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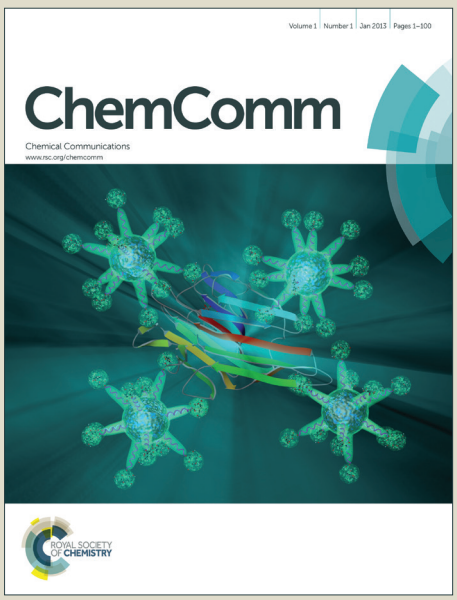

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ARTICLE TYPE

Stepwise synthesis of a Ru_4Cd_4 coordination cage using inert and labile subcomponents: introduction of redox activity at specific sites

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The kinetically inert mononuclear complex $[RuL_3](PF_6)_2$ (1:3 mixture of *fac* and *mer* isomers), with three pendant binding sites, reacts with labile Cd(II) ions to complete the assembly of a Ru_4Cd_4 cubic coordination cage in which reversible redox behaviour has been introduced at the Ru(II) sites.

The preparation and host-guest chemistry of coordination cages remains a particularly active field in modern supramolecular chemistry,[1,2] due a combination of elegant syntheses of new structures by self-assembly methods, as well as the useful functional behaviour – ranging from drug delivery[3] to catalysis[4] – that can arise from guest inclusion.

Despite recent progress in this field, most cage complexes are based on just two types of component, *i.e.* one type of metal ion and one type of bridging ligand. This limits the structural and functional and complexity that may be achievable. Given that the metal ions which form the basis of cage assemblies provide both structural information (*via* their preferences for specific coordination geometries) *and* possible functionality properties such as redox activity, magnetism, colour or luminescence),[5] efforts directed at assembling heterometallic cages – with control of which metal ions occupy which sites – are surprisingly limited.

So far, mixed-metal cages and related assemblies have been prepared by one of two strategies. The first involves use of unsymmetrical ligands possessing both hard and soft binding sites which will selectively bind to hard and soft metals, respectively.[6] The second involves the use of metal ions with different coordination preferences, such as a combination of octahedral and square-planar metal ions whose requirements can each be satisfied at different positions in the cage[7]. Both approaches allow the rational design of heterometallic structures with different metal ions at specific sites. However, these methods cannot be applied to cages (or other polynuclear assemblies) in which all metal ions have the same coordination environment, as the necessary differentiation between sites does not exist. Given the extensive family of homoleptic coordination cages that we have studied in recent years,[1c] with all metal ions in an octahedral tris-chelate coordination environment, we were interested to see if we could develop a route to formation of heterometallic analogues with control over which metal ion occupies which site.

Our strategy involves a combination of kinetically inert $[Ru^{2+}]$ and kinetically labile $[Cd^{2+}]$ metal centres. This allows inert Ru^{2+} complexes, which are pre-formed vertices of the cage, to be prepared first. These are then combined with labile Cd^{2+} ions to complete the assembly process, and the inertness of Ru(II) prevents any scrambling of metal ions between different sites. The use of a combination of 'inert + labile' components to control assembly of heteronuclear complexes with similar coordination sites is known in other contexts,[8] but application of this method to assembly of large cages remains undeveloped.

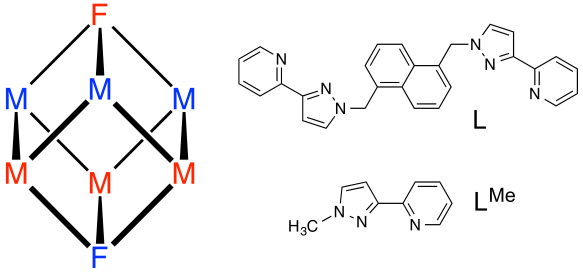

Fig. 1. Left: Schematic diagram of the cubic cage, showing the positions of the two *fac* (F) and six *mer* (M) metal centres. In the homonuclear cages all metal ions are the same; in the heteronuclear cage $[Ru_4Cd_4L_{12}]^{16+}$ the two types of metal ion are split over the red and blue sites, with each ion type occupying one *fac* and three *mer* centres. Right: the ligand L which connects two metal ions along each edge of the cage, and L^{Me}.

The cage we have used is a $[M_8L_{12}]X_{16}$ octanuclear 'cube' [M = Co, Cd; X = a mono-anion such as BF_4^-, ClO_4^- or BPh_4^-; L is the bis(pyrazolyl-pyridine) bridging ligand; Fig. 1]. We have reported several examples of such cages; all are based on a metal ion at each vertex of an approximate cube with the bridging ligand L spanning each of the twelve edges, giving each metal ion a tris(pyrazolyl-pyridine) coordination environment.[9] Importantly, the assembly requires that two of the metal ions (at either end of the long diagonal) have a *fac* tris-chelate geometry with the three pyridyl donors on one face of the octahedron and the three pyrazolyl donors on the other; whereas the other six metal ions have a *mer* tris-chelate geometry. With an inversion centre in the cage, this results in molecular S_6 symmetry with the C_3/S_6 axis through the two *fac* tris-chelate metal centres (Fig. 1).

The heterometallic analogue that we report here is $[Ru_4Cd_4L_{12}](ClO_4)_{16}$ in which the Ru(II) and Cd(II) centres alternate. Each type of metal ion occupies strictly one *fac* and three *mer* tris-chelate sites in the cage superstructure. The *fac* / *mer* geometric isomerism could add another layer of complexity to the problem of controlled preparation of a heterometallic cage, but in this particular case, it works to our advantage.

Our choice of 'inert' metal centre was Ru^{2+}, given its tractable synthetic chemistry: modestly high temperatures suffice for

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preparation of *N,N'*-donor tris-chelate complexes but the complexes are generally inert at room temperature. In addition incorporation of Ru^{2+} centres allows inclusion of a type of functional behaviour (redox activity) that is not normally associated with such cages. If we start with an inert $[RuL_3]^{2+}$ unit as a pre-formed vertex, with three pendant sites at which cage assembly can be propagated by binding to labile Cd^{2+} ions, it follows that it will not be possible to have two Ru^{2+} ions adjacent to one another along one edge of the cube. The same is clearly true for the Cd^{2+} ions given that all available free binding sites are at one end of a bridging ligand whose other terminus is occupied by a Ru^{2+} ion. The result must be strict alternation of the metal sites around the cube: this can be achieved in two ways which, due to the S_6 symmetry of the cube, are degenerate (Fig. 1). Consequently, a 3:1 mixture of *mer*:*fac* $[RuL_3]^{2+}$ isomers would provide four pre-formed corners of the cube as the correct isomers, as well as all twelve ligands necessary to complete the assembly. Addition of four equivalents of a labile metal ion that forms octahedral tris-chelate complexes will complete the cube assembly with each type of ion in predictable positions (Fig. 2).

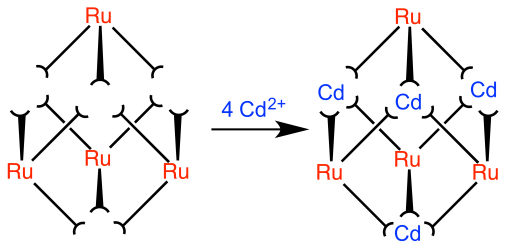

Fig. 2. Schematic diagram of the reaction between four pre-formed $[RuL_3]^{2+}$ complex units (each with three pendant binding sites) and four Cd^{2+} ions to complete assembly of the $[Ru_4Cd_4L_{12}]^{16+}$ cage. Arrangement of *fac* and *mer* centres is as shown in Fig. 1.

$[RuL_3](PF_6)_2$ was prepared by reaction of $RuCl_2(dmso)_4$ with > 3 equiv. L in refluxing ethylene glycol.† Given the non-symmetrical nature of the pyrazolyl-pyridine chelates, of course this forms as a mixture of *fac* and *mer* isomers. If there is no specific factor resulting in preference for one isomer over the other, a *fac*:*mer* ratio of 1:3 is expected. The ^{1}H NMR spectrum of $[RuL_3](PF_6)_2$ is consistent with this, showing four independent ligand environments in equal abundance.†,‡ In the $[RuL_3]^{2+}$ complex cation, each ligand uses only one of its two chelating sites so there are three pendant pyrazolyl-pyridine binding sites.

Conveniently for our purposes, this 1:3 *fac*:*mer* ratio of $[RuL_3](PF_6)_2$ isomers is precisely what is required in the cage if every alternate site is occupied by a Ru(II) centre. This is not generally true of other members of the cage family, which contains examples in which the metal tris-chelate centres are all *fac* and other examples in which the metal centres are all *mer*.[1d] Thus, no separation of isomers of $[RuL_3](PF_6)_2$ is needed: the as-prepared mixture can be used as it stands to provide the necessary cage subcomponents in the correct proportions.

The second step was to complete the assembly of the $[Ru_4Cd_4L_{12}]^{16+}$ cage by combining $[RuL_3](PF_6)_2$ with labile Cd^{2+} ions in a 1:1 ratio, *i.e.* four of each type of unit as the cage requires (Fig. 2). The twelve pendant bidentate binding sites from four $[RuL_3]^{2+}$ cations are exactly sufficient to combine with four Cd^{2+} ions (4 $[RuL_3]^{2+}$ + 4 Cd^{2+} = $[Ru_4Cd_4L_{12}]^{16+}$), and the only way in which cage assembly can be completed is if the Cd^{2+} and Ru^{2+} centres are strictly alternating, as shown in Fig. 2.

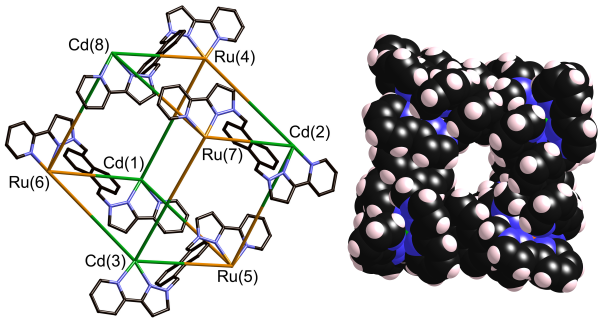

Fig. 3. Two views of the cage complex cation in the structure of $[Ru_4Cd_4L_{12}][ClO_4]_{16}$. Left: a view emphasizing the approximately cubic array of metal ions with four of the bridging ligands includes; right, a space-filling view of the complete cage.

Reaction of $[RuL_3](PF_6)_2$ (mix of isomers) with excess of $Cd(ClO_4)_2$ (to ensure completion of the assembly) in $MeNO_2$ at RT, followed by diffusion of di-isopropyl ether vapour into the solution, afforded a crop of small orange crystals. X-ray crystallographic analysis¶ revealed the structure of the expected octanuclear cage (Fig. 3).[9] The key issue is crystallographic location of the Ru^{2+} and Cd^{2+} ions at different sites in the cage, which is non-trivial given their similar electron density and size which could lead either to disorder or to mis-identification.

Two distinct pieces of crystallographic evidence confirmed the presence of four Ru^{2+} and four Cd^{2+} ions in the desired alternating arrangement. Firstly, these two ions should have different average M—N distances, with Ru—N distances shorter than Cd—N. The four metal positions identified as Ru^{2+} consistently had significantly shorter bond distances (average, 2.17 Å) than the four positions identified as Cd^{2+} (average, 2.23Å).† Secondly, correct assignment of Ru / Cd positions resulted in all eight metal ions having comparable isotropic displacement parameters; inversion of the assignment, *i.e.* deliberately mis-labelling Ru as Cd and *vice versa*, resulted in one set of displacement parameters being significantly larger than the other, as expected.

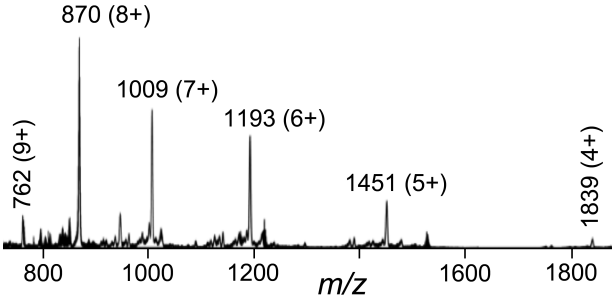

Fig. 4. Electrospray mass spectrum of $[Ru_4Cd_8L_{12}][ClO_4]_{16}$ showing a sequence of peaks corresponding to $[Ru_4Cd_4L_{12}(ClO_4)_{16-z}]^{z+}$, *i.e.* loss of 4 – 9 perchlorate anions from the complete complex.

The crystalline product was further analysed by ES mass spectrometry and ^{1}H NMR spectroscopy.† The ES mass spectrum reveals a series of peaks at *m/z* $[Ru_4Cd_4L_{12}(ClO_4)_{16-z}]^{z+}$ (z = 4 – 9) corresponding to the intact complex cation associated with varying numbers of anions (Fig. 4). High-resolution ES spectra give sets of peak clusters for the ions with z = 5, 6, 7 that match

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exactly what is expected.† A ^{1}H NMR spectrum of $[Ru_4Cd_4L_{12}](ClO_4)_{16}$ in CD_3NO_2 was not very informative as it contains 88 independent proton environments in the region 4.7 – 8.4 ppm;†,§ even at 800 MHz the signals overlap too much for meaningful assignment. However, a DOSY spectrum showed that all of the signals have the same diffusion constant, confirming the presence of a single large assembly in solution.†

Finally we investigated the electrochemical behaviour of the cage. The model complex $[Ru(L^{Me})_3](PF_6)_2$ (Fig. 1; separate *fac* and *mer* isomers)[10] shows a reversible Ru^{2+}/Ru^{3+} wave at +0.85 V *vs.* ferrocene / ferrocenium (Fc/Fc^+) for the *fac* isomer, and +0.81 V for the *mer* isomer – a difference of only 40 mV between the isomeric forms. For $[Ru_4Cd_4L_{12}](ClO_4)_{16}$ we observed a single symmetric wave at +0.96 V *vs.* Fc/Fc^+, which we ascribe to all four Ru^{2+}/Ru^{3+} couples that are coincident because of the absence of electronic coupling between the Ru centres. The separate processes for the *fac* and *mer* centres are also not resolved, but the wave is slightly broadened (ΔE_p = 120 mV).†

An important consequence of this redox activity is that the charge on the cage can be switched reversibly between charges of 16^+ and 20^+. Given that we recently demonstrated how binding of electron-rich organic guests involves a substantial contribution from charge-assisted hydrogen-bonding to the internal surface of the cage, at the position where the electrostatic potential is most positive,[9c] a reversible redox swing should affect the strength of the host/guest interaction and may provide a mechanism for controlling uptake and release of bound guests. Redox changes also offer the possibility of reversible changes in the luminescence[5a,9a] or chromic[5b] properties of the cage.

In conclusion, we have used a combination of kinetically inert and labile metal ions for the rational design and synthesis of a heterometallic Ru_4Cd_4 coordination cage, in which (i) the four Ru^{2+} and four Cd^{2+} ions occupy specific sites in the array; and (ii) we have introduced redox activity associated with the Ru^{2+} sites.

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Notes and references

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† Electronic Supplementary Information (ESI) available: crystallographic data in CIF format; bond distances and angles around the metal ions; further details of the crystallographic refinement; details of synthesis and characterisation; details of NMR and mass spectrometric characterisation of the cage; cyclic voltammograms. See DOI: 10.1039/b000000x/

‡ The *mer* isomer has no symmetry with all three ligands inequivalent; the *fac* isomer provides the fourth ligand environment with all three ligands equivalent due to the threefold symmetry but is only one-third as abundant. Hence we see signals for four independent ligand environments in equal abundance.

§ The homonuclear cages $[M_8L_{12}]X_{16}$ contain 44 proton environments because the two different ligand environments (connecting *fac/mer* and *mer/mer* metal centres, with six ligands in each environment) have no internal symmetry (ref. 9). In the Ru_4Cd_4 complex the symmetry is reduced by a further factor of two due to loss of the inversion centre.

¶ Crystal data for $[Ru_4Cd_4L_{12}](ClO_4)_{16}\bullet\{[Cd(H_2O)_6](ClO_4)\}_{0.5}\bullet 11MeNO_2\bullet 3H_2O$: $C_{347}H_{309}Cd_{4.5}Cl_{17}N_{83}O_{96}Ru_4$, M = 8441.94 g mol^{-1}, monoclinic, space group $P2_1/c$, a = 23.0027(14), b = 40.888(2), c = 50.529(3) Å, β = 100.989(3)°, U = 46653(5) Å^3, Z = 4, T = 100(2) K, λ(Mo-Kα) = 0.71073 Å. 325928 reflections were collected ($2\theta_{max}$ = 45°) which after merging afforded 61008 independent reflections with R_{int} = 0.176. Final $R1$ [$I > 2\sigma(I)$] = 0.130; $wR2$ (all data) = 0.378. See ESI for further details.

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