Dalton Transactions

COMMUNICATION

Cite this: *Dalton Trans.*, 2014, **43**, 14550

Received 1st August 2014,
Accepted 21st August 2014

DOI: 10.1039/c4dt02337d

www.rsc.org/dalton

Variation of guest selectivity within $[Fe_4L_4]^{8+}$ tetrahedral cages through subtle modification of the face-capping ligand†

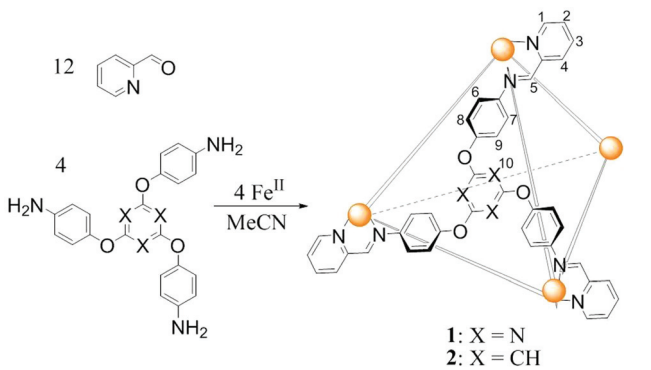
Alan Ferguson,*[a] Robert W. Staniland,[a] Christopher M. Fitchett,[a] Marie A. Squire,[a] Bryce E. Williamson[a] and Paul E. Kruger*[a,b]

We report here the host–guest behaviour of two isoelectronic $[Fe_4L_4]^{8+}$ 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. The high affinity for specific guests displayed by these cages bodes well for their use in separations,[2] ion binding,[3] 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, $[Fe_4L_4](BF_4)_8$, where **L** is the face-capping ligand derived from the sub-component self-assembly of 2,4,6-tris(4-aminophenoxy)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-aminophenoxy)triazine, 2-pyridinecarboxaldehyde and either $Fe(BF_4)_2$, $Fe(OTf)_2$, $Fe(PF_6)_2$ or $Fe(ClO_4)_2$ in MeCN solution in 4 : 4 : 12 stoichiometry yields $[Fe_4\mathbf{L1}_4]^{8+}$ cages, **1** (Scheme 1). Vapour diffusion of



Scheme 1 Sub-component self-assembly of tetrahedral cages from 2,4,6-tris(4-aminophenoxy)triazine or 1,3,5-tris(4-aminophenoxy)benzene, 2-pyridinecarboxaldehyde and Fe(II) in acetonitrile to yield the corresponding face-capped tetrahedra, $[Fe_4L_4]^{8+}$.

[a]*Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch 8140, New Zealand*
[b]*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 $[Fe_4L_4]^{8+}$ cages; structural data for $\{[BF_4^- \subset \mathbf{1}]^{7+}\text{–}[BF_4^-]_7\}\cdot 12MeCN\cdot H_2O$, $\{[OTf^- \subset \mathbf{1}]^{7+}[OTf^-]_7\}\cdot 5.63MeCN\cdot 3.88H_2O$ and $\{[\mathbf{2}]_2^{8+}[NTf^-]_{16}\}\cdot 46.17MeCN\cdot 6.5H_2O$; ^{19}F and ^1H NMR spectra of anion exchange studies, host–guest titration data and binding constant calculations. CCDC 1013078–1013080. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4dt02337d

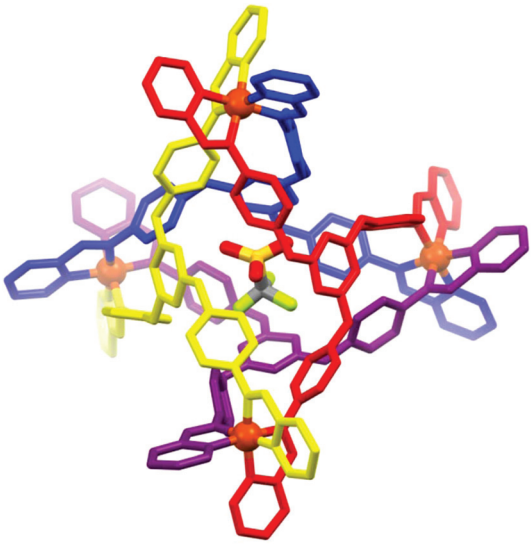


Fig. 1 Crystal structure of [OTf ⊂ **1**](OTf)$_7$, showing one orientation of the encapsulated OTf$^-$ anion. All hydrogen atoms, solvent molecules and lattice anions have been removed for clarity.

diisopropyl ether into the reaction mixtures containing either Fe(BF$_4$)$_2$ or Fe(OTf)$_2$ produced deep purple crystals suitable for single-crystal X-ray diffraction studies.†

The structure of [BF$_4$ ⊂ **1**](BF$_4$)$_7$ was refined in the triclinic space group $P\bar{1}$ (ESI†), while [OTf ⊂ **1**](OTf)$_7$ was refined in the monoclinic space group $C2/c$ (Fig. 1, ESI†). The encapsulated BF$_4^-$ anion shows strong F···π interactions (average F···centre-of-ring distance of 3.04 Å),[11] while the encapsulated OTf$^-$ anion is disordered over three positions. Each of the three orientations shows CF$_3$···π interactions at an average distance of 3.05 Å, which again suggests strong interaction despite the positional disorder. The average Fe···Fe distance within [BF$_4$ ⊂ **1**](BF$_4$)$_7$ and [OTf ⊂ **1**](OTf)$_7$ tetrahedra is 14.05 and 14.23 Å, whilst the accessible volumes of their cavities are 105 and 119 Å^3, respectively.[12] Clearly the flexible nature of the face-capping ligand allows the tetrahedron to adapt to better match the guest encapsulated within the cavity. The expansion of the cage within [OTf ⊂ **1**](OTf)$_7$ allows the larger OTf$^-$ anion to be encapsulated, although it is with a squeeze, as it occupies ~72% of the available volume, which is larger than that occupied by BF$_4^-$ in [BF$_4$ ⊂ **1**](BF$_4$)$_7$ (~51%), and lies outside that anticipated for optimal guest encapsulation (55 ± 9%).[13] Both complexes pack together *via* face-to-face π–π interaction between two neighbouring triazine rings to give a dimeric unit (ESI†).

The formation of BF$_4^-$, OTf$^-$, PF$_6^-$ and ClO$_4^-$ derivatives of the **L1**-based cage was also confirmed by NMR spectroscopy and mass spectrometry.† Each ^{1}H NMR spectrum shows a single set of peaks consistent with T point symmetry, while mass spectrometry confirms the presence of the [Fe$_4$**L1**$_4$]$^{n+}$ species. ^{19}F NMR spectroscopy reveals resonances for both 'free' and encapsulated ions in ~7 : 1 ratio for BF$_4^-$, OTf$^-$ and PF$_6^-$. While the encapsulation of ClO$_4^-$ is indicated by ^{1}H NMR spectroscopy and mass spectrometry data, it was definitively proven by the experiments reported below.

To assess the host–guest behaviour more fully we attempted to synthesise an empty cage using Fe(NTf$_2$)$_2$ featuring the larger triflimide anion but were unsuccessful. Several species were observed in the ^{1}H NMR spectrum, suggesting an important role for the smaller anions in templating the formation of this cage. Nonetheless, we devised a cycle of competition experiments to determine the relative binding affinities of anions across a range of potential guests. Beginning with [BF$_4$ ⊂ **1**](BF$_4$)$_7$ we added an equivalent of other potential anionic guests and tracked any changes in both the cage and anions by ^{1}H and ^{19}F NMR spectroscopy. Interestingly, we found that when a CD$_3$CN solution containing [BF$_4$ ⊂ **1**](BF$_4$)$_7$ was treated with an alternate anion (PF$_6^-$, ClO$_4^-$ or OTf$^-$) at room temperature there was no exchange of BF$_4^-$ for these 'competing' anions over several days. However, if the solutions were heated at 50 °C then exchange of the BF$_4^-$ guest occurred over a period of 12–18 hours for these competing anions. Both PF$_6^-$ and ClO$_4^-$ completely displaced the BF$_4^-$ anion as evidenced by the disappearance of the peak at δ −160.6 (due to bound BF$_4^-$), and the appearance of a doublet peak corresponding to encapsulated PF$_6^-$ at δ −73.3 and −75.2. OTf$^-$ displaced the BF$_4^-$ anion as demonstrated by the appearance of a new peak at δ −77.7, however, the two anions remain in equilibrium, as evidenced by the retention of a peak at δ −160.6 in the ^{19}F NMR spectrum, even after prolonged heating.

A series of competitive binding experiments were also conducted whereby all possible combinations of Fe(X)$_2$ salts (X = PF$_6^-$; OTf$^-$; ClO$_4^-$; BF$_4^-$) in 2 : 2 stoichiometry were reacted with the ligand sub-components (ESI†). As anticipated, only PF$_6^-$ was bound within the cavity when Fe(BF$_4$)$_2$ was used in combination with Fe(PF$_6$)$_2$. In the case of Fe(BF$_4$)$_2$ *vs.* Fe(OTf)$_2$, the cage selectively formed around the OTf$^-$ ion despite the earlier exchange experiment suggesting that a mixture of [BF$_4$ ⊂ **1**]$^{7+}$ and [OTf ⊂ **1**]$^{7+}$ might be observed. These experiments allowed the following binding preference for cage **1** to be determined: PF$_6^-$ > OTf$^-$ > ClO$_4^-$ > BF$_4^-$. Having established that BF$_4^-$ was the most weakly bound anion, we then introduced some solvent species (benzene, CHCl$_3$, CCl$_4$) to CD$_3$CN solutions of [BF$_4$ ⊂ **1**](BF$_4$)$_7$ to determine if they too could displace BF$_4^-$. However, none of these potential guests displaced BF$_4^-$, 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.[14]

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 [Fe$_4$**L2**$_4$]$^{8+}$ cages, **2** (Scheme 1). The face-capping ligand **L2** is iso-electronic with, and possesses near 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 Et$_2$O into the deep purple reaction mixture resulting from Fe(NTf$_2$)$_2$ produced crystals suitable for single-crystal X-ray diffraction

studies. The structure of $[\mathbf{2}](NTf_2)_8$ was refined in the monoclinic space group $P2_1/c$ (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 Å^3.[12] 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 NTf_2^- anion is too large to fit. The formation of the BF_4^-, OTf^-, NTf_2^-, PF_6^- and ClO_4^- derivatives of the **L2**-based cage has been confirmed by NMR spectroscopy and mass spectrometry. Each ^{1}H NMR spectrum shows one set of peaks consistent with *T* point symmetry, while mass spectrometry confirms the presence of $[Fe_4\mathbf{L2}_4]^{n+}$ species. ^{19}F NMR spectroscopy reveals that OTf^- and PF_6^- are bound within the cavity however; NTf_2^- and BF_4^- 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 ^{1}H 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 H^6, H^7, H^8, H^9 and H^{10} from the three ligand arms and the central benzene ring (Fig. 2 and Scheme 1). In its 'guest-free' form (BF_4^-, NTf_2^- and ClO_4^-) these peaks are noticeably broadened due to fluxional/rotational behaviour of the phenyl rings. However, in their 'guest-bound' form (OTf^- and PF_6^-) these peaks sharpen, resolve cleanly to doublets and either shift upfield (H^6, H^{10}) or down-field (H^7, H^8, H^9), suggesting the guests 'lock-down' the ligand arms to inhibit their dynamic behaviour (Fig. 2).

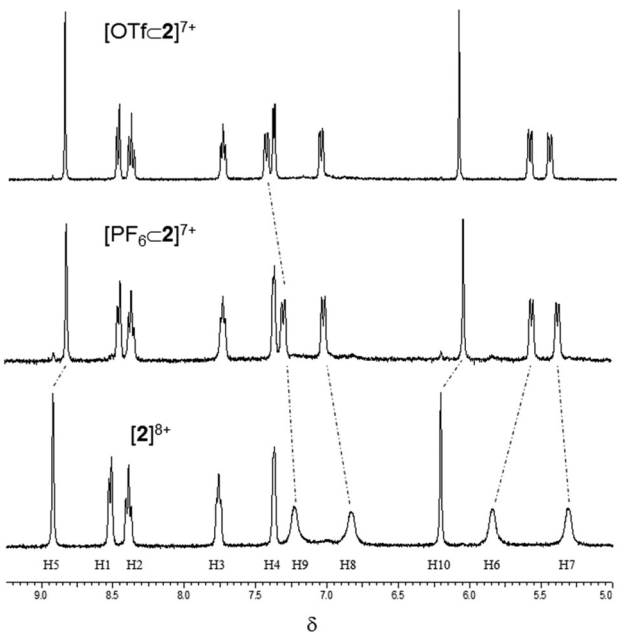


Fig. 2 Partial ^{1}H NMR spectra for the titration of 'guest-free' cage $[\mathbf{2}]^{8+}$ (bottom) with PF_6^- to give $[PF_6 \subset \mathbf{2}]^{7+}$ (middle) and then subsequently with OTf^- to give $[OTf \subset \mathbf{2}]^{7+}$ (top). (CD_3CN, 400 MHz, 298 K).

To better determine the host–guest behaviour of **2** a series of titrations were conducted whereby potential guests were added to 'guest-free' **2** in small increments and the host–guest formation was monitored through ^{1}H NMR spectroscopy (Fig. 2 and ESI†). Complete conversion to 'guest-bound' **2** occurred when OTf^- or PF_6^- were added (ESI†), however, incomplete conversion resulted when excess benzene was added (ESI†). No other guest trialled (BF_4^-, ClO_4^-, NTf_2^-, $CHCl_3$, CCl_4) was observed to bind. From these data binding constants for OTf^- and PF_6^- were determined as $9.9(\pm1.0) \times 10^4$ M^{-1} and $2.61(\pm0.16) \times 10^4$ M^{-1}, respectively.[15] The binding constant for benzene could not be determined due to overlap of peaks derived from **2** and $[\text{benzene} \subset \mathbf{2}]^{8+}$, however, from the ^{1}H NMR spectrum we estimate 1 : 1 stoichiometry.

A sequential guest exchange experiment was then performed and tracked through ^{1}H and ^{19}F NMR spectroscopy by firstly titrating PF_6^- against 'guest-free' **2** to yield $[PF_6^- \subset \mathbf{2}]^{7+}$, thereafter OTf^- was titrated against the newly formed $[PF_6^- \subset \mathbf{2}]^{7+}$ species to give $[OTf^- \subset \mathbf{2}]^{7+}$ (Fig. 2). From these experiments the order of guest binding preference for cage **2** was then determined as: $OTf^- > PF_6^- >$ benzene $\ggg BF_4^-$, ClO_4^-, NTf_2^-, $CHCl_3$, CCl_4.

In conclusion, it is clear that dramatic change in guest binding preference can be affected by subtle electronic change in the face-capping ligands in $[Fe_4L_4]^{8+}$ tetrahedral cages. The electron-poor triazine-based cage **1** has higher affinity for large anionic guests (that fit within its void) over small ones, although it will bind both with accommodating fashion. In contrast, however, cage **2** built from electron-rich face-capping ligands binds larger anions only and not small anions. Notably, it also binds benzene, a neutral guest, but of comparable size to OTf^- and PF_6^-. Clearly a subtle interplay between guest size, charge and the electronic nature of the host is operative and determines whether guest inclusion occurs. We are currently extending this study to include other face-capping ligands of varied electronic nature to screen 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.

Acknowledgements

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

1 H. Amouri, C. Desmarets and J. Moussa, *Chem. Rev.*, 2012, **112**, 2015; M. M. J. Smulders, I. A. Riddell, C. Browne and J. R. Nitschke, *Chem. Soc. Rev.*, 2013, **42**, 1728; M. D. Ward, *Chem. Commun.*, 2009, 4487.

2 E. Huerta, G. A. Metselaar, A. Fragoso, E. Santos, C. Bo and J. de Mendoza, *Angew. Chem., Int. Ed.*, 2007, **46**, 202; W. Meng, B. Breiner, K. Rissanen, J. D. Thoburn, J. K. Clegg and J. R. Nitschke, *Angew. Chem., Int. Ed.*, 2011, **50**, 3479.
3 R. Custelcean, *Chem. Commun.*, 2013, **49**, 2173; S. Goetz and P. E. Kruger, *Dalton Trans.*, 2006, 1277; D. A. McMorran and P. J. Steel, *Angew. Chem., Int. Ed.*, 1998, **37**, 3295.
4 J. E. M. Lewis, E. L. Gavey, S. A. Cameron and J. D. Crowley, *Chem. Sci.*, 2012, **3**, 778; Z. Ma and B. Moulton, *Coord. Chem. Rev.*, 2011, **255**, 1623; N. P. E. Barry, O. Zava, P. J. Dyson and B. Therrien, *Chem. – Eur. J.*, 2011, **17**, 9669.
5 M. Yoshizawa, J. K. Klosterman and M. Fujita, *Angew. Chem., Int. Ed.*, 2009, **48**, 3418; J. S. Mugridge, R. G. Bergman and K. N. Raymond, *J. Am. Chem. Soc.*, 2012, **134**, 2057.
6 Y. Fang, T. Murase, S. Sato and M. Fujita, *J. Am. Chem. Soc.*, 2013, **135**, 613.
7 S. Zarra, M. M. J. Smulders, Q. Lefebvre, J. K. Clegg and J. R. Nitschke, *Angew. Chem., Int. Ed.*, 2012, **51**, 6882.
8 H. Dube, D. Ajami and J. Rebek Jr., *Angew. Chem., Int. Ed.*, 2010, **49**, 3192; H. Dube and J. Rebek Jr., *Angew. Chem., Int. Ed.*, 2012, **51**, 3207.
9 M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi and K. Ogura, *Nature*, 1995, **378**, 469; Y. Inokuma, G. H. Ning and M. Fujita, *Angew. Chem., Int. Ed.*, 2012, **51**, 2379; M. Yoshizawa, M. Tamura and M. Fujita, *Science*, 2006, **312**, 251.
10 A. Ferguson, M. A. Squire, D. Siretanu, D. Mitcov, C. Mathonière, R. Clérac and P. E. Kruger, *Chem. Commun.*, 2013, **49**, 1597.
11 A. Frontera, *Coord. Chem. Rev.*, 2013, **257**, 1716.
12 PLATON VOIDS probe diameter 1.2 Å, grid 0.2 Å, A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7.
13 S. Mecozzi and J. Rebek Jr., *Chem. – Eur. J.*, 1998, **4**, 1 016.
14 B. L. Schottel, H. T. Chifotides and K. R. Dunbar, *Chem. Soc. Rev.*, 2008, **37**, 68.
15 Y. R. Hristova, M. M. J. Smulders, J. K. Clegg, B. Breiner and J. R. Nitschke, *Chem. Sci.*, 2011, **2**, 638.