Anion templated surface assembly of a redox-active sensory rotaxane†

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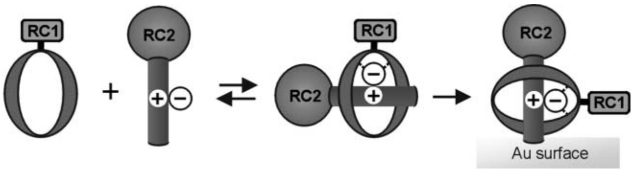
Anion templation is used to assemble novel redox-active bis-ferrocene functionalised rotaxane self-assembled monolayers (SAMs) on to gold electrode surfaces; after template removal, the unique SAM rotaxane binding domain is capable of selectively sensing chloride ions electrochemically.

Although mechanically bonded molecules such as rotaxanes and catenanes have enormous potential for use in applications based on nanometer-scale switching and motion,[1–5] the unique topological cavities intrinsic to these interlocked structures also make them of great interest in the molecular sensing arena.[6–10] In the majority of cases cationic and neutral species have been employed as efficient templates in mechanical bond construction.[11–14] The application of anions to direct supramolecular assembly, however, remains largely under-developed.[15–20]

We have recently reported a general method of using anions to template the formation of a range of pseudorotaxanes, rotaxanes and catenanes.[21,22] The assembly process is based on coupling anion recognition with ion-pairing where, in non competitive solvent media, a coordinatively unsaturated chloride anion of a tight ion-pair threading component facilitates the interpenetration of a pyridinium, imidazolium or guanidinium thread through the annulus of an isophthalamide macrocycle.[22]

Importantly, after chloride anion template removal the resulting interlocked assemblies contain unique topologically-defined hydrogen bond donating binding domains which exhibit a high degree of selectivity for the templating halide anion.

Herein we describe the first example of using anion templation for assembling rotaxane SAMs onto electrode surfaces. The fabrication of interlocked molecular structures as thin films, including the production of rotaxane self-assembled monolayers (SAMs) on electrodes and nanoparticle surfaces, is currently being intensely investigated.[23–30] To our knowledge, however, there exists no precedent for the use of any surface-assembled interlocked structure in chemical sensing.[31] We report here the chloride anion templated surface assembly of a novel redox-active rotaxane where two different ferrocene redox centres are covalently attached to the macrocycle wheel and thread axle. It is noteworthy that the electrochemical anion recognition behaviour of the rotaxane SAMs contrasts with that of the redox sensing properties of the individual components. The unique interlocked binding cavity of the rotaxane SAM, generated by axle threading, results in an amplified and selective response to chloride. The response to larger oxoanions, such as phosphate, which are unable to access the interlocked cavity, is switched off.



Scheme 1 Rotaxane SAM formation by surface stoppering (RC = redox centre).

The anion-templated surface-stoppering strategy used for redox-active rotaxane SAM formation is illustrated in Scheme 1. An anion binding macrocycle containing an appended ferrocene redox-active centre (RC1) and an ion-paired threading component, which also incorporates an appropriately designed novel bulky ferrocene redox-active stopper group (RC2) at one terminus and a surface tethering group at the other, are mixed in solution to form an anion-templated pseudorotaxane assembly. Introduction of a suitable substrate, such as a gold electrode, results in rotaxane SAM formation where the capture of both redox-active ferrocene functionalised macrocycle wheel and axle rotaxane components by the substrate can be probed electrochemically. The redox-active ferrocene-functionalised wheel and axle design components for the target rotaxane SAM are shown in Fig. 1.

The syntheses of the ferrocene appended isophthalamide macrocycle **1**, pentaphenylferrocene pyridinium nicotinamide chloride ion-pair thread $\mathbf{2^+Cl^-}$, and benzyl ion-pair analogue, $\mathbf{3^+Cl^-}$ (Fig. 1) are described in the Supplementary Information.

Preliminary ^{1}H NMR titration investigations in $CDCl_3$ and acetonitrile-d3 of **1** and $\mathbf{2^+Cl^-}$ revealed significant perturbations of

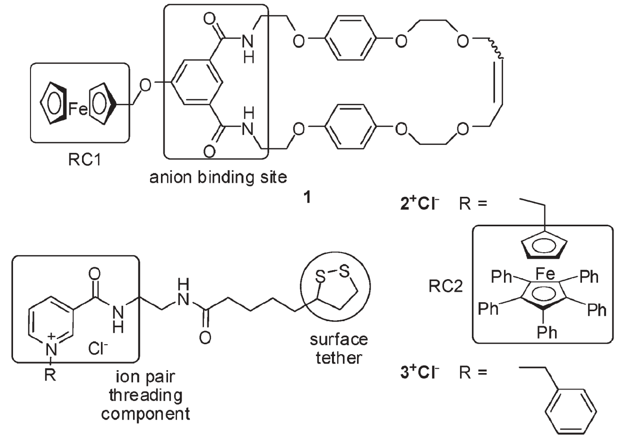


Fig. 1 Redox-active ferrocene-functionalised wheel and axle components.

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the amide and hydroquinone protons of **1** and the amide protons of **2^+**, indicative of pseudorotaxane formation. Rotaxane SAMs were formed by immersing gold electrodes into a 10 : 1 mixture (shifting the equilibrium in favour of rotaxane) of macrocycle **1** and thread **2^+Cl^-** in chloroform solution. The rotaxane SAM modified electrodes were sonicated in $CHCl_3$ to remove excess non-chemisorbed material and washed with 0.1 M $TBA^+PF_6^-$ in order to effect chloride exchange for hexafluorophosphate (to generate a chloride-responsive adlayer).

Square wave voltammetry facilitated characterisation of this adlayer with the resolution of both macrocycle and thread ferrocene redox waves (Fig. 2, and see Supplementary Information). Ellipsometry studies of the **$1/2^+Cl^-$** rotaxane monolayer indicated a thickness of 1.02 ± 0.30 nm, a figure broadly consistent with CACHE modelling. FTIR reflectance spectra (see Supplementary Information) of the pure axle (**2^+Cl^-**) monolayer showed strong absorbances at 706 cm^{-1} and 743 cm^{-1}, characteristic of phenyl C–H bond out-of-plane bending, a strong signal at 1676 cm^{-1}, characteristic of the amide carbonyl group stretch associated with the nicotinamide and amide groups, and phenyl C–H stretches at 3065 cm^{-1}. Evidence for the two-component nature of the threaded adlayer is provided by a resonance at 877 cm^{-1} (also observed in the solid state spectrum of **1**, but not observed in the spectrum of the **2^+Cl^-** monolayer), associated with the out-of-plane bending of the alkene C–H bonds of the macrocycle. Further evidence of macrocycle threading comes from a simultaneous shifting of the amide carbonyl stretching band centre towards lower wavenumbers and a broadening from fwhm = 30 cm^{-1} to 44 cm^{-1} (likely to be the result of a superimposition of the isophthalamide carbonyl stretches of **1** with the amide signals of compound **2^+Cl^-**).

The specific interlocked nature of the rotaxane film is further confirmed by Surface Plasmon Resonance (SPR) spectroscopy. Addition of a 0.8 mM solution of **1** in acetonitrile to a gold SPR chip modified with a monolayer of **3^+Cl^-** (unstoppered analogue of thread **2^+Cl^-**) led to a significant SPR response indicative of binding of the macrocycle at the surface (*i.e.* pseudorotaxane formation).[33] No plasmon response is observed for addition of macrocycle **1** to SPR chips modified with dodecanethiol monolayers or **2^+Cl^-** monolayers, which indicates that there is no non-specific binding of **1** at the surface, and that the pentaphenylferrocene group of **2^+Cl^-** does effectively act as a stopper, preventing the annulus of macrocycle **1** from passing over it. The results of this study are shown in Fig. 3.

The electrochemical anion sensing properties of the redox-active surface-confined rotaxane (**$1/2^+PF_6^-$**) were compared with those of the free macrocycle **1** in solution and SAM of the **$2^+PF_6^-$** thread alone. The addition of molar excesses of TBA^+ Cl^- and oxoanions $H_2PO_4^-$, HSO_4^- to acetonitrile solutions of free thread or SAMs of **$2^+PF_6^-$** resulted in only small electrochemical cathodic perturbation ($\Delta E < 10$ mV) of the pentaphenylferrocene redox couple. Diffusive cyclic voltammetric studies with macrocycle **1**, however, revealed the ferrocene redox couple to undergo significant cathodic shift[32] with $H_2PO_4^-$ (ΔE 45 ± 5 mV) and HSO_4^- (ΔE 15 ± 5 mV) and small perturbations ($\Delta E < 10$ mV) with Cl^- and AcO^-. These electrochemical anion recognition observations suggest that the relatively large tetrahedral dihydrogen phosphate anionic guest species "perches" on the periphery of the macrocycle *via* favourable amide–anion hydrogen bonding interactions in proximity to the aryl ether appended ferrocene redox centre.

The rotaxanated pentaphenylferrocene centre, RC2, exhibits electrochemical characteristics and responses to chloride and oxoanions broadly the same as SAMs of **$2^+PF_6^-$** alone. By contrast, the ferrocenyl appended macrocycle within the surface assembled rotaxane (**$1/2^+PF_6^-$**) exhibits a markedly greater electrochemical cathodic response to chloride of 40 ± 5 mV (Fig. 4). It is noteworthy that RC1 in the rotaxanated SAM is insensitive ($\Delta E < 5$ mV) to excess $H_2PO_4^-$ (Fig. 4) or any of the other basic oxoanions.[34] This suggests that chloride binding inside the interlocked cavity of the surface confined rotaxane results in a conformation where the macrocycle wheel's pendant ferrocene group is in proximity to the complexed halide anion, whereas the oxoanions are too large to penetrate the rotaxane binding pocket.

Preliminary electrochemical competition experiments in acetonitrile solutions reveal that these rotaxane SAMs are also capable of selectively detecting Cl^- in the presence of 100-fold excess amounts of $H_2PO_4^-$ and exhibit an appreciably greater detection

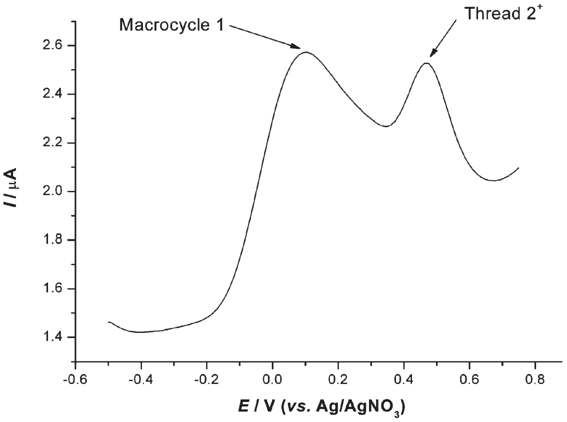

Fig. 2 Square wave voltammogram of a rotaxane SAM formed with macrocycle **1** (Ep 154 ± 15 mV) and thread **2^+Cl^-** (Ep 476 ± 15 mV) on a gold electrode (recorded with 100 mM TBA PF_6 in acetonitrile as the electrolyte). The macrocycle : axle peak charge ratios, which reflect the degree of axle threading, vary from 1 : 1.1 to 1 : 3.

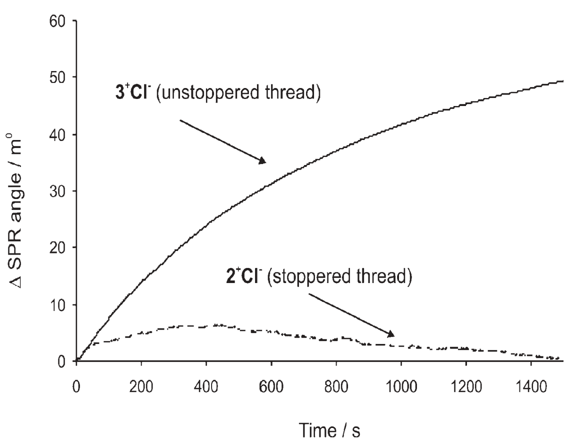

Fig. 3 Comparative SPR responses of **2^+Cl^-** (stoppered thread) and **3^+Cl^-** (unstoppered thread) modified SPR substrates to addition of macrocycle **1**. The response of the **3^+Cl^-** modified surface is indicative of pseudorotaxane formation.

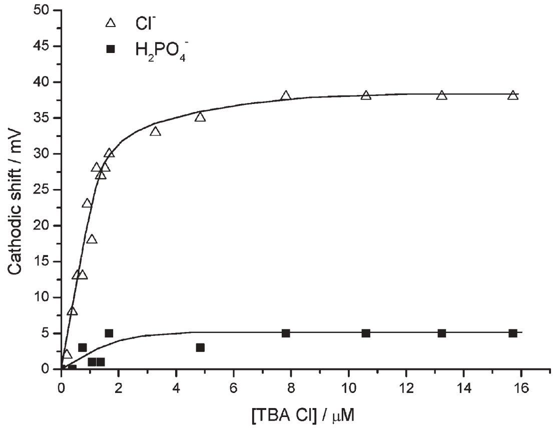

Fig. 4 The comparative voltammetric responses of the rotaxanated macrocycle ferrocene (in a SAM of $\mathbf{1/2^+PF_6^-}$) to chloride and dihydrogen phosphate (in acetonitrile).

sensitivity than that shown by the free macrocycle (LOD 0.2 µM for SAMs of $\mathbf{1/2^+PF_6^-}$; the free macrocycle is unresponsive at these levels). Importantly, this observed selective electrochemical sensing capability negates the possibility of intermolecular surface co-operative binding effects between neighbouring adsorbed molecules being responsible for chloride ion selectivity. The superior electrochemical response of rotaxane SAMs to Cl^- over $H_2PO_4^-$ (reversed compared to free **1**) mirrors the high degree of chloride anion selectivity of our previous rotaxanes prepared *via* chloride anion templation, where the mechanically bonded assemblies' unique interlocked binding domain excludes the larger, more basic, dihydrogen phosphate anion.[21]

In summary, we have demonstrated the first application of rotaxane SAMs in chemical sensing. Novel redox-active bis-ferrocenyl functionalised rotaxane SAMs can be assembled on to gold electrode surfaces using an anion-templated surface-stoppering methodology. The selectivity trends observed are markedly sensitive to axle threading and, with outlined SPR, FTIR and ellipsometry data, strongly supportive of the anion binding site being within the confines of the surface interlocked cavity. Such a potential anion sensing rotaxane system, by virtue of the bespoke interlocked binding cavity, has been shown to electrochemically recognise chloride anions selectively. The design and surface fabrication of interlocked SAM materials for sensory applications is continuing in our laboratories.

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