

An Ion-Pair Template for Rotaxane Formation and its Exploitation in an Orthogonal Interaction Anion-Switchable Molecular Shuttle**

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Despite significant advances^[1] in anion-template methods for the construction of mechanically interlocked molecules,^[2] the use of anions to induce changes in the relative positions of the components of catenanes and rotaxanes has proved particularly challenging,^[3] especially in comparison to the widespread success achieved with other stimuli.^[4–6] The few examples of anion-switchable molecular shuttles developed to date employ competition between the same types of weak interaction in both states of the molecule to achieve switching (solvation effects^[3d,e] or the anion outcompeting hydrogen-bonding acceptor groups of the macrocycle for donor groups on the thread^[3e,f]). Other features of anions, such as the propensity of halides to form strong coordination bonds to various transition metals, have yet to be exploited.^[7] Herein we report the serendipitous discovery of a new efficient template for rotaxane formation and its use in the assembly of a chloride-switchable molecular shuttle which exhibits excellent positional integrity (> 98 %) of the ring in both states that arises from orthogonal binding modes: direct intercomponent metal–ligand coordination in one state and a combination of tight ion pairing, aromatic stacking interactions, and CH...O and CH...Cl hydrogen bonding in the other.

The development of the new template for rotaxane formation was prompted by the chance observation that displacement of the acetonitrile ligand of $[(\mathbf{L1})\text{Pd}(\text{CH}_3\text{CN})]$ by the chloride ion of benzyl pyridinium chloride (**1-Cl**) was accompanied by encapsulation of the organic cation by the anionic PdCl-coordinated macrocycle $[(\mathbf{L1})\text{PdCl}]^-$ (Figure 1a).^[8] The threaded nature of the complex $[(\mathbf{L1})\text{PdCl}\cdot\mathbf{1}]$ in CDCl_3 was clearly apparent from ^1H NMR spectroscopy (a distinct upfield shift in the pyridinium resonances with respect

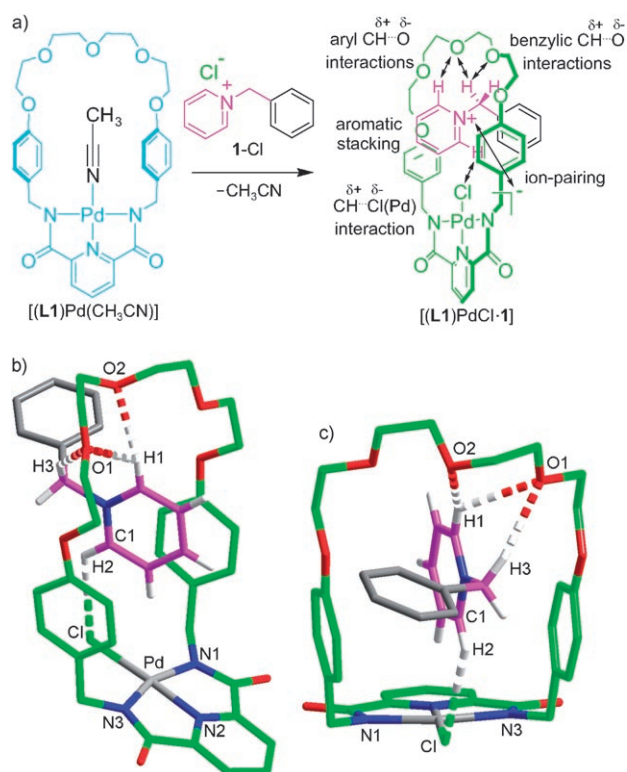


Figure 1. An allosteric anion-activated template for threading based on tight ion pairing reinforced through multiple other noncovalent interactions. a) Synthesis of pseudorotaxane $[(\mathbf{L1})\text{PdCl}\cdot\mathbf{1}]$. Reaction conditions: CH_2Cl_2 , 1 h, quantitative yield (use of **1-PF₆** instead of **1-Cl**, or using DMSO instead of CH_2Cl_2 , does not lead to pseudorotaxane formation). b) Side-on and c) face-on views of the X-ray crystal structure of $[(\mathbf{L1})\text{PdCl}\cdot\mathbf{1}]$.^[9] N blue, O red, Pd silver, Cl and the C atoms of the macrocycle green, pyridinium purple, and other C atoms gray. Selected bond lengths [Å] and angles [°]: N1–Pd 2.04, N2–Pd 1.93, N3–Pd 2.03, Cl–Pd 2.32, O1–H3 2.47, O1–H1 2.57, O2–H1 2.37; N1–Pd–N3 160.8, N2–Pd–Cl 176.4.

to those in **1-Cl** caused by shielding by the benzylic groups of the macrocycle, see the Supporting Information) and was also found to persist in the solid state (Figure 1b and c) from the X-ray crystal structure of single crystals grown from a saturated $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ solution.^[9]

The solid-state structure of $[(\mathbf{L1})\text{PdCl}\cdot\mathbf{1}]$ indicates that a broad range of noncovalent interactions are responsible for the assembly of the threaded architecture. In addition to the tight ion pair^[10] (the pyridinium nitrogen atom is within 4 Å of atoms in the first coordination sphere of the formally negatively charged metal complex), aromatic stacking interactions between the aromatic rings of the host and guest, aryl- and alkyl-CH...O hydrogen bonding between the polyether

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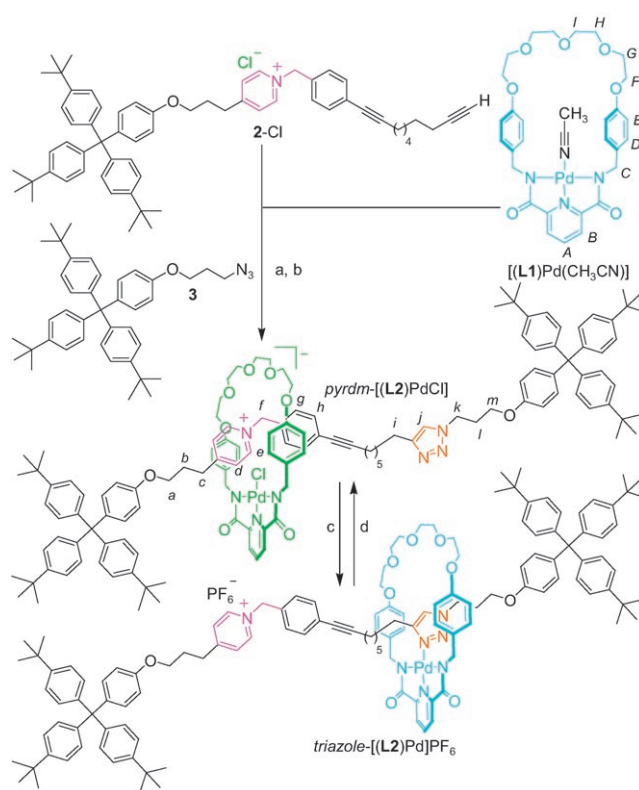
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oxygen atoms and protons on the carbon atoms adjacent to the pyridinium nitrogen atom (C–O distances 3.19–3.36 Å), and CH···Cl(Pd) second coordination sphere interactions^[7] (C–Cl distance 3.72 Å) all apparently contribute to the stability of the interpenetrated structure. Many of these primarily electrostatic interactions should be much weaker in more polar environments and, indeed, the ¹H NMR spectrum of [(L1)PdCl·1] (see the Supporting Information) shows the chloride anion is a vital component of the assembly process: [(L1)Pd(CH₃CN)] did not form a threaded complex when treated with 1-PF₆ in CH₂Cl₂, a result which suggested that the recognition motif could also be used as the basis of an anion-selective trigger.

A pyridinium chloride salt suitable for rotaxane synthesis (2-Cl) was prepared in four steps from 4-pyridinepropanol (see the Supporting Information). Treatment of [(L1)Pd(CH₃CN)] with 2-Cl in dichloromethane for one hour, followed by reaction with 3 by a Cu^I-catalyzed azide–alkyne 1,3-cycloaddition (CuAAC)^[11] in the presence of tris(benzyl-triazolylmethyl)amine (TBTA)^[12] and diisopropylethylamine (DIPEA) led to [(L2)PdCl] in 64% yield (Scheme 1). The mass spectrum of this product was strongly suggestive of a rotaxane, as the major peak, which corresponds to [(L2)Pd]⁺, does not fragment to the intact macrocycle and axle, as would be expected for a non-interlocked salt. The irreversible formation of a stoppered rotaxane was further confirmed when removal of palladium did not cause separation of the components (see the Supporting Information). Comparison of the ¹H NMR spectrum of [(L2)PdCl] (Figure 2b) with that of the chloride salt of the thread (Figure 2a), shows significant upfield shifts to the pyridinium resonances H_d, H_e, and H_f, and adjacent protons (H_a and H_c).^[13] Other signals of the thread show little change, which indicates that the anionic PdCl–macrocycle is located overwhelmingly over the pyridinium station, that is, the structure is *pyrdm*^[14]–[(L2)PdCl] (Scheme 1).

The triazole group introduced by the CuAAC reaction can also act as a ligating station for the palladium–macrocycle.^[15] Treatment of *pyrdm*–[(L2)PdCl] with AgPF₆ (1.1 equiv; Scheme 1, step c) smoothly precipitated AgCl and resulted in quantitative conversion into a new rotaxane, [(L2)Pd]PF₆, in which the chloride ligand had been replaced by the noncoordinating PF₆[−] counterion. A comparison of the ¹H NMR spectrum of [(L2)Pd]PF₆ (Figure 2c) with that of the PF₆ salt of the thread (Figure 2d) shows that the signals of the pyridinium station (H_{d–f}) appear at similar chemical shifts in the thread and rotaxane, while the triazole resonance (H_j) and adjacent protons (e.g., H_i) are shifted upfield in the rotaxane, which indicates that removal of the chloride ion from the palladium center is accompanied by translocation of the palladium–macrocycle component to



Scheme 1. Synthesis and operation of chloride-switchable molecular shuttle [(L2)Pd]⁺: a) CH₂Cl₂, 1 h; b) 3 (1.1 equiv), [Cu(CH₃CN)₄]PF₆ (0.2 equiv), TBTA (0.25 equiv), DIPEA (1 equiv), CH₂Cl₂/CH₃CN (7:1), 18 h, 64% (from 2-Cl); c) AgPF₆ (1.1 equiv), acetone, 18 h, quantitative; d) Bu₄NCl (1.5 equiv), CHCl₃, quantitative.

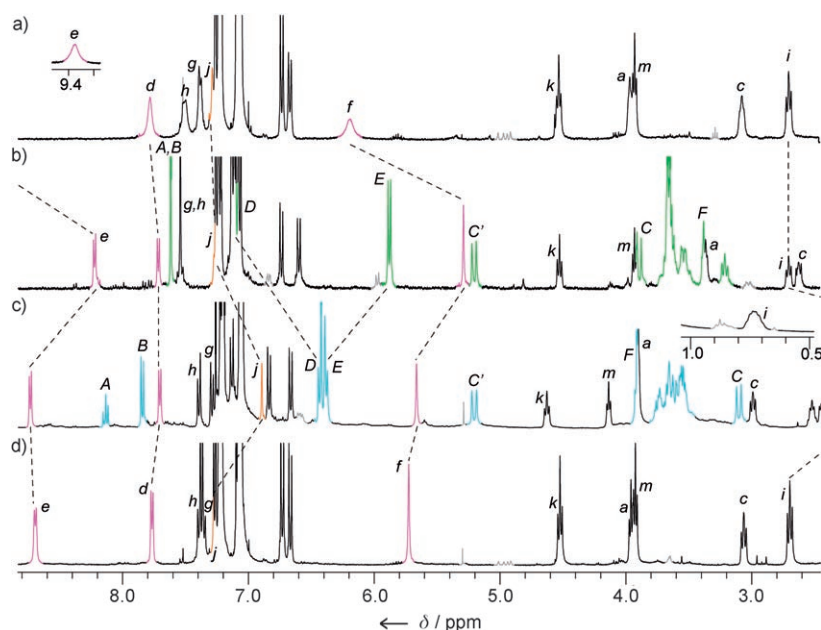


Figure 2. Partial ¹H NMR (400 MHz, CDCl₃, 298 K) spectra of a) chloride salt of the thread,^[13] b) *pyrdm*–[(L2)PdCl], c) *triazole*–[(L2)Pd]PF₆, and d) PF₆[−] salt of the thread. The assignments correspond to the lettering shown in Scheme 1. Signals shown in gray arise from impurities and residual solvents.

give triazole-[(L2)Pd]PF₆. Simple addition of tetrabutylammonium chloride to triazole-[(L2)Pd]PF₆ in chloroform (Scheme 1, step d) reverses this process to afford a product with identical physical and spectroscopic properties to the original rotaxane, pyrdm-[(L2)PdCl].

The chance discovery of a molecular recognition motif that is triggered by the formation of an anion–palladium coordination bond has been exploited as both an efficient rotaxane-forming template and as the basis for a chloride-switchable molecular shuttle. The use of wholly different and orthogonal binding modes in the two states of the shuttle leads to exceptional positional integrity of the ring in both forms. Anion-activated allosteric templates could lead to new developments in sensors, logic gates, transport agents, and molecular machines.

Experimental Section

Experimental procedure for the preparation of pyrdm-[(L2)PdCl]: 2-Cl (59 mg, 0.066 mmol) and [(L1)Pd(CH₃CN)] (50 mg, 0.073 mmol) were stirred for 1 h in CH₂Cl₂ (7 mL) prior to the addition of 3 (43 mg, 0.073 mmol) and DIPEA (11 µL, 0.066 mmol). A solution of TBTA (9 mg, 0.017 mmol) and [Cu(CH₃CN)₄]PF₆ (6 mg, 0.0147 mmol) in CH₃CN (1 mL) was added and the reaction mixture allowed to stir for a further 18 h. After this time the volatile compounds were removed under reduced pressure and the residue taken up in CH₂Cl₂ (10 mL). The resulting solution was washed with saturated NH₄Cl (3 × 10 mL) and the aqueous phase re-extracted with CH₂Cl₂ (3 × 5 mL). The combined organic extracts were concentrated under reduced pressure and subjected to flash chromatography on silica gel (0–3% MeOH in CH₂Cl₂ as eluent) to give pyrdm-[(L2)PdCl] as a bright yellow solid (89 mg, 64%). For compound characterization, full synthetic details for all precursors, and the switching experiments, see the Supporting Information.

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