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Inflating face-capped Pd<sub>6</sub>L<sub>8</sub> coordination cages<sup>†</sup>

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Tritopic metalloligands were used to form two  $Pd_6L_8$ -type coordination cages. With molecular weights of more than 15 kDa and  $Pd \cdots Pd$  distances of up to 4.2 nm, these complexes are among the largest palladium cages described to date.

Geometrical considerations are of central importance in synthetic metallosupramolecular chemistry.<sup>1</sup> Metal complexes are characterized by the number and the orientation of the available coordination sites, and ligands are categorized by the orientation of the coordinate vectors. Knowing these parameters, it is possible to make a prediction of what kind of structure will form during the self-assembly process. Besides geometry, there are other factors such as template effects<sup>2</sup> or steric interactions,<sup>3</sup> which can influence the self-assembly process. However, geometrical analyses have been remarkably successful in predicting and rationalizing the outcome of metal-based self-assembly.

The absolute size of a ligand is irrelevant for a geometrical analysis. In principle, it should be possible to expand the size of a metallosupramolecular structure by increasing the size of the ligands, while keeping the number and orientation of the coordinate vectors constant. However, there is an obstacle. Larger ligands are typically more flexible, which makes the orientation of the coordinate vectors less defined. This flexibility could allow the formation of other assemblies along with – or instead of – the targeted structure.

It should be noted that for some metal–ligand assemblies, ligand flexibility is more of an issue than for others. For example, it is possible to form  $Pd_nL_{2n}$ -type coordination cages by combination of  $Pd^{2+}$  ions with ditopic N-donor ligands. There are reports on very large structures with n = 12, 24, or  $30,^4$  but the assembly process is very sensitive to the relative orientation of the coordinate vectors of the two N-donors.<sup>5</sup>

The combination of Pd<sup>2+</sup> ions with divergent,<sup>6</sup> tritopic N-donor ligands is expected to give assemblies of the general

formula  $Pd_{3n}L_{4n}$ . The assembly with the lowest number of building blocks,  $Pd_3L_4$ , can only form if some of the ligands act as chelates (two of the three N-donors bind to the same  $Pd^{2+}$ ion).<sup>7</sup> If the N-donor position does not allow the formation of a chelate, the resulting assembly will contain at least six  $Pd^{2+}$  ions and eight ligands.<sup>8</sup> Since it is straightforward to design tritopic ligands which cannot form chelates,  $Pd_{3n}L_{4n}$  complexes appear to be a good starting point if the aim is to create particularly large assemblies based on ligands with nanoscale dimensions.

For this study, we have used the tritopic ligands L1 and L2 (Scheme 1). These metalloligands<sup>9</sup> contain three diamagnetic  $Fe^{II}$  clathrochelate complexes. We have previously shown that  $Fe^{II}$  clathrochelates are robust and versatile building blocks for supramolecular chemistry.<sup>3*a*,10</sup> A key advantage of these complexes is the ease of synthesis, because clathrochelates are formed in metal-templated multicomponent reactions.<sup>11</sup> This advantage is particularly evident for L1 and L2, which were prepared by one-pot reactions using readily accessible or commercially available starting materials. Specifically, the synthesis



Scheme 1 One-pot synthesis of the metalloligands L1 and L2. The yields are calculated based on the triboronic acid as limiting reagent.

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was performed by heating a mixture of  $\text{FeCl}_2$  (4 eq.), nioxime (12 eq.), 3-pyridylboronic acid (5 eq.) and a triboronic acid (1 eq.) in a solvent mixture of chloroform, methanol, and acetone (30:7:1) (Scheme 1). Substoichiometric amounts of the triboronic acid were used to limit the formation of oligomers. As a consequence, a mono clathrochelate complex with two pyridylboronate ester caps was the major product for this reaction. Since this complex is much smaller than L1 and L2, it can be separated by size exclusion chromatography. The yields of the desired tritopic ligands are 57% (L1) and 49% (L2), respectively, when calculated based on the triboronic acid as limiting reagent.

L1 and L2 were characterized by NMR spectroscopy and high-resolution mass spectrometry (for details, see the ESI†). In addition, both compounds were analysed by single crystal X-ray diffraction. The results show that the N-donor atoms of L1 are approximately 2.2 nm apart (Fig. 1). The presence of the additional phenyl spacers increases this value to 2.9 nm for ligand L2.

The coordination cages **1** and **2** were prepared by combining ligand **L1** or **L2** (4 eq.) with  $[Pd(CH_3CN)_4](BF_4)_2$  (3 eq.) in DMSO- $d_6$  (Scheme 2). Since the ligands are poorly soluble in DMSO- $d_6$ , suspensions were initially obtained, which turned into clear orange solutions after heating at 70 °C overnight. The <sup>1</sup>H NMR spectra of the solutions showed broad and not very well defined peaks, which is not unusual for large cage complexes in a



**Fig. 1** Molecular structures of the ligands **L1** (top) and **L2** (bottom) as determined by single crystal X-ray diffraction. Hydrogen atoms and solvent molecules are omitted for clarity. Grey: C; blue: N; green: B; red: O; and orange: Fe.



viscous solvent.<sup>4a,5b,8b,12</sup> Processing the data of the <sup>1</sup>H DOSY NMR also posed some problems related to the broad and overlapping peaks. Nonetheless, the DOSY spectra did confirm the formation of complexes with a uniform diffusion coefficient.

For both reactions, clear evidence for the formation of  $Pd_6L_{8^-}$  type complexes was obtained by mass spectrometry. The MS analyses were performed on a hybrid LTQ Orbitrap FTMS instrument operated in the positive ionization mode. The HESI-II probe in an Ion Max ion source was modified in order to perform cold-spray ionization (CSI), a variant of electrospray ionization operated at low temperature.<sup>13</sup> CSI-MS can be used to prevent decomposition of labile supramolecular structures and was shown to be crucial for such measurements. Using this methodology, the major peaks observed in the 1200–2600 *m*/*z* mass range were attributed to  $[Pd_6L_8]^{12+}$  complexes with a variable number of  $BF_4^-$  anions (Fig. 2 and ESI,† Fig. S16).

Cage 1 was characterized by single crystal X-ray diffraction, and graphic representations of the cationic  $[Pd_6(L1)_8]^{12+}$  complex are depicted in Fig. 3 and 4. The location of most anions and solvent molecules is ill defined in the electron density map, and the solvent-masking program in OLEX2 was applied to treat this disorder.<sup>14</sup>

The six Pd ions are positioned at the vertices of an octahedron, and the ligands panel the eight faces. The maximum  $Pd \cdots Pd$  distance is 3.3 nm. This value is larger than what is



Fig. 2 CSI-HRMS of cage 2 in 10% DMSO-d<sub>6</sub> in CH<sub>3</sub>CN.



Fig. 3 Molecular structure of cage **1** as determined by single crystal X-ray diffraction. Hydrogen atoms,  $BF_4^-$  anions, and solvent molecules are omitted for clarity. Grey: C; blue: N; green: B; red: O; cyan: Pd and orange: Fe.

found for other  $M_6L_n$  cages (M = Pd, Pt) reported in the Cambridge Crystallographic Data Center (CCDC) (for a more detailed analysis, see the ESI†). The cage features only small openings, because the bulky side chains of the clathrochelate complexes are in close proximity to each other (Fig. 4, left side). The size of the cavity is estimated to be around  $2.8 \times 10^3 \text{ Å}^3$ , as determined by the use of the VOIDOO software.

Single crystals for the larger cage **2** were also obtained. Unfortunately, we were not able to obtain diffraction data of good quality, despite testing different crystals and various experimental set-ups (including synchrotron radiation). On two occasions, it was possible to determine the size of the unit cell (~193 000 Å<sup>3</sup>, see ESI<sup>†</sup>), but we were not able to solve the structure.

In order to estimate the size of cage 2, we have constructed a molecular model using the Spartan software. The results show that the maximum  $Pd \cdots Pd$  distance for this cage is around 4.2 nm. As expected, the cage shows much larger openings compared to what was found for 1 (Fig. 4).

To conclude, we have investigated if it is possible to inflate coordination cages by increasing the size of the ligand. On purpose, we have chosen  $Pd_6L_8$ -type cages for our study. Due to geometric constraints, these complexes are not likely to undergo a structural reorganization into smaller aggregates. We have



**Fig. 4** Space fill representation of cage **1** (left), as determined by X-ray diffraction, and of cage **2** (right), as obtained by molecular modelling. Solvent molecules are omitted for clarity. Grey: C; blue: N; green: B; red: O; cyan: Pd; orange: Fe and white: H.

synthesized two large, tritopic N-donor ligands by using clathrochelate complexes as key structural elements. Upon combination with Pd<sup>2+</sup> ions, we were indeed able to form Pd<sub>6</sub>L<sub>8</sub>-type coordination cages. One cage was characterized by single crystal X-ray diffraction. With a maximum Pd···Pd distance of 3.3 nm, this complex represents the largest  $M_6L_n$  cage (M = Pd, Pt) in the CCDC database. The second cage is even larger ( $Pd \cdots Pd_{max} \sim 4.2 \text{ nm}$ ), but unfortunately we were not able to obtain diffraction data of sufficient quality to solve the structure (despite using synchrotron radiation). This failure is indicative of one key challenge when working with metallosupramolecular structures of this size: the structural characterization becomes exceedingly difficult. For the present study, we have focused on structural aspects, but it is clear that very large cages offer interesting opportunities in terms of function (e.g. encapsulation of large guests). Investigations in this direction are ongoing in our laboratory.

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## Conflicts of interest

There are no conflicts to declare.

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