## Two-component control of guest binding in a self-assembled cage molecule<sup>†</sup>

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A self-assembled  $M_2L_4$  palladium-pyridyl cluster with a "paddle-wheel" structure shows binding affinity in competitive organic solvents for neutral organic guests that possess both the correct size and electrostatic complementarity.

Metal-ligand interactions have been used to create a number of self-assembled host molecules.<sup>1</sup> For example, one of the most common structural linkages uses pyridine-Pd<sup>II</sup> contacts, taking advantage of the square-planar geometry of the coordinatively saturated metal center.<sup>2</sup> These systems can form host : guest inclusion complexes that have been exploited for a variety of purposes. Examples include controlling reaction rates,<sup>3</sup> isolating reactive intermediates<sup>4</sup> and unstable species,<sup>5</sup> or altering reaction pathways.<sup>6</sup> The guest binding is most often controlled by interactions between guest and the aromatic ligands used to form the cluster walls. Water-soluble clusters have been shown to be highly effective hosts for aromatic hydrocarbon species due to the hydrophobic effect,<sup>7</sup> whereas negatively charged clusters with electron rich walls often favor the binding of organic cations.<sup>8</sup> The binding of desired guests in organic solvents is rarer, as the solvent often outcompetes the binding of other added species. Above all, fully enclosed clusters are shape-selective, and only bind species that fit in the cavity. The metals used to form the clusters are coordinatively saturated, and generally seen as structural vertices, not used to aid guest binding. Here we report a paddle-wheel shaped metal-ligand cluster that uses weak electrostatic interactions between metal and guest as well as steric effects to control binding selectivity.

The ligand **3** was synthesized *via* Sonogashira coupling of 1,3-diethynylbenzene and 3-bromopyridine.<sup>9</sup> Upon addition of Pd(NO<sub>3</sub>)<sub>2</sub> to a solution of ligand **3** in DMSO- $d_6$ , <sup>1</sup>H NMR analysis showed the formation of a new complex **4** (see Fig. 1and 4c). This complex is kinetically stable, and symmetric; the integrals for each of the protons on the ligand remain unchanged, and each peak remains sharp, indicating the formation of only one complex. Cluster formation was only observed with a weakly ligated palladium source. Three counterions proved suitable for the synthesis of the complex; nitrate, triflate and tetraphenylborate. Palladium chloride was

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Fig. 1 Synthesis of  $M_2L_4$  "paddle-wheel" cluster 4; its minimized structure indicating the resultant cavity (SPARTAN; AM1 forcefield) and a minimized structure of the 4-terephthalonitrile complex.

unreactive, and treatment with  $Pd(OAc)_2$  gave an intractable solid. The solubility properties of the complex were highly dependent on counterion— $4 \cdot (NO_3)_4$  was only soluble in DMSO, although mixtures of DMSO and small amounts of water, acetone and chloroform were tolerated. Complexes  $4 \cdot (BPh_4)_4$  and  $4 \cdot (OTf)_4$  also showed some solubility in acetone, methanol and acetonitrile.

X-Ray quality crystals of  $4 \cdot (OTf)_4$  were obtained from slow evaporation from acetonitrile solution, and show that the cluster forms a symmetrical "paddle-wheel" structure (Fig. 2).<sup>10,11</sup> The structure shows the presence of one disordered triflate group in the interior cavity of the cluster. There is a



**Fig. 2** ORTEP representation of the X-ray diffraction structure of cluster **4**. One disordered triflate molecule is present in the cavity, and has been removed for clarity.

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significant amount of open space in the unit cell between clusters, with the interstitial space between cluster subunits filled with disordered acetonitrile solvent and triflate ions (see ESI<sup>†</sup>).

Electrospray mass spectrometric analysis was also possible if performed under gentle ionization source conditions (see ESI†). Analysis of 4 (NO<sub>3</sub>)<sub>4</sub> showed the presence of two species,  $[M + 2NO_3]^{2+}$  and  $[M + 3NO_3]^+$ , where  $M = Pd_2L_4$ . The triflate salt 4 (OTf)<sub>4</sub> proved far more stable, and an ESI-MS spectrum (Fig. 3) could be obtained of the cluster alone, with the loss of one triflate ion (*i.e.*  $[4 (OTf)_3]^+$ ). Both of these peaks displayed the correct isotope pattern for the cluster containing two Pd atoms. Interestingly, even though the *m*-pyridine group can freely rotate and could be expected to adopt a number of orientations, formation of polymers or other oligomers has not been observed,<sup>12</sup> indicating the favorability of the paddle-wheel structure. Most selfassembled metal-ligand clusters are designed so that the ligand has as few degrees of freedom as possible to prevent the formation of different aggregates.<sup>1c</sup> This is not necessary here, as the self-assembly process forms only one species.

The cluster is stable in air at room temperature in both the solid state and DMSO solution for months, and no special handling precautions are necessary. It is stable at elevated temperatures for hours, although prolonged heating over 70 °C caused decomposition. Exchange NMR spectroscopy<sup>13</sup> of a 1 : 1 mixture of cluster **4** and ligand **3** in DMSO- $d_6$  (see ESI †) showed no evidence of ligand exchange on the NMR timescale, so it is reasonable to suggest that the cluster stays intact for a period of at least minutes at room temperature.<sup>14</sup>

The presence of highly disordered anion in the cavity interior led us to study the solution-phase host : guest properties of the cluster. The cluster has a cavity approximately 6 Å wide and 10 Å deep, suggesting that molecules such as *p*-xylene would fit in the cavity. Unfortunately, the cluster displayed no affinity towards suitably sized hydrocarbons such as naphthalene, *p*-xylene or toluene. On the other hand, addition of 1,4dicyanobenzene caused an upfield shift in the NMR spectrum of the nitrate salt of host. Guest exchange was rapid on the NMR timescale (the cluster retains an averaged  $D_{4h}$  symmetry by NMR), and only changes in host chemical shift could be observed. Benesi–Hildebrand analysis<sup>15</sup> gave a binding affinity of 11.1 M<sup>-1</sup>. The most shifted peak (colored red in Fig. 4d–f) was assigned to the proton H<sub>1</sub>, pointing into the center of the



**Fig. 3** ESI-MS spectrum of  $4 \cdot (OTf)_4$ . (a) observed and (b) calculated isotope pattern for  $[4 \cdot (OTf)_3]^+$ .



**Fig. 4** Downfield regions of <sup>1</sup>H NMR spectra (400 MHz, DMSO- $d_6$ , 298 K) of (a) ligand **3**; (b) Pt cluster **5**; (c) Pd cluster **4**; (d) 1.7 mM cluster **4** + 1.7 mM terephthalonitrile, (e) 1.7 mM cluster **4** + 14 mM terephthalonitrile, and (f) 1.7 mM cluster **4** + 28 mM terephthalonitrile.

cavity. The protons on the periphery of the cluster were only slightly affected.

To explore this behavior further, we exposed the cluster to a series of neutral guests; the results are displayed in Table 1. A "two-component" pattern in guest binding was observed. Only species of the correct size and shape displayed binding, and then only if there was a suitable lone-pair containing donor group present. Two donor groups are not necessary for binding, as 4-tolunitrile and benzonitrile showed similar binding affinities to terephthalonitrile. 1,4-Difluorobenzene also showed binding, indicating that a nitrile is not the only coordinating group tolerated. Interestingly, dichlorobenzene showed no binding affinity, although 4-chlorobenzonitrile did. Strong ligands such as pyridine, N,N-dimethylaminopyridine, aniline or aliphatic amines destroyed the cluster, forming an unidentified insoluble Pd complex and leaving free ligand to be observed in the <sup>1</sup>H NMR spectrum. The cluster was tolerant to excess nitrile. Addition of a 50-fold excess of the nitriles in Table 1 did not show appreciable dissociation of cluster, and  $4 (OTf)_4$ 

**Table 1** Binding affinities for guests in cluster  $4 \cdot (NO_3)_4^a$ 

Guest	$K_{\rm a}/{ m M}^{-1}$	
Terephthalonitrile	11.1	
4-Chlorobenzonitrile	12.4	
Benzonitrile	10.2	
4-Tolunitrile	9.9	
1,4-Difluorobenzene	7.8	
1,4-Dichlorobenzene	0	
<i>p</i> -Xylene	0	
1,4-Dicyanobutane	0	
1,6-Dicyanohexane	0	
Acetonitrile	0	
<sup><i>a</i></sup> 298 K, [4] = 2 mM, DMSO- $d_6$ .		

was suitably tolerant to acetonitrile solvent to allow crystal growth.

The presence of an electron pair donor group was not all that was required for binding. Small nitriles such as acetonitrile gave no binding (even in the solid state), nor did flexible dinitriles such as 1,4-dicyanobutane or 1,6-dicyanohexane. These species are too long to fit in the pocket without unfavorable alkyl chain compression.<sup>16</sup> Molecular modeling of the 4-NC–C<sub>6</sub>H<sub>4</sub>–CN complex shows that the guest causes slight deformation of the cluster to allow binding. This is consistent with the observation that species with extra "width" such as 1,2,4,5-tetracyanobenzene and 1,8-dicyanoanthracene show no binding affinity, even though they are of the correct "height".

The binding affinity of neutral guests is moderate, mainly due to the competitive interaction between host and the solvent and counterion. Both  $4 \cdot (NO_3)_4$  and  $4 \cdot (OTf)_4$  have limited solubility in solvents other than DMSO, which can also occupy the host cavity and is present in far greater concentration than the guests in Table 1. Nitrate cluster  $4 \cdot (NO_3)_4$  was the most effective host. The use of host  $4 \cdot (OTf)_4$ lowered the binding affinities further, presumably due to additional competition from the counterion, as seen in the solid-state structure. The smaller nitrate ion can only partially fill the cavity, allowing other species to bind more effectively.

In order to study the effect of guest : metal interaction further, we studied the other group 8 metals as cluster termini. No discrete cluster formation was observed upon treatment with Ni(II) salts, however Pt cluster 5 (Fig. 4b) was successfully synthesized (by treatment of 3 with  $PtCl_2/AgNO_3$  in DMSO- $d_6$ followed by filtration) and exposed to the guests in Table 1. This cluster has the same properties (although slightly smaller changes in chemical shift upon addition of metal salt to ligand 3) as Pd cluster 4. Pt<sup>II</sup>, however, is less Lewis acidic than Pd<sup>II</sup>, and so the affinity of 5 for donor guests would be expected to be much smaller than that of 4. Indeed, addition of both terephthalonitrile and difluorobenzene showed no change in the <sup>1</sup>H NMR spectra with over 100-fold excess of guest (no decomposition was observed). This lowered affinity for Lewis donor guests removes one component of the "two-component" recognition, and so no host : guest behavior is observed. This behavior is unusual; most host : guest binding in metal-ligand systems comes from size and shape complementarity of the hydrophobic effect. Structures such as covalently linked metal-bisporphyrins<sup>17</sup> can complex strong ligands such as pyridines or DABCO, but binding weak donors such as organofluorides is unprecedented, especially in competitive solvents such as DMSO.

In summary, we have created a new self-assembled  $M_2L_4$  palladium–pyridyl cluster with a "paddle-wheel" motif, and showed its affinity for guests with both the correct size and electronic complementarity. Further studies of these systems are underway in our laboratory.

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- 11 Crystal data:  $[C_{80}H_{48}N_8Pd_2]^{4+}[CF_3SO_3]^{4-}$  (4·(OTf)<sub>4</sub>), CCDC 768969, M = 2399.95, monoclinic, space group Cm (no. 8), a = 27.6097(22) Å, b = 15.0085(12)Å, c = 14.2322(11) Å,  $\beta = 107.6573(11)^\circ$ , V = 5619.7(8) Å<sup>3</sup>, Z = 2, calculated density  $D_c = 1.418$  g cm<sup>-3</sup>, colorless prism fragment (0.40 × 0.38 × 0.35 mm) coated with paratone oil, T = 100(2) K, 44 210 reflections measured (0.71 Å resolution), 16961 unique ( $R_{int} = 0.0236$ , completeness = 99.7%), final  $R_1 = 0.0326$ ,  $wR_2 = 0.0877$  with intensity  $I > 2\sigma$  (I).
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