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Published paper

A tetrameric hetero-octanuclear cyclic helicate formed from a bridging ligand with two inequivalent binding sites†

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A bis-bidentate bridging ligand H₂L with inequivalent hard and soft binding sites (catecholate and pyrazolyl-pyridine, respectively) reacts with a mixture of Ti(IV) and Zn(II) ions to afford an octanuclear heterometallic Ti₄Zn₄ cyclic helicate formed from four dinuclear (TiZn(μ-L)₂) units connected in a ring via methoxide ions.

Self-assembly is a regularly exploited method in coordination chemistry to combine large numbers of components in one edifice. This is illustrated particularly well in the formation of coordination cages or capsules from labile metal ions and simple bridging ligands, with (for example) Fujita’s ‘nanosphere’ forming from 72 component parts, i.e. 24 metal ions and 48 ditopic bridging ligands. An example from our own group is a series of M₄₈L₃₄ cages which contain forty components in a single assembly, and many other groups have reported self-assembled molecular species of comparable complexity.

An important characteristic of most such assemblies is that, despite their structural complexity and the large number of component parts that assemble, they often contain only two types of component with all metal ions being the same and all ligands being the same. This inevitably limits the functional behaviour that can be built into the assemblies. We can imagine that a greater range of functional behaviour could be achieved if the component parts themselves have some useful function such as redox activity or magnetism for metal ions, or conformational switchability or luminescent excited states for ligands. Accordingly it is of value to investigate self-assembled systems containing three or more types of component part, as a way of increasing the possibilities for functional behaviour in self-assembled complexes.

There are many ways in which self-assembly of >2 different types of component can be achieved using orthogonal interactions to avoid unwanted combinations of subcomponents. In terms of simple metal/ligand combinations, this could mean one type of metal ion that selects for a mixture of two types of ligand during the assembly process, for either geometric or electronic reasons. This principle is illustrated by Lehn’s Cu(I)-based cylindrical assemblies and related trigonal-prismatic structures from Severin and Mukherjee in which each metal ion connects to two different types of ligand. Alternatively, it could mean one ligand that selects for a mixture of different metal ions. This can be achieved if the ligand has two different binding sites which attract different types of metal ion, and this is well known in (for example) heteronuclear double or triple helicates based on bridging ligands with two different binding pockets.

Additional examples have come from the groups of Shionoya, Wang, and Raymond. Shionoya and co-workers used a ligand with a pyridyl group as one terminus and a catecholate (cat²⁻) as the other; the pyridyl coordinates to Pd(II) and the catecholate to Ti(IV), to give heterometallic cages or rings depending on stoichiometry and reaction conditions. Wang and co-workers used a pyridyl/acetyleacetone ligand to prepare an Al(acac)₃ unit with pendant pyridyl groups which combined with Pd(II) ions to form a heterometallic cubic cage. Raymond and co-workers used a simple ligand with phosphine and catechol binding sites which combines with a mixture of Ti(IV) and Pd(II) ions; the resulting Ti₂Pd₃L₆ assembly forms not only because of the preferences of the ‘hard’ and ‘soft’ metal cations for the catecholate and phosphine binding sites respectively, but also exploits the stereochemical preferences of the metal ions – octahedral for Ti(IV) and square planar for Pd(II).

It is this last strategy that we exploit in this work. We have used ligands containing bidentate pyrazolyl-pyridine (pypz) termini as the basis of an extended family of self-assembled coordination cages using relatively soft M²⁺ cations which form [M(pypz)₂]³⁺ vertices. In contrast, Raymond and Albrecht have used ligands containing catecholate termini that combine with harder metal cations to form anionic cages based on [M(cat)]⁻ vertices. We report here the preparation of a new bridging ligand which combines ‘hard’ catecholate and ‘soft’ pyrazolyl-pyridine termini connected to an aromatic spacer. This opens up new possibilities to prepare heterometallic assemblies based on two types of metal.
ion with differing affinities for the two types of terminus, and as a first example we present the example of an unusual heterometallic cyclic helicate which is a cyclic tetramer of dinuclear double helicate subunits.

The new ligand H$_2$L is shown in Scheme 1 along with a disconnection into component parts which forms the basis of the synthetic strategy. The catechol terminus is connected to the aromatic spacer via an amide linkage formed between an aromatic amine and an acyl chloride; the pyrazolyl-pyridine unit is connected via reaction of the deprotonated pyrazole unit with a $-\text{CH}_2\text{Br}$ group on the central spacer. The full synthesis is shown in Scheme 2 and starts from 3-amino-benzyl alcohol. Boc protection of the amine group allows the alcohol to be converted to a $-\text{CH}_2\text{Br}$ group, to which the pyrazolyl-pyridine unit is connected to give 3. Removal of the Boc group liberates the amine which condenses with the acyl chloride group of 5 to attach the dimethoxybenzene group to the central spacer (6); the final step is removal of the methyl groups with BBr$_3$ to liberate the catechol of H$_2$L. All new compounds were fully characterised by standard methods (see ESI).

The $^1$H NMR spectrum of H$_2$L in d$_6$-DMSO confirmed its structure; an expansion of the aromatic region (with assignments) is in ESI. The ES mass spectrum showed a molecular ion at $m/z$ 387 (M + H)$^+$. Crystals of H$_2$L (as its hydrobromide salt) were grown by diffusion of diethyl ether vapour into a solution in MeOH/CHCl$_3$ and the crystal structure is shown in Fig. 1. There is one complete ligand (and one HBr) in the asymmetric unit. The catechol oxygen atoms are arranged syn to the amide carboxyl, as this allows the formation of a 6-membered hydrogen-bonded ring with a catechol O–H bonded to the carboxyl oxygen O(43). Raymond and co-workers have reported this effect with their catecholamide ligands.$^{15}$ The crystal structure also reveals that the bromide anion forms a variety of close contacts with protonated ligand molecules (numerous H⋯Br contacts of ca. 2.9–3 Å involving CH and NH bonds), with one interaction being notably shorter than the others: this is an N$^+$⋯H⋯Br$^-$ hydrogen bond involving a protonated pyridine ring [N(11)⋯Br(1), 3.21 Å; H(11)⋯Br(1), 2.41 Å].

We combined H$_2$L with a mixture of Zn($^{n}$) and Ti($^{iv}$) salts, which are expected to interact with the pypz and catecholate termini respectively. There could be many ways in which the ligands arrange around this combination of metal ions to match their electronic preferences. H$_2$L·HBr, Zn(BF$_4$)$_2$ and Ti(O$_{\text{iPr}}$)$_4$ were...
combined in a 3 : 1 : 1 ratio in MeOH with a few drops of Et$_3$N.$^\S$

Stirring at room temperature quickly afforded an orange
precipitate which was filtered off and washed with MeOH and
ether. Crystallisation by diffusion of MeOH vapour into a dmf
solution of the complex afforded X-ray quality orange plates; the
resulting structure is shown in Fig. 3 and 4.

The complex has the formulation [Ti$_4$Zn$_4$L$_8$(μ-OMe)$_8$]
·4MeOH·4dmf and has an unusual structure which is a square
array of four heterodinuclear {TiZnL$_2$}$_2^+$ double helicates that are
connected head-to-tail [i.e. Zn(n) terminus to Ti(iv) terminus] by a
pair of methoxide bridges. Each double helicate fragment – an
edge of the square assembly – has the two bridging ligands
oriented in the same direction, such that the Zn(n) ion is
coordinated by two pzpy units at one end and the Ti(iv) ion is
coordinated by two cat$_2^-$ units at the other, i.e. the ligands are
arranged so as to define ‘hard’ and ‘soft’ binding pockets. There
are two crystallographically independent types of double helicate
unit, one containing Ti(1)/Zn(2) and the other containing Ti(2)/
Zn(1), with Ti…Zn separations of 9.67 and 9.63 Å respectively; as
such the tetrameric {TiZnL$_4$}$_4$ array has crystallographically-imposed
twofold symmetry. The Ti(2)/Zn(1) double helicate unit is shown in
wire-frame and space-filling modes in Fig. 2. Weak interactions
between ligands (π-π and CH…π) within each double helicate
subunit are evident; for example Fig. 2a illustrates a
π-stacking interaction between a phenyl spacer of one ligand and a
coordinated pyrazolyl-pyridine unit of the other.

All four dinuclear double helicates units have the same sense of
twist within the assembly, i.e. the whole tetrameric assembly is
homochiral. A pair of bridging methoxide ions connecting each
helicate to the next in the cyclic tetramer means that each Zn(n)
ion has an N$_4$O$_2$ donor set and each Ti(iv) ion has an O$_6$ donor set.
The Zn(1)…Ti(1) and Zn(2)…Ti(2) separations across the methoxide
bridges in the ZnTi(μ-OMe)$_2$ units are 3.18 and 3.20 Å respectively.
Individual bond lengths and angles around the approximately
octahedral metal ions are unremarkable. Fig. 3 shows the entire
complex, with the two Zn(1)/Ti(2) double helicates (approximately
vertical in the figure) shown with blue and green bridging ligands,
and the two Zn(2)/Ti(1) double helicates (approximately horizontal
in the figure) shown with purple and gold ligands. A space-filling
view is in Fig. 4, and Fig. 5 shows just the octanuclear metal

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**Fig. 1** Molecular structure of H$_2$L·HBr. Non-H atoms are shown with 40% thermal ellipsoids, the hydrogen-bond between the protonated pyridine and the bromide anion is shown with a dotted line. Atoms labeled ‘#’ are at equivalent position (−x, 1 − y, z).

**Fig. 2** Two views of one of the four dinuclear double helical subunits that form the edges of tetrameric assembly. (a) A wire-frame view showing the atomic numbering scheme; the methoxide ligands are shown (but not the adjacent atoms to which they bridge). Atoms labeled ‘#’ are at equivalent position (−x, y, 0.5 − z). (b) A space-filling view from the same perspective, with one of the ligands shown in paler colours for clarity (methoxide ligands omitted).

**Fig. 3** A view of the complete tetrameric assembly. The dinuclear double helicate units are shown with the atoms of each ligand coloured green/blue or purple/gold; Zn = grey; Ti = cyan; O = red; C = black.
skeleton and the methoxide bridges that hold the four double helicates together.

Once formed, the crystals are highly insoluble and can only be redissolved in a strongly competitive solvent like DMSO; ES mass spectra on the resultant solutions showed, unsurprisingly, only fragments with no evidence for the intact complex under those conditions.

Cyclic helicate structures in general are now well known\textsuperscript{16} but this example is unprecedented for two reasons. Firstly, a one-pot reaction results in formation of a cyclic tetramer (C = black, O = red). Atoms labelled ‘#’ are at equivalent position (−x, y, 0.5 − z).

Fig. 4 A space-filling view of the whole complex [Ti\textsubscript{4}Zn\textsubscript{4}L\textsubscript{8}(μ-OMe)\textsubscript{8}] with the bridging ligands coloured as in Fig. 3 (the individual dinuclear double helicate components are green/blue or purple/gold).

\textsuperscript{‡} Preparation of [Ti\textsubscript{4}Zn\textsubscript{4}L\textsubscript{8}(μ-OMe)\textsubscript{8}]·4MeOH·4dmf. A solution of Ti(O\textsubscript{2}Pr\textsubscript{4})\textsubscript{4} (8.5 mg, 0.03 mmol) was added to a stirred solution of H\textsubscript{2}L (39 mg, 0.1 mmol) in MeOH (3 cm\textsuperscript{3}) causing the solution to turn yellow. A solution of Zn(BF\textsubscript{4})\textsubscript{2}-6H\textsubscript{2}O (10.2 mg, 0.03 mmol) in MeOH (2 cm\textsuperscript{3}) was then added. Excess Et\textsubscript{3}N (1 cm\textsuperscript{3}) was added and the mixture was stirred in the dark at room temperature for 24 h. A fine orange precipitate was collected and washed with MeOH. X-Ray quality crystals were grown by slow diffusion of MeOH into a solution of the complex in DMF. Yield: 13 mg, 0.003 mmol, 46%. Found: C, 54.3; H, 3.9; N, 11.3%. Calcd. For C\textsubscript{61}H\textsubscript{48}B\textsubscript{15}N\textsubscript{34}O\textsubscript{38}Ti\textsubscript{4}Zn\textsubscript{8}: C, 54.8; H, 3.8; N, 11.1%.


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