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Preparation of a porphyrinic bis(pyridyl aldehyde) and its supramolecular complexes[†]

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Shape-specific molecular assemblies require the preparation of the constituent building blocks with the necessary properties to bias exclusive formation of the proposed structures. In this work, a novel linear porphyrin dialdehyde was synthesised and used to assemble a supramolecular grid *via* Cu(I) heteroleptic phenanthroline/pyridyl imine complexation, and a tetrahedral cage *via* Fe(II) pyridyl imine coordination.

Relatively simple building blocks (in terms of size, symmetry and available functional groups) provide access to a remarkable array of molecular assemblies.¹ Our objective has been to introduce complexity into the design of our building blocks (larger size, spectroscopically active fragments, and metal binding sites for orthogonal coordination) in order to access assemblies with more interesting properties and scope for incorporation of non-symmetrical components to give multi-component, heteroleptic assemblies, however, introduction of such complexity can present synthetic challenges. Guided by the elegant work of Schmittel and co-workers, we adopted the heteroleptic phenanthroline/pyridyl imine Cu(I) complex motif² as the coordinating components of one assembly, while also demonstrating the suitability of our building block for the formation of a tetrahedral cage with Fe(II)/pyridyl imine corners. In our work, the required pyridyl aldehyde functionalities were carried through the synthesis as acetals, and revealed under mild conditions that did not demetallate the zinc porphyrin - a reaction for which there is only a single previous example.³ The synthesis and solution state characterisation (by nuclear magnetic resonance spectroscopy and mass spectrometry) of the assemblies and the various building blocks is described below.

The scope for introducing a number of different amines to potential building blocks offers access to structural diversity, while

the ability of metal ions to influence the equilibrium of imine formation provides a method for control of the self-assembly process. Using a porphyrinic aldehyde, rather than a porphyrinic amine, mitigates the potential issue of self-coordination in the case of zinc porphyrins which are otherwise attractive targets due to the possibility of using axial ligation of nitrogen donors as an additional coordination motif.^{4,5} As aldehydes are relatively sensitive functionalities, their inclusion into subcomponents for supramolecular chemistry can sometimes prove problematic. There are few reports of porphyrins bearing pyridyl aldehyde substituents,^{6,7} and none that we are aware of having been used for metal-imine complexation in supramolecular assemblies.

Improving synthetic access to porphyrinic pyridyl aldehydes provides functional components for incorporation into supramolecular systems, in which porphyrins can play important roles such as catalysts,⁸ chromophores for molecular photonic devices,⁹ and structural motifs.¹⁰ The reactions we used to generate functionalised porphyrins were relatively simple, however we encountered unexpected challenges in terms of the solubility of our desired products and the introduction of a pyridyl aldehyde functionality, so in this report we outline the synthesis of linear porphyrin dialdehyde **1** which address these practical limitations (see also supplementary information section 1).

The final structure of **1** was dictated by several iterations of our synthetic route in which solubilising hexyloxy chains were found to be vital to offset the poor solubility properties (and overlapping chromatographic mobility) of the pyridyl aldehyde substituents, and the choice of protecting group for the aldehyde was based around the requirement for a very mild deprotection that would not cause concomitant demetallation of the porphyrin.

To synthesise a porphyrin core with the desired properties (see supporting information), benzaldehyde **2** was condensed with dipyrromethane **3** under the standard Lindsey conditions¹¹ (figure 1). While many previous literature examples make use of 3,5-dialkyloxyaryl groups to improve porphyrin solubility,^{12–14} there is also precedent for use of the 2,6-disubstituted variant,¹⁵ which we used in the hope that additional cofacial hin-

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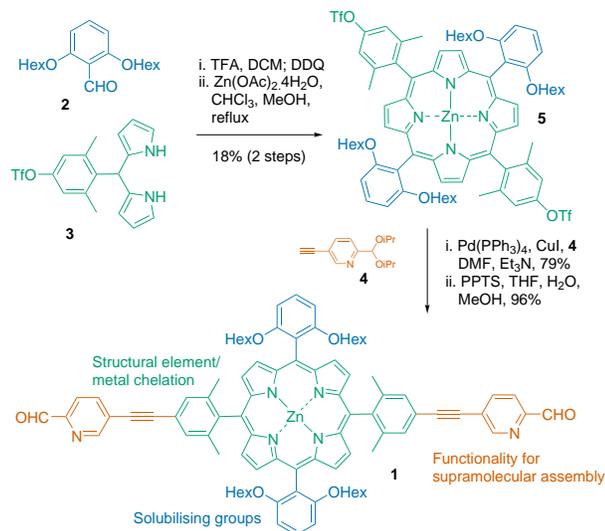


Fig. 1 Preparation of **1** from synthetically accessible starting materials (**2**, **3**, **4** and **5**) that impose the necessary structural and chemical properties for the proposed molecular assemblies.

drance would lead to enhanced solubility. An additional advantage is that **2** was readily available in two steps from resorcinol. Dipyrromethane **3** imparts the required cross-coupling functionality for further elaboration by introduction of a triflate group, and its 2,6-dimethyl substitution pattern prevents regioisomeric scrambling of the porphyrinogen during the synthesis, ensuring the exclusive formation of a single product. Zinc porphyrin **5** was obtained by treating the freebase porphyrin with zinc acetate in chloroform/methanol.

After introduction of the protected pyridyl aldehyde functionalities *via* a Sonogashira coupling with alkyne **4**, the diisopropyl acetals were hydrolysed under mild conditions to afford linear porphyrin dialdehyde **1** in an overall yield of 76% from triflyloxy porphyrin **5**. In contrast, we found that the harsher deprotection conditions required for the analogous dimethyl acetal also led to loss of the chelated zinc ion from the porphyrin under all of the various conditions that were attempted for this reaction (supporting information, section 2).

Once the basic building block had been isolated and characterised, the assembly of the molecular architectures was followed step-by-step to confirm the integrity of our methodology (see supporting information, section 7). The monophenanthroline-copper complex of porphyrinic bisphenanthroline **6** (prepared *via* the Sonogashira coupling between a known substituted phenanthroline¹⁶ and a bis(4-iodophenyl) porphyrin¹¹) was formed by combining **6** with two equivalents of Cu(I)(MeCN)₄PF₆ in DCM (figure 2). Sequential addition of **1** and *p*-anisidine resulted in the generation of pyridyl imine metal chelation motifs that satisfy the remainder of the coordination sphere the Cu⁺ ions, similar to the previously reported phenanthrolines complexes.² The geometric and stoichiometric constraints imposed by this binding motif led to the exclusive formation of the desired square structure.

The resulting square supramolecular grid was characterised by ESI-MS, for which the measured isotope pattern is in excellent

agreement with the simulation (figure 2), confirming the structure under the experimental conditions (see supporting information, section 3).

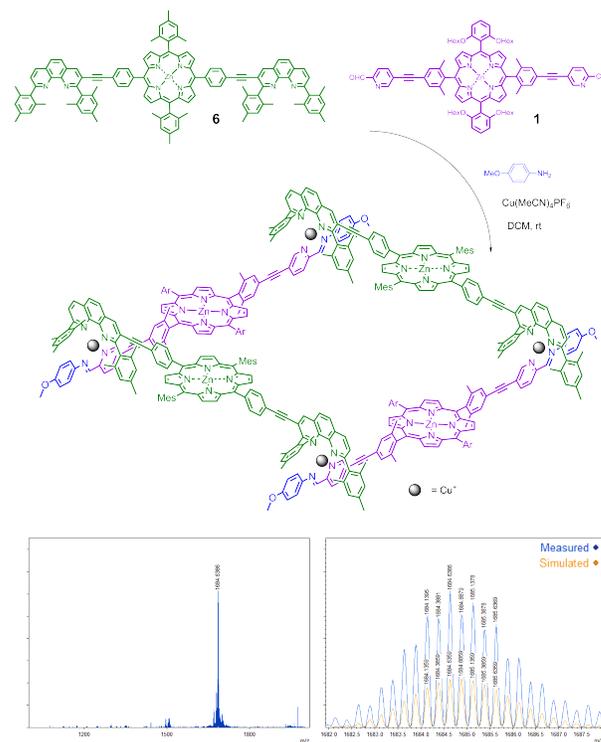


Fig. 2 Formation of a square metallocuprous grid through combination of **1** and **6** with *p*-anisidine and Cu(I). ESI-MS showing the recorded and simulated *m/z* values for the structure shown.

Further evidence for the formation of the assembly in solution is provided by NMR spectroscopy (supporting information, section 4), in which characteristic resonances are identified in response to metal coordination, relative to the free ligand. For example, several through-space interactions are visible in the NOESY spectrum of the grid that are diagnostic of the formation of the Cu(I) pyridyl imine/phenanthroline coordination complex (figure 3, supporting information section 5).

Key through-space interactions confirming the formation of the imine, which then coordinates to the phenanthroline *via* the Cu(I) metal, are the intramolecular correlation between protons 22 and 21 (demonstrating the formation of the imine bond); correlations between mesityl methyl groups 9 with *p*-anisidine protons 20 and 21 (boxes A and B) and 1 with 22 (box C); and between mesityl methyl groups 3 with pyridyl aldehyde proton 25 (box D). Loss of symmetry within the phenanthroline mesityl groups is demonstrated by three different mesityl methyl environments (box G), all of which show through-space correlations with their two adjacent mesityl aromatic protons. Correlations E and F provide intermolecular correlations allowing the identification of porphyrin *meso*-aryl groups.

Porphyrin dialdehyde **1** was also used for the formation of a tetrahedral cage complex through use of Fe(II)(BF₄)₂·6H₂O as the metal salt, in combination with *p*-anisidine for the imine formation in acetonitrile, similar to the structures reported by the

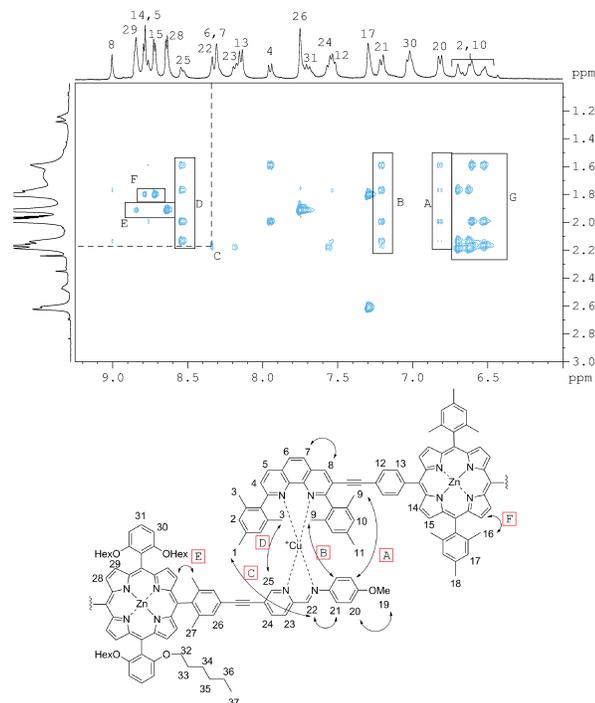


Fig. 3 Region of the NOESY spectrum of the square grid with key correlations marked. The complex is shown in a flattened view for clarity.

Nitschke group.^{17,18} The measured and simulated ESI-MS spectra are in good agreement (figure 4), and the stoichiometry of the M_4L_6 cage is confirmed by the presence of a 7^+ charge peak in the ESI-MS, corresponding to the complex associated with a single PF_6^- counterion (supporting information, section 3). The 1H -NMR spectrum of the assemblies may be complicated due to the possibility of different isomers (supporting information section 6 provides examples for the grid structure), and for this reason the 1H -NMR spectrum of the tetrahedral cage contains more peaks than might be expected in characteristic regions of the spectrum, although key through-space correlations from the imine proton demonstrate the coordination environment around the Fe(II) centre. Tetrahedral complexes such as these have variously been used for encapsulation¹⁹ and catalysis²⁰ and provide a useful structural motif that in assemblies such as our tetrahedral cage allows face specific coordination either inside or outside the cavity with synthetic control over the periphery of the edge components.

In conclusion, linear porphyrin dialdehyde **1** was successfully synthesised using a solubilising porphyrinic core in combination with a mild deprotection of a labile acetal that allowed incorporation of the pyridyl aldehyde moieties. This dialdehyde was used to generate a pair of supramolecular structures: a square grid and a tetrahedron, of mass 6739 Da and 9843 Da respectively, using two different metal-organic coordination motifs (heteroleptic phenanthroline-pyridyl imine Cu(I) complexes and octahedral coordination around an Fe(II) ion respectively). Dialdehyde **1** rep-

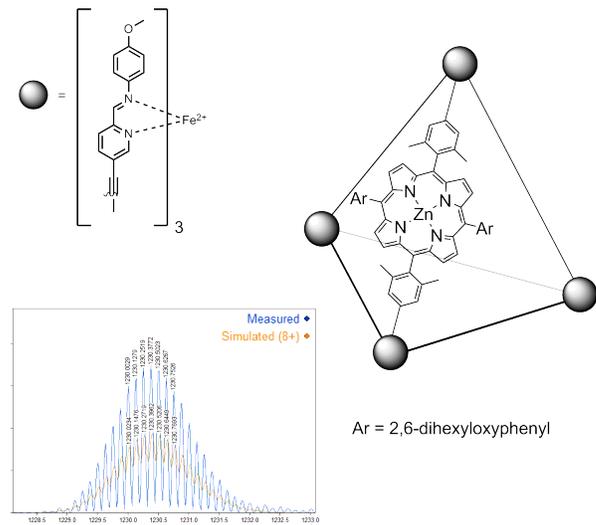


Fig. 4 Formation of a supramolecular tetrahedral cage from **1**, *p*-anisidine and Fe(II).

resents one of only very few reports of porphyrins bearing pyridyl aldehyde functionalities for use in supramolecular systems that are key to our approach for molecular assemblies.

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