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Integrative Sorting

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Synthesis and characterisation of an integratively self-sorted $[\text{Fe}_4\text{L}_6]^{8+}$ tetrahedron†

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Isolating metal–organic cage structures which incorporate more than one distinct ligand has been challenging due to competing pressures from narcissistic and social sorting phenomena. Here we report the first example of exclusive formation of a single tetrahedral product from a reaction mixture containing two different bidentate ligands. Exclusive formation of the tetrahedron, which incorporates one unique metal vertex, relies on a triamine to orientate the heteroditopic ligand. Inclusion of perchlorate counterions during the self-assembly process is also found to be a requirement if social sorting is to be avoided. The C_3 -symmetric structure is characterised by HR-MS, NMR spectroscopy and X-ray crystallography, and provides proof of principle for use of heteroditopic ligands in classical M_4L_6 supramolecular structures, opening exciting possibilities for their use in separation, storage and catalysis applications.

Within a subcomponent mixture, self-sorting principles can control the spontaneous self-assembly process and promote the formation of specific products.^{1,2} This phenomenon is prevalent throughout nature, governing processes such as base pairing in DNA,³ the self-fractioning of white blood cells in human blood⁴ and the highly-ordered, spontaneous grouping of alike neurons during foetal brain development.⁵ Recently there has been a growing interest in understanding and controlling complex self-sorting phenomenon in synthetic systems.^{6–12} In the field of metallo-supramolecular architectures the desire to controllably generate complex structures with unusual and useful functionality has led researchers to explore incorporation of reduced symmetry ligands^{13–17} as well as the formation of heteroleptic structures.^{18–24} Generation of discrete structures from these components requires that ligands are controllably orientated through sorting phenomena.

Self-sorting processes have been defined as either narcissistic or integrative,^{25,26} where narcissistic self-sorting describes

the phenomenon of self-association^{2,27} and integrative self-sorting describes the combination of multiple different structural components within a single system.^{11,27} Commonly these terms are applied to the self-assembly of complexes from more than one homoditopic ligand, however, the self-assembly of reduced symmetry heteroditopic ligands can also be defined using these descriptors. In the latter case it is the coordination environment around the metal ion that is considered.^{7,11} For systems where neither narcissistic nor integrative sorting dominates, it is also possible to generate equilibrium mixtures containing several thermodynamic products of similar energies. This socially sorted mixture is termed a dynamic library.^{8,28} Gaining control over sorting to enable inclusion of more than one ligand within a metal–organic structure can however be challenging as narcissistic associations often dominate.^{27–30} For heteroditopic ligands orientation of the ligand with respect to the metal centre can be governed using steric and electronic arguments to bias either narcissistic or integrative sorting.^{11,14,31}



Scheme 1 Left: Self-assembly of a heteroleptic tetrahedral cage **C1** by integrative sorting. Right: Formation of homoleptic cage **C2** and the mononuclear complex **C3**. Exclusive formation of **C1** or social sorting is possible when using **L1**, **L2**, TREN and Fe(II) starting materials.

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Herein we detail self-assembly reactions incorporating two similar ligands (Scheme 1; **L1** and **L2**) with a choice of amine and iron(II) salt. The system is shown to display integrative sorting generating **C1** exclusively when TREN and iron perchlorate are employed in the self-assembly reaction. Alternatively, social sorting to form a mixture of two tetrahedral cages **C1** and **C2**, and the mononuclear complex **C3**, is observed when iron triflimide is used in place of iron perchlorate.

The bisbidentate ligands **L1** and **L2** both bind octahedral metal ions through their bidentate N^N binding sites. Ligand 1 (**L1**) contains two bipyridine binding sites and was previously reported to form $[M^{n+}_4L_6]^{4n+}$ tetrahedral architectures in the presence of octahedrally coordinating metal ions including Fe(II)³² and Co(III).³³ Ligand 2 (**L2**) features a bidentate bipyridyl binding site at one end and a pyridine aldehyde moiety capable of reacting with a range of amines to generate a bidentate pyridylimine at the other.³⁴ The relative orientation of the bidentate binding sites in these ligands is comparable, leading us to hypothesize the ligands could be interchanged within $[M_4L_6]^{8+}$ tetrahedra.

To the best of our knowledge, the Fe₄L₆ tetrahedron (**C1**), which incorporates both **L1** and **L2**, is the only example of an M₄L₆ tetrahedron formed through integrative sorting behaviour. Incorporation of **L1** and **L2** generates a structure which has overall C₃-symmetry and incorporates one unique vertex which may allow for introduction of functionality not possible at the *tris*(bipyridine) sites,³⁵ or affect host guest binding through alteration of guest access and egress.³⁶

In initial studies **L1**, **L2**, Fe(CLO₄)₂ and the monoamine *p*-toluidine were combined in CD₃CN to determine if the system displayed any self-sorting behaviour. Analysis of the ¹H NMR from this reaction showed major peaks corresponding to the homoleptic cage, **C2**, alongside a broad baseline. Mass spectrometric analysis supported the formation of a library of M₄L₆ tetrahedra with between three and six **L1** ligands incorporated (Fig. S5, ESI[†]). No evidence for formation of cages with greater than three equivalents of **L2** was found suggesting that under the conditions of ionisation cages incorporating significant numbers of this component are less stable.

We next added one equivalent of TREN (T; *tris*(2-aminoethyl)amine) per four metal centres to the library generated with *p*-toluidine, hypothesising that the triamine would displace three equivalents of *p*-toluidine and orientate three pyridyl imines around one metal centre (Fig. 1). Analysis of the ¹H NMR spectrum following addition of TREN (Fig. S4, ESI[†]) indicated formation of a single set of resonances corresponding to **C1**, in addition to those of the liberated *p*-toluidine. Single crystals of **C1** (Fig. 2) were grown through slow diffusion of diethyl ether into acetonitrile over the course of seven days. Measurement of the Fe(II) to N bond lengths in the crystal structure of **C1** did not indicate any significant bond strain. All bond lengths were consistent with coordination of low-spin Fe(II) within a N⁶ coordination environment. Moreover, these values were comparable with those obtained from the single crystal structure of homoleptic tetrahedron **C2** (Fig. S32, ESI[†]).

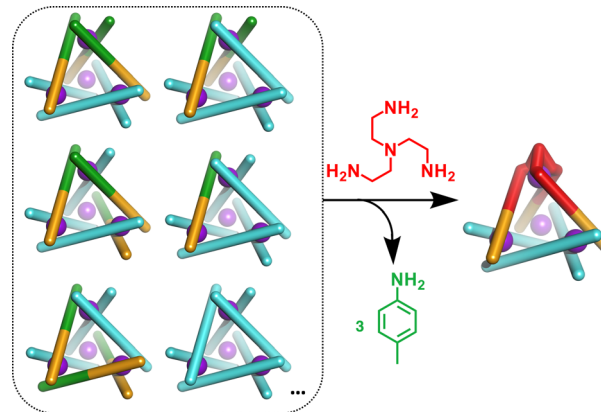


Fig. 1 Displacement of *p*-toluidine (3 equiv.) by TREN (red) to generate **C1** exclusively from a library of cages. The initial library includes a mixture of cages with varying numbers and orientations of **L1** and **L2**.

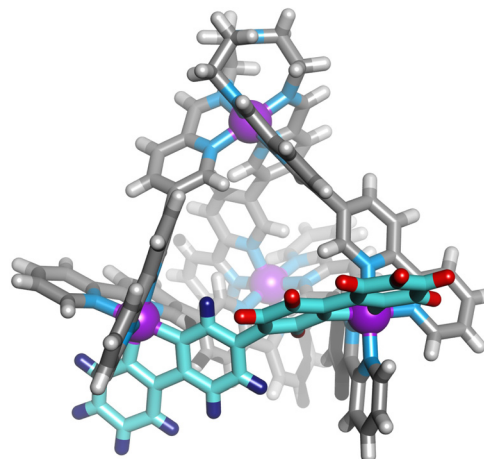


Fig. 2 Single crystal X-ray structure of the cationic portion of **C1**. The two different bipyridine environments on **L1** are coloured blue and red. Counterions and solvent removed for clarity.

Assignment of the ¹H NMR spectrum revealed that upon incorporation in **C1**, the two adjacent bipyridine units of **L1** became inequivalent, consistent with formation of the C₃-symmetric tetrahedral architecture (Fig. 2). Refinement of the single crystal X-ray data did not provide definitive evidence for encapsulation of the perchlorate counterion, however, structurally related M₄L₆ tetrahedra have been reported to bind perchlorate anions with high affinity.^{33,37}

To try and better understand the factors governing the *p*-toluidine to TREN amine exchange process we next added three equivalents of 2-pyridinecarboxaldehyde and one equivalent of TREN per Fe(II) ion to a solution of purified **C2** constituted from **L1** and Fe(II). After heating the mixture at 65 °C for 24 hours the ¹H NMR spectrum contained no evidence of **C2** (Fig. S22, ESI[†]). Analysis of the reaction mixture confirmed exclusive formation of a mononuclear *tris*pyridylimine complex, and the displaced **L1** ligand precipitated from solution following decomplexation. We therefore propose that



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