



Cite this: *Chem. Commun.*, 2014, 50, 12189

Received 15th July 2014,
Accepted 21st August 2014

DOI: 10.1039/c4cc05465b

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A six-component metallocupramolecular pentagon *via* self-sorting†

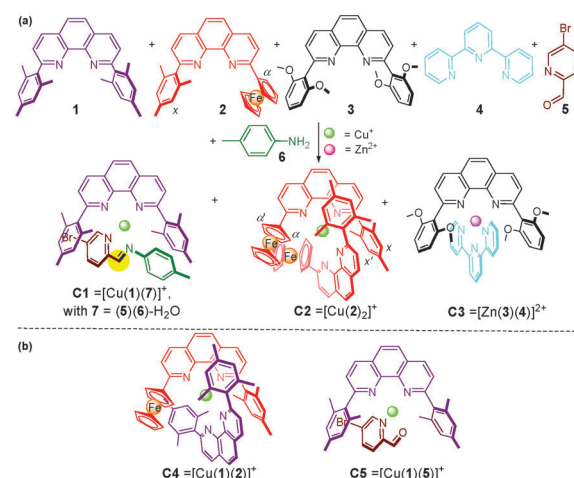
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The six-component pentagon P1 with its five dynamic vertices was conceived on the basis of three different orthogonal metal complex units in a 1-fold complete self-sorting of four linear ligands and two metal ions without using directional bonding.

Nature ingeniously uses self-assembly and self-sorting¹ to orchestrate the correct spatial and functionally active arrangement of multiple building blocks in superstructures that are elementary for life.^{1b} For instance, both the storage and utilisation of a cell's genetic information require a specific base sequence of DNA and thus an error-free base pairing (= self-sorting).² In comparison to this impressive accomplishment, artificial supramolecular self-assembly^{1,3} is presently reaching its limits at three- to five-component nano-architectures^{4,5} with only a single discrete structure being known composed of more components.⁶

Herein, we report on the *de novo* design (Schemes 1 and 2) and synthesis of the unprecedented six-component metallo-supramolecular pentagon **P1**. So far, pentagons have been developed as two- or three-component pentametalacycles^{7,8} predominantly based on the directional bonding⁹ approach rendering the pentagonal architecture a rather difficult target due to a lack of 108° angles at metal centres.^{3a,7} In contrast, the 1-fold complete^{1c} (= integrative)^{4b} self-sorting approach presented here enforces the pentagonal architecture **P1** simply due to the implementation of three different dynamic complexation units **C1–C3** in combination with entropic optimisation (Schemes 1 and 2).

To construct the odd number of vertices in **P1**, we chose to implement one homoleptic **C2** and two heteroleptic cornerstones



Scheme 1 (a) 3-Fold complete self-sorting of the orthogonal complexes **C1–C3** from an eight-component library. (b) Chemical structure of complexes **C4** and **C5**.

C1 and **C3**, the latter complexation units being derived from the HETPHEN (heteroleptic bisphenanthroline complex) and HETTAP (heteroleptic terpyridine and phenanthroline complex) tool box.¹⁰ As a key challenge, the dynamic homoleptic coordination centre **C2** should be fully orthogonal¹¹ to **C1** and **C3**, because otherwise detrimental cross-talk will generate unsolicited structures. To preevaluate the required self-sorting,¹ the archetypical ligands **1–6** representing the interacting termini at the cornerstones were assessed in combination with suitable metal ions (*i.e.* Cu⁺ and Zn²⁺ ions) (Scheme 1).

At the start, we established the 2-fold complete self-sorted formation of both **C1** = [Cu(1)(7)]⁺ and **C3** = [Zn(3)(4)]²⁺ as dynamic HETPHEN¹² and HETTAP complexes from a seven component library (see ESI,† Fig. S21), *i.e.* from **1:3:4:5:6:Cu⁺:Zn²⁺** = **1:1:1:1:1:1:1**, in a similar fashion to what has been observed in a related library.⁶

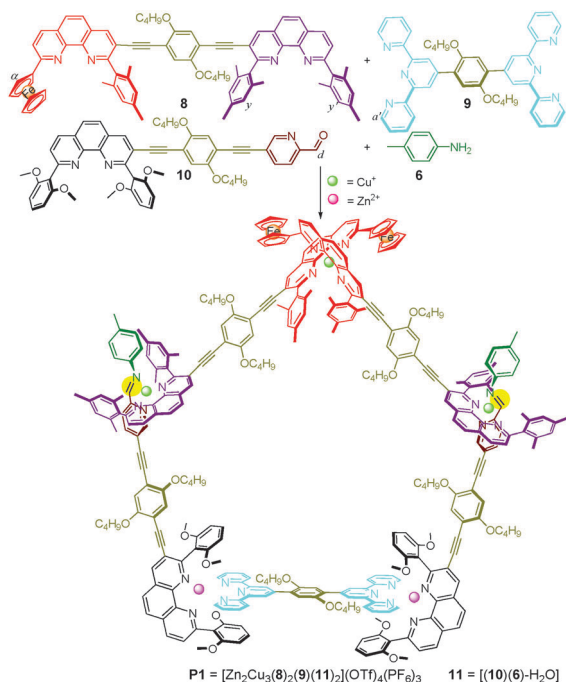
Formation of complex **C2** = [Cu(2)₂]PF₆ (Scheme 1) may seem problematic at first due to the front shielding of 2-ferrocenyl-9-mesityl-[1,10]-phenanthroline (**2**), but the surprisingly high

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† Electronic supplementary information (ESI) available: Experimental procedures and spectroscopic data of all new ligands and complexes, solid state structure of **C2**. CCDC 1013251. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc05465b





Scheme 2 Synthesis of six-component pentagon **P1**.

association constant $\log \beta_{\text{C2}} = 11.0 \pm 0.35$ should warrant clean preparation of **C2** from a 2 : 1 mixture of **2** and $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ in CD_2Cl_2 . Indeed, **C2** formed readily as evidenced by ESI-MS (electrospray ionisation mass spectrometry), multi-nuclear NMR data and single-crystal X-ray analysis (see ESI†). The latter reveals Cu^+ in a distorted tetrahedral geometry with the planes of both ligands being almost perpendicular ($\theta_z = 79^\circ$).¹³ In **C2**, the Cu–N_{phen} bond distances are in the range of 2.051(5)–2.063(6) Å.

Valuable information about **C2** in solution was extracted from the ¹H-NMR. It revealed that the mesityl ($\alpha\text{-H}$, $\delta = 7.06$ ppm) and ferrocenyl ($\alpha\text{-H}$, $\delta = 5.19$ ppm) protons being homotopic in ligand **2** are diastereotopic in **C2** (see ESI,† Fig. S14) as indicated by the two sets at $\delta = 5.60$ and 6.45 ppm (for mesityl, *i.e.* x and $x'\text{-H}$) and $\delta = 5.62$ and 5.01 ppm (for ferrocenyl, α and $\alpha'\text{-H}$).

After proving the clean formation of **C2**, we decided to evaluate 2-fold complete self-sorting^{1c} scenarios in presence of **C2**, *i.e.* the orthogonal formation of **C1** + **C2** and **C2** + **C3** pairs, as a prerequisite for the required 3-fold complete self-sorting (Scheme 1). At first, we surveyed the stoichiometry dependence of the complexation involving a mixture of Cu^+ and ligands **1** & **2**. For example, addition of 1.0 equiv. of $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ to a 1 : 2 mixture of **1** and **2** in CD_2Cl_2 endowed clean formation of a 1 : 1 mixture of **C2** and ligand **1** (see ESI,† Fig. S16). In contrast, an equimolar mixture of **1**, **2** and $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ yielded both **C2** (*ca.* 30%) and **C4** = $[\text{Cu}(\mathbf{1})(\mathbf{2})]\text{PF}_6$ (*ca.* 15%) (Scheme 1b),[‡] suggesting that the complex of both shielded phenanthrolines **1** and **2** is not kinetically impeded, as often observed with other bulky phenanthrolines (see ESI,† Fig. S17).¹⁰ Presumably, the higher front strain in **C4** = $[\text{Cu}(\mathbf{1})(\mathbf{2})]\text{PF}_6$ with regard to that in **C2** drives the selective formation of the **1** + **C2** pair over the alternative **2** + **C4** pair.¹⁴

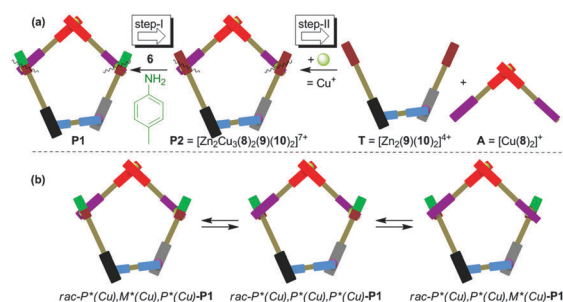
To verify the relative energetics of **C2** and **C4**, we added the slim ligand **5** and $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ (each 1 equiv.) to a mixture of **C2** + **1** (1 : 1) furnishing **C5** = $[\text{Cu}(\mathbf{1})(\mathbf{5})]\text{PF}_6$ (Scheme 1b) without interference with **C2** (see ESI,† Fig. S18), while the alternative pair **C4** + $[\text{Cu}(\mathbf{2})(\mathbf{5})](\text{PF}_6)$ (1 : 1) is not observed. Further addition of 1 equiv. of *p*-toluidine (**6**) to a 1 : 1 mixture of **C2** and **C5** completed the $[\text{Cu}(\mathbf{1})]^+$ assisted formation of the iminopyridine ligand **7** (= $(\mathbf{5})(\mathbf{6})\text{-H}_2\text{O}$),¹² thereby furnishing a mixture of **C2** and **C1** (1 : 1) demonstrating their required orthogonality¹¹ (Scheme 1, Fig. S19, ESI†).

To test the interference-free formation of **C2** and **C3** (Scheme 1), we added 1 equiv. of **C2** to a 1 : 1 : 1 mixture of **3**, **4** and $\text{Zn}(\text{OTf})_2$ and refluxed for 2 h in CH_2Cl_2 . The ¹H-NMR and ESI-MS analysis of the reaction mixture confirmed their orthogonality (see ESI,† Fig. S20). Based on our prior knowledge,⁶ we suggest that the observed selectivity is largely guided by the preferred coordination number of zinc(II) (*i.e.* six) and copper(I) ions (*i.e.* four).^{14,15} Indeed, one more time the additional $\text{Zn} \cdots \text{OME}$ interaction present in **C3**⁶ provides a suitable pseudo-octahedral geometry to the Zn^{2+} ions, thus enthalpically enforcing the observed HETTAP complex **C3**.¹⁴

Considering the above insights, we finally examined the required 3-fold complete self-sorting process^{1c} (Scheme 1) using ligands **1**–**6** as well as Cu^+ and Zn^{2+} ions. To our delight, full orthogonality of the complexes **C1**–**C3** was established through ¹H-NMR and ESI-MS data (see ESI,† Fig. S23 and S41), thus providing a sound basis for the requested orthogonality of the dynamic corners in **P1** (Scheme 2). The observed selectivity is achieved by the precise amalgamation of stoichiometry, steric and electronic effects, π – π interactions, metal-ion coordination specifics and metal-templated reversible imine bond formation in a one-pot process.

Besides the orthogonal formation of five dynamic corner-stones, the clean synthesis of **P1** also requires full positional control, with each of the five metal–ligand corners finding their unique location in **P1** (Scheme 2). Accordingly, the three ditopic ligands **8**–**10** were designed and prepared (see ESI†).

Bearing in mind that the pair **C2** + **C5** is orthogonal as well (**C5** = $[\text{Cu}(\mathbf{1})(\mathbf{5})]\text{PF}_6$, *vide supra*), we chose first to synthesise the pentagon **P2** = $[\text{Zn}_2\text{Cu}_3(\mathbf{8})_2(\mathbf{9})(\mathbf{10})_2](\text{OTf})_4(\text{PF}_6)_3$ as precursor and then to prepare **P1** *via* a post-self-assembly modification approach,¹⁶ *i.e.*, **P2** → **P1**, in presence of *p*-toluidine (**6**) (**P1** : **6** = 1 : 2; Scheme 3a, step-I). This approach also facilitates our



Scheme 3 (a) Retrosynthesis of pentagon **P1**. (b) Cartoon representation of the three different stereoisomers of **P1**.



characterisation of **P1** (*vide infra*). A retrosynthetic analysis of **P2** suggests that it can be viewed as a combination of the angular subunit **A** = [Cu(**8**)₂](PF₆) and the tweezer subunit **T** = [Zn₂(**9**)(**10**)₂](OTf)₄ linked together by two dynamic C5-type copper(i) complexation sites (Scheme 3a, step-II).¹² As a result, we first inspected the reaction between ligand **8** and [Cu(CH₃CN)₄](PF₆) (2 : 1) in CD₂Cl₂ at 25 °C that furnished a clear red solution of **A**. Characterisation of **A** was established from the ESI-MS spectrum that showed one major peak at *m/z* = 2392.2 Da, corresponding to [Cu(**8**)₂]⁺ (Fig. S42, ESI†). A ¹H-NMR analysis of the reaction mixture substantiated the proposed C2-type binding motif (see Schemes 1 and 3a) in **A** by showing two sets of diastereotopically different ferrocenyl (α-H) protons of ligand **8** (Scheme 2), appearing at δ = 5.03 and 5.61 ppm (*cf.* in **C2** δ = 5.01 and 5.62 ppm), see Fig. 1a. In contrast, other diagnostic resonances, *e.g.* *y* and *y'*-H of the 2,9-dimesitylphenanthroline cores appear at a similar region to that of free ligand **8** (*y* and *y'*-H in **A**: δ = 6.92 and 6.94 ppm, and in **8**: δ = 6.96 and 6.98 ppm), thus excluding the possibility of an alternative C4-type (*vide supra*) binding motif in **A**.

The reaction of ligands **9**, **10** and Zn(OTf)₂ (1 : 2 : 2), carried out at reflux temperature for 2 h in CH₂Cl₂/CH₃CN = 4 : 1 to destroy erroneously formed [Zn(terpy)₂]²⁺ complexes,¹⁷ quantitatively produced the HETTAP based tweezer **T** (Scheme 3) that was characterised from ¹H-NMR, ¹H-¹H COSY NMR, and ESI-MS data (see ESI†). For example, the ESI-MS spectrum of the crude reaction mixture exhibited two major peaks at *m/z* = 872.5 and 1382.8 Da for [Zn₂(**9**)(**10**)₂](OTf)_n⁽⁴⁻ⁿ⁾⁺ with *n* = 1, 2, respectively, that clearly supported the characterisation of **T**. The formation of HETTAP complex units, *i.e.* [Zn(**10**_{phenAr2})(**9**_{terpy})]²⁺ at each dynamic corner of **T** was further confirmed by the characteristic upfield shifts of the protons at the phenanthroline (*e.g.* OCH₃: δ = 2.95 and 2.97 ppm, see Fig. 1b) and the terpyridine protons (*e.g.* *a'*-H: δ = 7.63 ppm) in **T**, as compared to those in free **10** (OCH₃: δ = 3.71 and 3.73 ppm) and **9** (*a'*-H: δ = 8.87 ppm).^{5c} Notably, the aldehyde protons in **T** experience no upfield shift in comparison with that in ligand **10** (*e.g.* *d*-H in **T**: δ = 10.02 ppm, and *d*-H in **10**: δ = 10.05 ppm). Thus, the terminal picolin-aldehyde units are available for extra functionalisation.

As conceived, the angular subunit **A** (1 equiv.) with its two free 2,9-dimesitylphenanthroline terminals, tweezer **T** (1 equiv.) with its two picolinaldehyde units, and 2 equiv. of [Cu(CH₃CN)₄](PF₆) were cleanly reacted to the five-component supramolecular pentagon **P2** (Scheme 3a, step-II) after heating to reflux for 2 h in CH₂Cl₂ (see ESI†). The characterisation and purity of the

pentametallacycle **P2** was verified from ESI-MS, ¹H-NMR, ¹H-¹H COSY NMR, DOSY NMR and elemental analysis. For example, the ESI-MS spectrum of the reaction mixture exhibited three major peaks at *m/z* = 1057.6, 1358.5 and 1861.2 Da, for [Zn₂Cu₃(**8**)₂(**9**)(**10**)₂](OTf)_n⁽⁷⁻ⁿ⁾⁺ with *n* = 2, 3 and 4, respectively, that clearly supported the full characterisation of **P2**, while a single diffusion coefficient at *D* = 3.8 × 10⁻¹⁰ m² s⁻¹ in the DOSY NMR provided evidence for its purity (see ESI,† Fig. S33 and S44).

A comparison among the ¹H-NMR spectra of **A**, **T** and **P2** (see ESI,† Fig. S31, Table S1) demonstrates that all the abovementioned diagnostic peaks for **A** and **T** complexation units show up also in identical regions for **P2**, thus confirming the existence of both C3- and C2-type corners in **P2** (see Fig. 1a–c). In addition, the significant upfield shifts of the mesityl protons in **P2** (*y* and *y'*-H: δ = 6.50 and 6.58 ppm) as compared to those in **A** (*y* and *y'*-H: δ = 6.92 and 6.94 ppm) and of aldehyde protons (*d*-H: δ = 9.47 and 9.45 ppm) as compared to those in **T** (*d*-H: δ = 10.02 ppm) further support the formation of two C5-type complex units. The observed 1 : 19 ratio (see ESI†) of the aldehyde protons in **P2** proposes the existence of two§ diastereomers (Scheme 3b, see ESI,† Fig. S30), due to the three stereogenic axes at copper(i) centres.

Finally, the two C5-type complex units in **P2** were interrogated in a post-self-assembly functionalisation as indicated in Scheme 3, step-I. Indeed, the six-component pentametallacycle **P1** with its two constitutionally dynamic imine sites (Scheme 2) was cleanly obtained upon addition of 2 equiv. of **6** to a solution of **P2** in CD₂Cl₂, as evidenced by ESI-MS (*m/z* = 1093.2, 1403.1 and 1920.6 Da for [Zn₂Cu₃(**8**)₂(**9**)(**11**)₂](OTf)_n⁽⁷⁻ⁿ⁾⁺ with *n* = 2, 3 and 4, respectively), ¹H-NMR (Fig. 1d), DOSY NMR (*D* = 3.2 × 10⁻¹⁰ m² s⁻¹) and elemental analysis (see ESI†). To our satisfaction, full integrative self-sorting (Scheme 2) was equally effective when we examined the formation of **P1** from its precursor ligands **6**, **8**–**10** and metal ions (Cu⁺ and Zn²⁺) at correct stoichiometric onset (see ESI†). MM⁺ force field computations on **P1** and **P2** provided some insight in their structure as scalene pentagons. Taking the metal–metal distance as a measure, the five corners of **P2** are separated by 1.51, 1.68, 1.74, 1.74 and 1.76 nm in the energy minimised structure and by 1.51, 1.68, 1.74, 1.74 and 1.75 nm in **P1** (see ESI†).

In summary, the present study describes the clean and 1-fold complete (integrative) self-sorted synthesis of the unprecedented five- and six-component supramolecular pentagons **P1** & **P2**. The generality of the present approach, devoid of control through directional bonding, is currently under investigation for the construction of 3D structures.

We are indebted to the DFG and Universität Siegen for financial support and to Dr S. Pramanik/Universität Siegen for his help in the synthesis of ligands **2** and **16** (precursor of **8**).

Notes and references

‡ In the ¹H-NMR spectrum (see ESI†), we observed additional signals representing the free ligand **1** (*ca.* 30%) and [Cu(**1**)](PF₆) (*ca.* 25%). Thus, the mixture contains **C2** : **C4** : **1** : [Cu(**1**)](PF₆) = 30 : 15 : 30 : 25.

§ Considering the structures, the isomers (*P**, *M**, *P**) and (*P**, *P**, *M**) could be magnetically equivalent, thus one cannot exclude the formation of all three possible diastereomers.

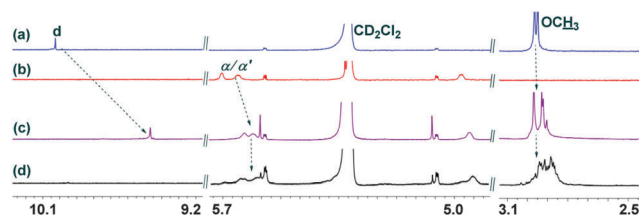


Fig. 1 Partial ¹H NMR spectrum for comparison (400 MHz, CD₂Cl₂, 298 K) of (a) **T**, (b) **A**, (c) **P2** and (d) **P1**.



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- 17 $[\text{Zn}(\text{terpy})_2]^{2+}$ forms in rivalry to the desired HETTAP complexes.

