Synthesis of a [2]rotaxane through first- and second-sphere coordination†

Barry A. Blight, James A. Wisner* and Michael C. Jennings

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In an effort to expand the application of a new template from interpenetrated to interlocked molecular species, we report the synthesis of a new [2]rotaxane by means of both first- and second-sphere coordination of a palladium(II) dichloride subunit.

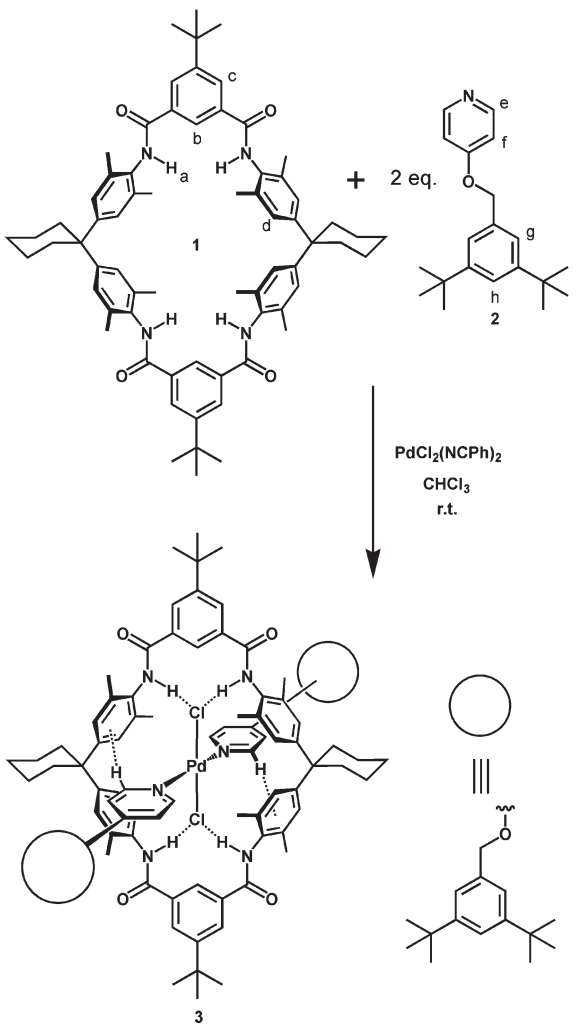
The synthesis of mechanically bonded molecules, such as rotaxanes and catenanes, has benefited enormously over the past two decades from the introduction of a template methodology.[1] In the specific case of rotaxanes, metal centres have been used either as part of the organizational template or as covalent attachment points within the organic skeletons that generally make up the majority of the interlocked superstructures.[2] Herein, we describe a rare example of [2]rotaxane formation where the metal centre fulfils both functions at the same time.

In a recent publication, we employed second-sphere coordination as a template in the formation of a series of [2]pseudorotaxanes, which were composed of a tetralactam "wheel"-shaped molecule interpenetrated by various sterically unencumbered *trans*-palladium(II) dihalide coordination complexes.[3] The main driving force for their interaction was second-sphere coordination of the halide ligands by the amide protons of the macrocycle *via* hydrogen bonding. Considering the facility of this template in our initial investigation, our attention has turned to its application in the synthesis of interlocked products.

The most straightforward manner in which to transform the aforementioned system from an interpenetrated arrangement to an interlocked one is likely to be the generation of palladium complexes that incorporate ligands with sterically demanding terminal groups. Such an arrangement maintains the original template in its entirety in the final structure. To this end, 4-(3,5-di-*tert*-butyl-benzyloxy)pyridine (**2**) was synthesized easily from readily available starting materials in 45% yield over two steps. The 3,5-di-*tert*-butyl-benzyl group thus acts as a "stopper" in the final product to prevent, in the absence of ligand exchange, dissociation of the assembled components.

The synthesis of the desired [2]rotaxane is an exceedingly simple procedure (Scheme 1). Two equivalents of tetralactam macrocycle **1**[4] were dissolved simultaneously with one equivalent of *trans*-bis-benzonitrilepalladium(II) dichloride[5] at room temperature in $CHCl_3$. Two equivalents of ligand **2** were then added and the reaction stirred for another 4 hours. The excess macrocycle was easily recovered by selective crystallization from $CHCl_3$ solution at low temperature, and the final product was obtained by precipitation from the remaining mother liquor with hexanes to give putative [2]rotaxane **3** in 89% yield. This product is completely stable in $CHCl_3$ solution over a period of three months and can be chromatographed, if necessary, on silica (EtOAc/$CHCl_3$) with no loss of integrity.

The ^{1}H NMR spectrum of the material in $CDCl_3$ thus obtained is supportive of the interlocked nature of the complex (Figure 1), in



Scheme 1 Synthesis and structure of [2]rotaxane **3**, depicting the interlocked geometry templated by second-sphere coordination of the metal halides.

Department of Chemistry, The University of Western Ontario, Chemistry Building, 1151 Richmond Street, London, ON, Canada N6A 5B7. E-mail: jwisner@uwo.ca; Fax: +1 519 661 3022
† Electronic supplementary information (ESI) available: Synthetic protocols and spectral details for compounds **2**, **3** and **4**. See DOI: 10.1039/b610243c

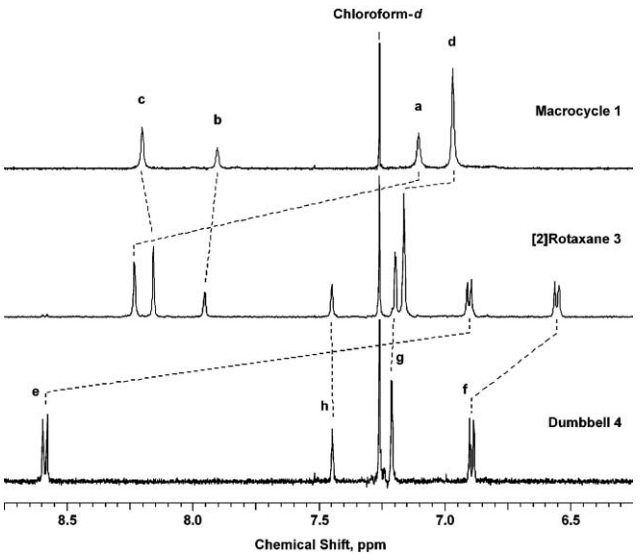


Fig. 1 The aromatic region of the ^{1}H NMR spectra (400 MHz, 298 K) of free macrocycle **1** (top), [2]rotaxane **3** (middle) and free dumbbell **4** (bottom). Illustrated are the observed perturbations in chemical shift between free and interlocked components (dashed lines). NOESY experiments were performed to allow individual ^{1}H NMR assignments.

comparison to the isolated components **1** and pre-formed "dumbbell" *trans*-bis-(4-(3,5-di-*tert*-butyl-benzyloxy)pyridine)palladium(II) dichloride (**4**). Hence, the macrocyclic amide protons H_a shift downfield to δ 8.23 ($\Delta\delta$ = 1.10) as a result of hydrogen bonding to the chloride ligands. The *ortho*-protons of the pyridine rings H_e are involved in CH–π interactions with the aryl side walls of the macrocycle, shifting them upfield to δ 6.90 ($\Delta\delta = -1.69$). These shifts are of the same quality as those observed upon pseudorotaxane formation, but exaggerated in this context due to the interlocked nature of the constituents. Notably, an admixture of **1** and **4** together in $CHCl_3$ does not produce any change in their spectra, effectively ruling out a non-interlocked complex geometry for **3**. Analysis by CSI-MS displays a peak at *m*/*z* 895.5 ($[M + 2\ H]^{2+}$) that does not appear in simple solutions of **1** and **4** under the same conditions, further supporting the presence of **3** in solution.

Confirmation of the interlocked geometry was obtained from the solid state structure by single crystal X-ray diffraction.[6] Pale yellow crystals suitable for analysis were grown by slow diffusion of di-*iso*-propyl ether into a concentrated $CHCl_3$ solution of **3**. The [2]rotaxane crystallized in the space group *P*(-1) to yield the expected interlocked structure (Figure 2). The structure differs from the previously reported [2]pseudorotaxanes in that the central $PdCl_2$ axis is displaced entirely to one face of the macrocyclic cavity in a nested arrangement. This disposition results in only one of the pyridyl rings of the two neutral ligands being included in the cavity itself. In order to accommodate this geometry and still engage in hydrogen bonding with the chloride ligands, the amide groups of the isophthalamide subunits in the macrocyclic component all deviate in the same direction from coplanarity with their associated aryl rings by 19–32°. The four amides engage in hydrogen bonds to the chloride ligands of the metal complex (Figure 3: N–Cl = 3.49 (A), 3.66 (B), 3.45 (C) and 3.36 Å (D), and N–H–Cl = 162 (A), 153 (B), 152 (C) and 155° (D)), as anticipated

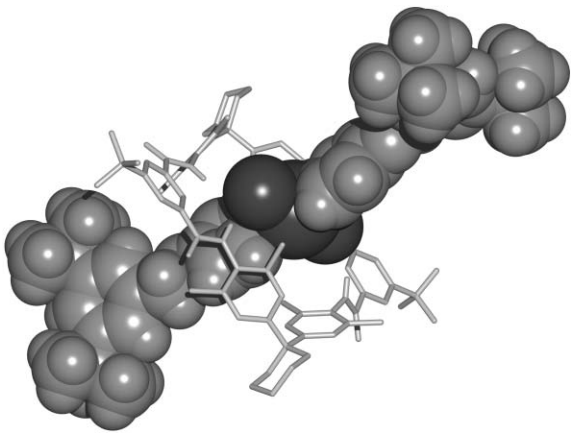


Fig. 2 Space-filling/stick representation of the solid-state structure of [2]rotaxane **3**, illustrating the interlocked geometry of the components (light grey sticks, macrocycle; medium grey space-filling, pyridyl ligands; dark grey space-filling, $PdCl_2$ subunit).

in the original template design. Unfortunately, there is no evidence in the solid state of the CH–π interactions, whose effects are observed in the NMR spectrum, though it is likely the weak nature of these forces has been overwhelmed by crystal packing effects in this case.

In summary, we have self-assembled a new [2]rotaxane through a combination of first- and second-sphere coordination. Based on the characterization of **3**, we have also demonstrated that this template displays an analogous mode of complexation when compared to the subsequent [2]pseudorotaxane. From this, we can conclude that second-sphere coordination is a viable route for the production of these types of interlocked molecular species. We are currently investigating the further development of this template for the formation of catenanes, and molecular devices such as shuttles or switches.

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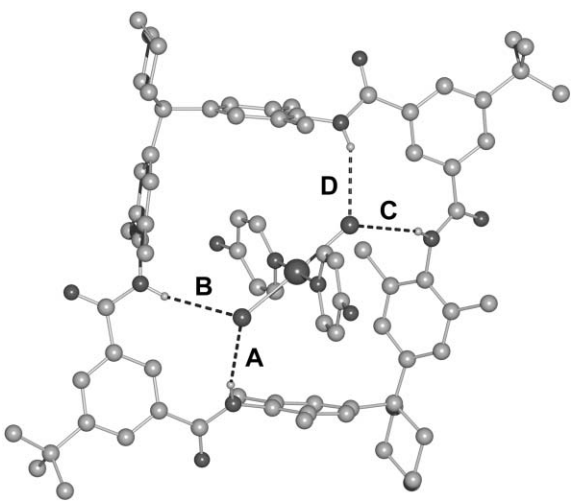

Fig. 3 Ball-and-stick representation of the interior of the macrocyclic cavity of **3** in the solid state. All of the C–H hydrogen atoms have been removed for clarity. NH···Cl hydrogen bonds are indicated by dashed lines.

Notes and references

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6 Crystal structure data for [2]rotaxane **3**: $C_{108}H_{134}Cl_2N_6O_6Pd$, M = 1789.58, triclinic, space group $P(-1)$, a = 17.2816(4), b = 20.3272(8), c = 20.7318(94) Å, α = 107.11(0), β = 100.24(0), γ = 113.61(0)°, V = 6003.15(9) Å^3, Z = 2, ρ_{calc} = 1.2351 g cm^{-3}, $2\theta_{max}$ = 50.06°, Mo-Kα radiation (λ = 0.71073 Å), T = 123 K, Z = 2. Pale yellow crystal of dimensions 0.48 × 0.20 × 0.08 mm. 39451 total reflections, 20806 unique reflections (R_{int} = 0.051), R_1 = 0.0674, wR_2 = 0.1981[$I > 2\sigma(I)$], R_1 = 0.1049, wR_2 = 0.1981, GOF(F^2) = 1.027, N_o/N_v = 20806/1306 with $I > 2\sigma(I)$. Data obtained from a programmed hemisphere scan routine on a Nonius Kappa-CCD diffractometer. Lorentz and polarization correction, followed by a multiscan (HKL SCALEPACK: Z. Otwinowski and W. Minor, *Methods Enzymol.*, 1997, **276**, 307–326) absorption correction, were applied to the data (μ = 0.389 mm^{-1}, min./max. transmission = 0.8354/0.9714). The structure was solved by Patterson methods, followed by difference Fourier syntheses, to find the remaining atoms. Refinement was by full-matrix least-squares methods using SHELXTL-NT 6.1 (G. M. Sheldrick, *SHELXTL-NT 6.1*, Madison, WI, 2000). CCDC 611645. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b610243c.