This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Variation of guest selectivity within \([\text{Fe}_4\text{L}_4]^{8+}\) tetrahedral cages through subtle modification of the face-capping ligand.

Alan Ferguson\(^a\)*, Robert W. Staniland\(^a\), Christopher M. Fitchett\(^a\), Marie A. Squire\(^a\), Bryce E. Williamson\(^a\), and Paul E. Kruger\(^a,b\)

Received (in XXX, XXX) Xth XXXXXXXXXX 200X, Accepted Xth XXXXXXXXXX 200X
First published on the web Xth XXXXXXXXXX 200X
DOI: 10.1039/b000000x

We report here the host-guest behaviour of two isoelectronic \([\text{Fe}_4\text{L}_4]^{8+}\) tetrahedral cages that differ only in the nature of their face-capping ligand and possess either triazine (L1) or benzene (L2) cores. Crystallography reveals these hosts to be flexible and adaptable, while NMR spectroscopy shows them to be selective and discriminating in their host-guest behaviour.

The synthesis of molecular cages has produced an impressive variety of species, many of which are capable of selectively binding guest molecules within their cavities.\(^1\) Selectivity is based upon an interplay between host and guest to achieve the best complementarity between size, shape, bonding and electronic factors with the ‘best fit’ yielding highest stability.\(^2\) The high affinity for specific guests displayed by these cages bodes well for their use in separations,\(^3\) ion binding,\(^4\) drug delivery\(^4\) and catalysis.\(^5\) Importantly, the host-guest chemistry of these nano-capsules can be modified through change of the organic components or by external perturbation. For example, the incorporation of large ancillary groups on the cage forming ligands has been shown to compress the cavity volume and alter the selectivity and motion of the encapsulated guests.\(^6\) Likewise, it is possible to regulate guest exchange kinetics by capping the apertures through which guest ingress/egress occurs.\(^7\) Further, it has been shown that light can be used to reversibly control encapsulation processes whereby photo-isomerisation of a guest causes it to be ejected from the host because of shape incompatibility.\(^8\) Moreover, the use of electron-poor ligands in the synthesis of cages has rendered them capable of binding organic molecules in aqueous media and to accelerate Diels-Alder reactions.\(^9\)

We recently reported the first tetrahedral cage to show spin crossover (SCO) behaviour, \([\text{Fe}_4\text{L}_4](\text{BF}_4)_8\), where L is the face-capping ligand derived from the sub-component self-assembly of 2,4,6-tris(4-aminophenoxo)triazine and 2-imidazolecarboxaldehyde, along with preliminary \[^{19}F\] NMR data tracking the ingress/egress of the BF\(_4^−\) guest.\(^10\) Naturally, the switchable paramagnetic nature of this cage impinged upon its host-guest behaviour. To more fully delineate the influences that SCO behaviour has upon guest exchange a thorough study of the host-guest behaviour of related diamagnetic cages is required. We report here the synthesis, structural characterisation and varied host-guest behaviour of two cages featuring iso-electronic ligands with either electron-poor triazine-ring (L1) or electron-rich benzene-ring (L2) cores (Scheme 1).

The self-assembly of 2,4,6-tris(4-aminophenoxo)triazine, 2-
A series of competitive binding experiments were also conducted whereby all possible combinations of Fe(X)₂ salts (X = PF₆⁻, OTF⁻, ClO₄⁻, BF₄⁻) in 2:2 stoichiometry were reacted with the ligand sub-components (ESI). As anticipated, only PF₆⁻ was bound within the cavity when Fe(BF₄)₂ was used in combination with Fe(PF₆)₂. In the case of Fe(BF₄)₂ vs. Fe(OTF)₂, the cage selectively formed around the OTF⁻ ion despite the earlier exchange experiment suggesting that a mixture of [BF₄Cl]⁺ and [OTf⁻Cl]⁺ might be observed. These experiments allowed the following binding preference for cage 1 to be determined: PF₆⁻ > OTF⁻ > ClO₄⁻ > BF₄⁻.

Having established that BF₄⁻ was the most weakly bound anion, we then introduced some solvent species (benzene, CHCl₃, CCl₄) to CD₂CN solutions of [BF₄Cl]₁(BF₄)₂ to determine if they too could displace BF₄⁻. However, none of these potential guests displaced BF₄⁻, which is not too surprising given the highly cationic nature of the cage and the fact that the cage walls within 1 are replete with electron-poor triazine-rings that interact strongly with anionic species.

We next used electron-rich 1,3,5-tris(4-aminophenoxy)-benzene in combination with 2-pyridinecarboxaldehyde in the sub-component self-assembly reaction with Fe(II) salts to yield a series of [FeL₂]⁺⁺ cages, 2, (Scheme 1). The face-capping ligand L₂ is iso-electron-rich with, and possesses nearby identical metric parameters to, L₁. Any variation in binding affinity of the cages could then be attributed to differences in their electron- rich vs. poor nature. Vapour diffusion of Et₂O into the deep purple reaction mixture resulting from Fe(NTf₂)₂ produced crystals suitable for single-crystal X-ray diffraction studies. The structure of [2](NTf₂)₈ was refined in the monoclinic space group P2₁/c (ESI). There are two crystallographically distinct cages in the asymmetric unit, with average Fe-Fe separations of 14.29 and 14.40 Å, respectively. These Fe-Fe distances result in an increased cavity volume in 2 relative to 1 of 148 and 150 Å³. It was not possible to determine the exact nature of the encapsulated guest due to significant disorder, but we suspect solvent molecules reside within the cavity as the NTf₂⁻ anion is too large to fit. The formation of the BF₄⁻, OTf⁻, NTf₂⁻, PF₆⁻ and ClO₄⁻ derivatives of the L₂-based cage has been confirmed by NMR spectroscopy and mass spectrometry. Each ¹H NMR spectrum shows one set of peaks consistent with T point symmetry, while mass spectrometry confirms the presence of [FeL₂]⁺⁺ species. ¹⁹F NMR spectroscopy reveals that OTf⁻ and PF₆⁻ are bound within the cavity however; NTf₂⁻ and BF₄⁻ are not (or are in rapid exchange) due to the presence of only one peak within their spectra consistent with ‘free’ anion.

Comparison of the ¹H NMR spectra of 2 in its ‘guest-free’ or ‘guest-bound’ forms reveals interesting differences in many proton resonances but most significantly in the peaks for the phenyl protons H₆, H₇, H₈, H₉ and H₁₀ from the three ligand arms and the central benzene ring (Fig. 2 and Scheme 1). In its ‘guest-free’ form (BF₄⁻, NTf₂⁻ and ClO₄⁻) these peaks are noticeably broadened due to fluxional/rotational behaviour of the phenyl rings. However, in their ‘guest-bound’ form (OTf⁻ and PF₆⁻) these peaks sharpen, resolve cleanly to doublets and either shift upfield (H₇, H₁₀) or down-field (H₆, H₈, H₉), suggesting the guests ‘lock-down’ the ligand arms to inhibit their dynamic behaviour (Fig. 2).

To better determine the host-guest behaviour of 2 a series of titrations were conducted whereby potential guests were

---

**Fig. 1** Crystal structure of [OTf⁻1](OTf)₂, showing one orientation of the encapsulated OTf⁻ anion. All hydrogen atoms, solvent molecules and lattice anions have been removed for clarity.
Notably, it also binds benzene, a neutral guest, but of binding preference can be affected by subtle electronic change although it will bind both with accommodating fashion. In large anionic guests (that fit within its void) over small ones, when OTf$^-$ or PF$_6^-$ observed to bind. From these data binding constants for OTf$^-$ host is operative and determines whether guest inclusion occurs. We are currently extending this study to include other additional anionic and neutral guest preferences with the view to include related SCO cages to study the interplay between host-guest and SCO behaviour. We will report results from these studies in due course.

The authors gratefully acknowledge the Royal Society of New Zealand Marsden Fund for financial support. We also thank the New Zealand synchrotron group for funding and Dr Tom Caradoc-Davies (Australian synchrotron) for assistance.

**Notes and references**

Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch 8140, New Zealand.

MacDiarmid Institute for Advanced Materials and Nanotechnology.

Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch 8140, New Zealand. E-mail: paul.kruger@canterbury.ac.nz

†Electronic Supplementary Information (ESI) available: Synthesis and characterization of [Fe$_2$L$_{44}$]$^{12+}$ cages; Structural data for [{BF$_4$}(L$_4$)$_2$]-12MeCN-H$_2$O, [{OTf$^-$}(L$_4$)$_2$]-5.63McCN3.88H$_2$O and [{PF$_6$}(L$_4$)$_2$]-4.17MeCN-6.5H$_2$O; $^{13}$C and $^1$H NMR spectra of anion exchange studies, host-guest titration data and binding constant calculations. Crystal structures available in CIF format under CCDC deposition numbers 1013078-1013080. See DOI: 10.1039/b000000x/


