (3 × 100 mL), sat. $NaHCO_{3(aq)}$

solution (2 × 100 mL) and H_2O (2 × 100 mL). The organic fraction was dried over $MgSO_4$, the solvent removed *in vacuo* and then purified by silica gel column chromatography (pentane–EtOAc 4 : 1 to 1 : 1) to yield iodo-arene **2** as a white solid (1.44 g, 46%). Mp = 100 °C; δ_H(300 MHz, $CDCl_3$) 8.15 (2H, s, isophthalamide Ar*H*^{4} & *H*^{6}) 8.06 (1H, s, isophthalamide Ar*H*^{2}), 6.42 (2H, t, ^3J = 5.3 Hz, N*H*), 3.40–3.46 (4H, m, NHCH_2CH_2), 1.56–1.66 (4H, app quartet, NHCH_2CH_2), 1.29–1.42 (12H, m, 3 × CH_2), 0.88–0.92 (6H, m, CH_3); δ_C(75.5 MHz, $CDCl_3$) 165.5, 138.5, 136.7, 124.4, 94.3, 40.4, 31.5, 29.4, 26.7, 22.5, 14.0; *m/z* (ES) 459.1517 ([M + H]$^+$, $C_{20}H_{32}IN_2O_2$ requires 459.1509), 459 (98%, [M + H]$^+$), 476 (12, [M + NH_4]$^+$), 481 (98, [M + Na]$^+$), 491 (65, [M + CH_3OH + H]$^+$), 497 (44, [M + K]$^+$), 513 (100, [M + CH_3OH + Na]$^+$).

***N*^{1}, *N*^{3}-Dihexyl-5-ferrocenylisophthalamide (3).** Ferroceneboronic acid (232 mg, 1.00 mmol) was added to DME (9 mL) in a 20 mL microwave vial (containing a stirring bar). To this was added **2** (458 mg, 1.00 mmol), then 3 M $NaOH_{(aq)}$ solution (1 mL). This mixture was then degassed thoroughly for 20 min with nitrogen. $PdCl_2$(dppf) (7 mg, 0.01 mmol) was then added, the microwave vial capped, and the vial subjected to microwave irradiation at 150 °C for 30 min. The reaction mixture was then diluted with $CHCl_3$ (100 mL) and H_2O (25 mL). The organic layer was separated and washed with H_2O (3 × 50 mL), dried over $MgSO_4$, solvent removed *in vacuo* and then purified by silica gel column chromatography (hexane–EtOAc 1 : 0 to 2 : 1) to yield compound **3** as a dark orange solid (303 mg, 59%). Mp = 68–70 °C; δ_H(300 MHz, $CDCl_3$) 7.97 (2H, d, ^4J = 1.5 Hz, isophthalamide Ar*H*^{4} & *H*^{6}), 7.87 (1H, t, ^4J = 1.5 Hz, isophthalamide Ar*H*^{2}), 6.32 (2H, t, ^3J = 5.1 Hz, N*H*), 4.72 (2H, t, ^3J = 1.8 Hz, Fc Cp*H*), 4.38 (2H, t, ^3J = 1.8 Hz, Fc Cp*H*), 4.05 (5H, s, Fc Cp'*H*), 3.45–3.52 (4H, app quartet, NHCH_2CH_2), 1.60–1.70 (4H, m, NHCH_2CH_2), 1.31–1.46 (12H, m, 3 × CH_2), 0.89–0.93 (6H, m, CH_3); δ_C(75.5 MHz, $CDCl_3$) 167.0, 141.2, 135.1, 127.1, 121.9, 83.1, 69.7, 69.6, 66.6, 40.3, 31.5, 29.5, 26.7, 22.5, 14.0; *m/z* (ES) 517.2513 ([M + H]$^+$, $C_{30}H_{41}FeN_2O_2$ requires 517.2517), 517 (100%, [M + H]$^+$), 539 (19, [M + Na]$^+$), 549 (31, [M + CH_3OH + H]$^+$), 571 (14, [M + CH_3OH + Na]$^+$).

***N*^{1}, *N*^{3}-Bis(2-(4-(2-(allyloxy)ethoxy)phenoxy)ethyl-5-ferrocenylisophthalamide (5).**

Route A. Ferroceneboronic acid (230 mg, 1.00 mmol) was added to DME (9 mL) in a 20 mL microwave vial (containing stirring bar). To this was added iodo-arene compound **4** (731 mg, 1.00 mmol), then 3 M $NaOH_{(aq)}$ solution (1 mL). This mixture was then degassed thoroughly for 20 min with nitrogen. $PdCl_2$(dppf) (7 mg, 0.01 mmol) was then added, the microwave vial capped, and the vial subjected to microwave irradiation at 150 °C for 30 min. The reaction mixture was then diluted with $CHCl_3$ (100 mL) and H_2O (25 mL). The organic layer was separated, washed with H_2O (3 × 50 mL) and dried over $MgSO_4$, the solvent removed *in vacuo* and then purified by silica gel column chromatography (hexane–EtOAc 1 : 1 to 1 : 2) to yield **5** as an orange oil (156 mg, 20%).

Route B. Diphenol compound **9** (250 mg, 0.40 mmol), 2-(allyloxy)ethyl 4-methylbenzenesulfonate (207 mg, 0.81 mmol) and K_2CO_3 (123 mg, 0.89 mmol) were suspended in dry CH_3CN (15 mL) and heated under a nitrogen atmosphere for 60 h. The reaction was cooled to room temperature, filtered and the solvent removed *in vacuo*. The residue was dissolved in CH_2Cl_2, filtered and then dried ($MgSO_4$), the solvent removed *in vacuo*, and the product isolated after silica gel column chromatography (CH_2Cl_2–CH_3OH 98 : 2) as an orange oil (151 mg, 48%).

δ_H(300 MHz, $CDCl_3$) 7.99 (2H, d, ^4J = 1.5 Hz, isophthalamide Ar*H*^{4} & *H*^{6}), 7.90 (1H, t, ^4J = 1.5 Hz, isophthalamide Ar*H*^{2}), 6.86 (8H, app s, hydroquinone Ar*H*), 6.78 (2H, t, ^3J = 5.9 Hz, N*H*), 5.88–6.01 (2H, m, C*H*═CH_2), 5.19–5.35 (4H, m, CH═CH_2), 4.72 (2H, app s, Fc Cp*H*), 4.39 (2H, app s, Fc Cp*H*), 4.07–4.15 (12H, m, 3 × CH_2), 4.04 (5H, s, Fc Cp'*H*), 3.88 (4H, app quartet, NHCH_2), 3.78 (4H, m, CH_2); δ_C(75 MHz, $CDCl_3$) 167.1, 153.2, 152.6, 141.3, 134.7, 134.5, 127.4, 122.1, 117.4, 115.6, 115.3, 82.9, 72.3, 69.7, 68.5, 68.0, 67.1, 66.7, 66.6, 39.8; *m/z* (ES) 811.2652 ([M + Na]$^+$, $C_{44}H_{48}FeN_2NaO_8$ requires 811.2653), 789 (3%, [M + H]$^+$), 806 (100, [M + NH_4]$^+$), 811 (67, [M + Na]$^+$).

***N*^{1}, *N*^{3}-Bis(2-(4-benzyloxy)phenoxy)ethyl)-5-iodoisophthalamide (7).** 5-Iodoisopthalic acid (1.55 g, 5.32 mmol) was suspended in $SOCl_2$ (20 mL) and refluxed for 16 h under a drying tube. The excess $SOCl_2$ was removed by distillation, and the crude diacid chloride (a brown oil) was then added in dry CH_2Cl_2 (75 mL), to a solution of 2-(4-benzyloxy)phenoxy)ethanamine **6** (2.59 g, 10.6 mmol) and NEt_3 (2.69 g, ~ 4 mL, 26.6 mmol) in dry CH_2Cl_2 (75 mL) at 0 °C, and then stirred at room temperature for 1 h under a nitrogen atmosphere. The reaction mixture was then washed with 10% $HCl_{(aq)}$ (3 × 150 mL), sat. $NaHCO_3$ (150 mL) and brine (150 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was subjected to silica gel column chromatography (CH_2Cl_2–CH_3OH 98 : 2), and then the resulting solid washed with EtOAc to give **7** as a white solid (1.83 g, 46%). Mp = 160 °C; δ_H(300 MHz, $CDCl_3$) 8.22 (2H, d, ^4J = 1.5 Hz, isophthalamide Ar*H*^{4} & *H*^{6}), 8.11 (1H, t, ^4J = 1.5 Hz, isophthalamide Ar*H*^{2}), 7.32–7.44 (10H, m, benzyl Ar*H*), 6.83–6.93 (8H, m, hydroquinone Ar*H*), 6.69 (2H, t, ^3J = 5.6 Hz, N*H*), 5.02 (4H, s, CH_2), 4.10 (4H, t, ^3J = 5.0 Hz, OCH_2), 3.82–3.87 (4H, app. quartet, NCH_2); δ_C(75 MHz, d_6-DMSO) 164.6, 152.6, 152.5, 138.1, 137.3, 136.3, 128.4, 127.7, 127.6, 126.0, 115.7, 115.4, 94.6, 69.2, 66.3 (1 peak missing *C*NH - coincidental with solvent); *m/z* (ES) 765.1427 ([M + Na]$^+$, $C_{38}H_{35}IN_2NaO_6$ requires 765.1432), 801 (100%, [M + CH_3CN + NH_4]$^+$ - only assignable peak observed in low resolution mass spectrum.

***N*^{1}, *N*^{3}-Bis(2-(4-benzyloxy)phenoxy)ethyl)-5-ferrocenylisophthalamide (8).** Ferroceneboronic acid (230 mg, 1.00 mmol) was added to DME (9 mL) in a 20 mL microwave vial (containing a stirring bar). To this was added **6** (743 mg, 1.00 mmol), then 3 M $NaOH_{(aq)}$ solution (1 mL). This mixture was then degassed thoroughly for 20 min with nitrogen. $PdCl_2$(dppf) (7 mg, 0.01 mmol) was then added, the microwave vial capped, and the vial subjected to microwave radiation at 150 °C for 30 min. The reaction mixture was then diluted with $CHCl_3$ (100 mL) and H_2O (25 mL). The organic layer was separated, washed with H_2O (3 × 50 mL), and dried over $MgSO_4$. The solvent was removed *in vacuo* and then purified by silica gel column chromatography (CH_2Cl_2: CH_3OH 99 : 1) to yield **8** as a foaming orange solid (303 mg, 59%). Mp: phase transitions at 68 °C and 120 °C; δ_H(300 MHz, $CDCl_3$) 8.00 (2H, d, ^4J = 1.5 Hz, isophthalamide Ar*H*^{4} & *H*^{6}), 7.90 (1H, t, ^4J = 1.5 Hz, isophthalamide Ar*H*^{2}), 7.32–7.44 (10H, m, benzyl Ar*H*), 6.86–6.94 (8H, m, hydroqunione Ar*H*), 6.71–6.75 (2H, t, ^3J = 5.7 Hz, N*H*), 5.02 (4H, s, CH_2), 4.72–4.73 (2H, m, Fc Cp*H*), 4.38–4.39 (2H, m, 2H, Fc Cp*H*), 4.13–4.16 (4H, m, OCH_2), 4.04 (5H, s, Fc Cp'*H*), 3.87–3.92 (4H,

app. quartet, NCH_2); δ_C(75 MHz, $CDCl_3$) 167.1, 153.3, 152.7, 141.4, 137.1, 134.8, 128.5, 127.9, 127.4, 122.1, 115.9, 115.4, 82.9, 70.6, 69.7, 69.7 (sic), 67.2, 66.7, 39.8. (1 Ar*C* peak missing); *m*/*z* (ES) 823.2436 ([M + Na]$^+$, $C_{48}H_{44}FeN_2NaO_6$ requires 823.2442), 823 (7%, [M + Na]$^+$), 859 (100, [M + CH_3CN + Na]$^+$).

***N*^{1}, *N*^{3}-Bis(2-(4-hydroxyphenoxy)ethyl)-5-ferrocenylisophthalamide (9).** To a solution of **8** (400 mg, 0.50 mmol) dissolved in $CHCl_3$–CH_3OH (1 : 1, 20 mL) was added 10% Pd/C (10% by wt, 40 mg), and the reaction was stirred under an atmosphere of H_2 for 16 h. The reaction mixture was filtered through Celite®, the solvent removed *in vacuo*, to leave the product as a foaming orange solid (310 mg, quant.). Mp > 148 °C (dec.); δ_H(300 MHz, *d*$_6$-DMSO) 8.94 (2H, s, O*H*), 8.87 (2H, t, ^3J = 5.6 Hz, N*H*), 8.20 (1H, t, ^4J = 1.5 Hz, isophthalamide ArH^2), 8.13 (2H, d, ^4J = 1.5 Hz, isophthalamide ArH^4 & H^6), 6.65–6.82 (8H, m, hydroquinone Ar*H*), 4.93 (2H, t, ^3J = 1.9 Hz, Fc Cp*H*), 4.43 (2H, t, ^3J = 1.9 Hz, Fc Cp*H*), 4.02–4.07 (9H, m, Fc Cp'*H* & OCH_2), 3.60–3.66 (4H, app. quartet, NCH_2); δ_C(75 MHz, *d*$_6$-DMSO) 166.0, 151.4, 151.2, 139.9, 134.6, 126.7, 124.1, 115.8, 115.5, 83.4, 69.5, 69.4, 66.6, 66.6 (sic) (1 peak missing *C*NH - coincidental with solvent); *m*/*z* (ES) 643.1504 ([M + Na]$^+$, $C_{34}H_{32}FeN_2NaO_6$ requires 643.1502), 643 (5%, [M + Na]$^+$), 679 (100, [M + CH_3CN + NH_4]$^+$). In addition, 619 (100%, [M − H]$^-$), 655 (43, [M + Cl]$^-$) observed in negative polarity mass spectrum.

Chloride salt of rotaxane (1$^+$Cl$^-$). Macrocycle precursor **5** (81 mg, 0.10 mmol) and **10**$^+$Cl$^-$ (110 mg, 0.10 mmol) were added to dry CH_2Cl_2 and stirred for 30 min under a nitrogen atmosphere. Grubbs 2nd generation catalyst (8.1 mg) was added, stirred under a constant flow of nitrogen for 16 h. The reaction solvent was removed *in vacuo*, and after purification by two prep silica gel TLC plates (CH_2Cl_2–CH_3OH 96 : 4, then EtOAc), rotaxane **1**$^+$Cl$^-$ was isolated as an orange solid (48 mg, 25%). Mp > 230 °C (dec.); δ_H(300 MHz, $CDCl_3$): 10.30 (2H, s, py N*H*), 9.68 (1H, s, pyridinium ArH^4), 9.25 (2H, s, pyridinium ArH^2 & ArH^6), 8.77 (1H, s, isophthalamide ArH^2), 8.55 (2H, s, isophthalamide N*H*), 8.26 (2H, s, isophthalamide ArH^4 & ArH^6), 7.84 (4H, d, ^3J = 8.8 Hz, stopper NHAr*H*), 7.06–7.26 (30H, m, stopper Ar*H*), 6.45 (4H, d, ^3J = 8.9 Hz, hydroquinone Ar*H*), 6.20 (4H, d, ^3J = 8.9 Hz, hydroquinone Ar*H*), 5.96 (2H, br s, C*H*═C*H*), 4.68 (2H, app s, Fc Cp*H*), 4.32 (5H, app s, Fc Cp*H* & N$^+$CH_3), 4.19 (4H, br s, CH_2), 4.05 (app s, 4H, CH_2), 4.00 (5H, s, Fc Cp'*H*), 3.75–3.85 (12H, m, 3 × CH_2), 1.32 (36H, s, (CH_3)$_3$); δ_C(125.8 MHz, $CDCl_3$) 168.9, 158.1, 153.4, 151.9, 148.4, 146.9, 145.2, 144.8, 143.5, 140.4, 139.4, 134.8, 134.0, 133.4, 131.8, 131.1, 130.6, 129.9, 129.0, 127.4, 125.8, 124.3, 122.1, 120.4, 114.8, 114.5, 71.0, 69.3, 68.0, 66.1, 63.8, 48.8, 40.6, 34.3, 31.4 (in addition evidence of broad peaks attributed to the four Cp*C*); *m*/*z* (ES) 1800.8585 ([M − Cl]$^+$, $C_{116}H_{122}FeN_5O_{10}$ requires 1800.8541), 1801 (100%, [M − Cl]$^+$).

Hexafluorophosphate salt of rotaxane (1$^+$PF$_6^-$). Rotaxane **1**$^+$Cl$^-$ (72 mg, 0.039 mmol) was dissolved in $CHCl_3$ (15 mL), and then vigorously shaken with 0.1 M NH_4PF_6 (10 × 10 mL), then washed with H_2O (3 × 10 mL). The organic layer was separated, then dried over $MgSO_4$, with the solvent subsequently removed *in vacuo* to yield rotaxane **1**$^+$PF$_6^-$ as a yellow-orange solid (59 mg, 78%). Mp > 220 °C (dec.); δ_H(300 MHz, $CDCl_3$) 9.23 (2H, s, pyridinium N*H*), 8.90 (1H, s, pyridinium ArH^4), 8.54 (2H, s, pyridinium ArH^2 & ArH^6), 8.19–8.21 (3H, m, isophthalamide ArH^2 & ArH^4 & ArH^6), 7.61 (4H, d, ^3J = 8.8 Hz, stopper Ar*H*), 7.08–7.29 (32H, m, stopper Ar*H* & isophthalamide N*H*), 6.48 (4H, t, ^3J = 8.9 Hz, hydroquinone Ar*H*), 6.37 (4H, t, ^3J = 8.9 Hz, hydroquinone Ar*H*), 5.98 (2H br s, C*H*═C*H*), 4.73 (2H, s, Fc Cp*H*), 4.37 (2H, s, Fc Cp*H*), 4.31 (3H, s, N$^+$CH_3) 4.04–4.06 (9H, m, Fc Cp'*H* & CH_2) 3.93 (4H, t, ^3J = 4.4 Hz, CH_2), 3.86 (4H, m, CH_2), 3.81 (4H, m, CH_2) 3.70–3.72 (4H, m, CH_2), 1.31 (s, 36H, (CH_3)$_3$); δ_C(125.8 MHz, $CDCl_3$) 167.0, 158.3, 152.8, 152.0, 148.6, 146.8, 145.3, 144.0, 143.4, 141.8, 141.3, 134.3, 134.3 (sic), 134.1, 132.0, 131.0, 130.6, 130.4, 128.5, 127.4, 125.9, 124.4, 121.6, 120.1, 115.5, 114.7, 83.2, 70.8, 69.7, 69.5, 69.3, 67.7, 66.9, 66.8, 63.9, 49.6, 39.7, 34.3, 31.4; δ_F(282.4 MHz, $CDCl_3$) –69.9 (d, ^1J = 714 Hz, P*F*$_6$); δ_P(121.5 MHz, $CDCl_3$) –143.9 (septet, ^1J = 714 Hz, *P*F$_6^-$); *m*/*z* (ES) 1800.8605 ([M − PF$_6$]$^+$, $C_{116}H_{122}FeN_5O_{10}$ requires 1800.8541), 1801 (100%, [M − PF$_6$]$^+$).

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