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

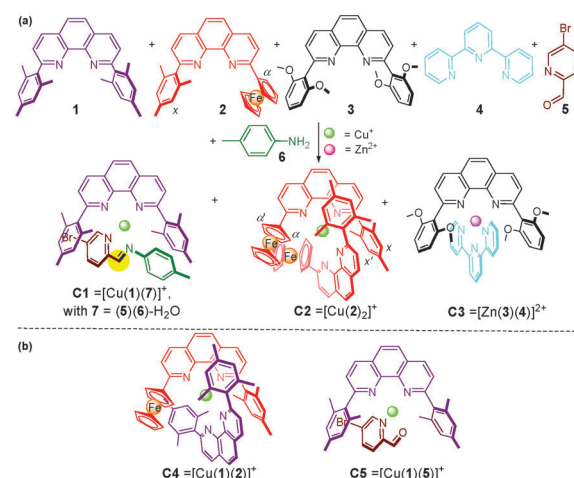
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The six-component pentagon **P1 with its five dynamic vertices was conceived on the basis of three different orthogonal metal complex units in a 1-fold complete self-sorting of four linear ligands and two metal ions without using directional bonding.**

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

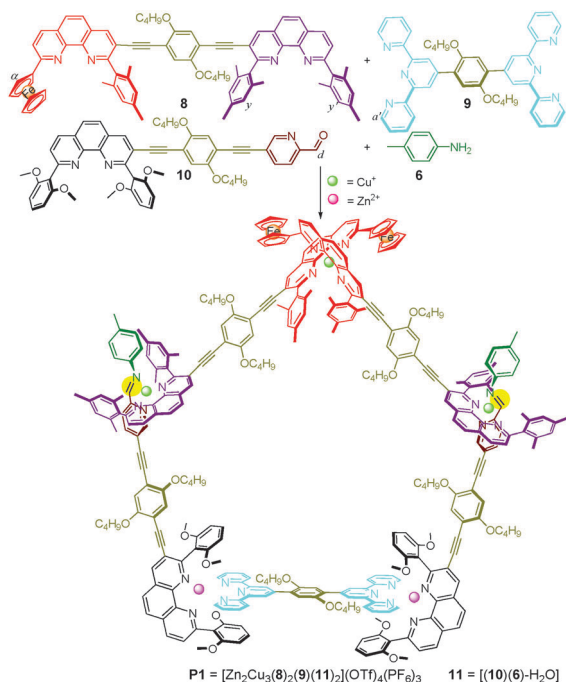
Formation of complex **C2** = [Cu(2)₂]PF₆ (Scheme 1) may seem problematic at first due to the front shielding of 2-ferrocenyl-9-mesityl-[1,10]-phenanthroline (**2**), but the surprisingly high

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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 ($x\text{-H}$, $\delta = 7.06$ 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

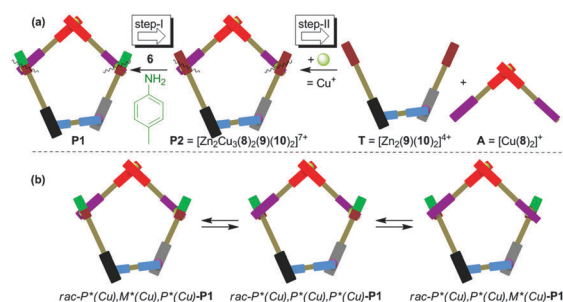
To verify the relative energetics of **C2** and **C4**, we added the slim ligand **5** and $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ (each 1 equiv.) to a mixture of **C2** + **1** (1 : 1) furnishing **C5** = $[\text{Cu}(\mathbf{1})(\mathbf{5})]\text{PF}_6$ (Scheme 1b) without interference with **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.

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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.

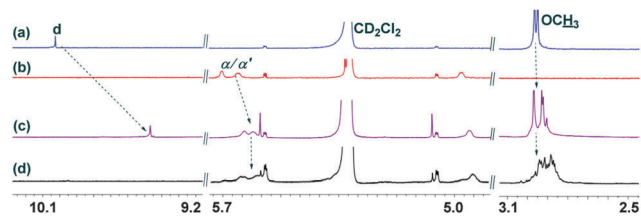


Fig. 1 Partial ¹H NMR spectrum for comparison (400 MHz, CD₂Cl₂, 298 K) of (a) **T**, (b) **A**, (c) **P2** and (d) **P1**.



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

