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

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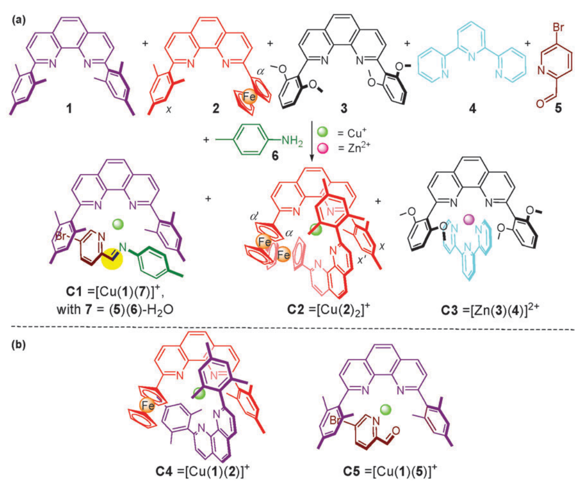
The six-component pentagon P1 with its five dynamic vertices was conceived on the basis of three different orthogonal metal complex units in a 1-fold completive self-sorting of four linear ligands and two metal ions without using directional bonding.

Nature ingeniously uses self-assembly and self-sorting[1] 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 pentametallacycles[7,8] pre-dominantly based on the directional bonding[9] 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 completive[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 completive 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 orthogonal[11] 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 Zn^{2+} ions) (Scheme 1).

At the start, we established the 2-fold completive self-sorted formation of both **C1** = $[Cu(\mathbf{1})(\mathbf{7})]^+$ and **C3** = $[Zn(\mathbf{3})(\mathbf{4})]^{2+}$ as dynamic HETPHEN[12] and HETTAP complexes from a seven component library (see ESI,† Fig. S21), *i.e.* from $\mathbf{1}:\mathbf{3}:\mathbf{4}:\mathbf{5}:\mathbf{6}:Cu^+:Zn^{2+} = 1:1:1:1:1:1:1$, in a similar fashion to what has been observed in a related library.[6]

Formation of complex **C2** = $[Cu(\mathbf{2})_2]PF_6$ (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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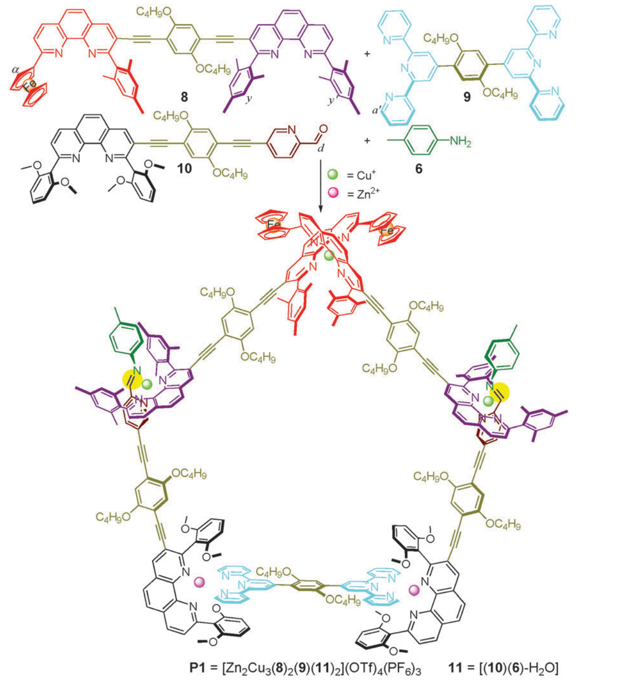


Scheme 2 Synthesis of six-component pentagon **P1**.

association constant log $\beta_{\mathbf{C2}}$ = 11.0 ± 0.35 should warrant clean preparation of **C2** from a 2 : 1 mixture of **2** and $[Cu(CH_3CN)_4]PF_6$ 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 (θ_z = 79°).[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 ^{1}H-NMR. It revealed that the mesityl (*x*-H, δ = 7.06 ppm) and ferrocenyl (α-H, δ = 5.19 ppm) protons being homotopic in ligand **2** are diastereotopic in **C2** (see ESI,† Fig. S14) as indicated by the two sets at δ = 5.60 and 6.45 ppm (for mesityl, *i.e.* *x* and *x*′-H) and δ = 5.62 and 5.01 ppm (for ferrocenyl, α and α′-H).

After proving the clean formation of **C2**, we decided to evaluate 2-fold completive 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 completive 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 $[Cu(CH_3CN)_4]PF_6$ 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 $[Cu(CH_3CN)_4]PF_6$ yielded both **C2** (*ca.* 30%) and **C4** = $[Cu(\mathbf{1})(\mathbf{2})]PF_6$ (*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** = $[Cu(\mathbf{1})(\mathbf{2})]PF_6$ with regard to that in **C2** drives the selective formation of the **1** + **C2** pair over the alternative **2** + **C4** pair.[14]

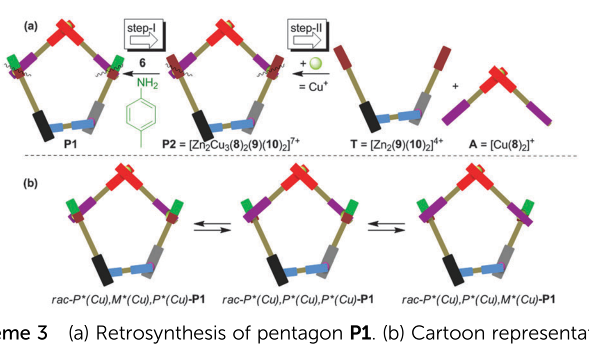
To verify the relative energetics of **C2** and **C4**, we added the slim ligand **5** and $[Cu(CH_3CN)_4]PF_6$ (each 1 equiv.) to a mixture of **C2** + **1** (1 : 1) furnishing **C5** = $[Cu(\mathbf{1})(\mathbf{5})]PF_6$ (Scheme 1b) without interference with **C2** (see ESI,† Fig. S18), while the alternative pair **C4** + $[Cu(\mathbf{2})(\mathbf{5})](PF_6)$ (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 $[Cu(\mathbf{1})]^+$ assisted formation of the iminopyridine ligand **7** (= (**5**)(**6**)–H_2O),[12] thereby furnishing a mixture of **C2** and **C1** (1 : 1) demonstrating their required *orthogonality*[11] (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 $Zn(OTf)_2$ and refluxed for 2 h in CH_2Cl_2. The ^{1}H-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 Zn···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 completive 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 ^{1}H-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 cornerstones, 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** = $[Cu(\mathbf{1})(\mathbf{5})]PF_6$, *vide supra*), we chose first to synthesise the pentagon **P2** = $[Zn_2Cu_3(\mathbf{8})_2(\mathbf{9})(\mathbf{10})_2](OTf)_4(PF_6)_3$ 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**)$_2$](PF$_6$) and the tweezer subunit **T** = [Zn$_2$(**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(CH$_3$CN)$_4$]PF$_6$ (2 : 1) in CD_2Cl_2 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 ^{1}H-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 CH_2Cl_2/CH_3CN = 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 ^{1}H-NMR, ^{1}H–^{1}H 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 [Zn$_2$(**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**$_{\text{phenAr2}}$)(**9**$_{\text{terpy}}$)]$^{2+}$ at each dynamic corner of **T** was further confirmed by the characteristic upfield shifts of the protons at the phenanthroline (*e.g.* OC*H*$_3$: 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** (OC*H*$_3$: 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 picolinaldehyde 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(CH$_3$CN)$_4$]PF$_6$ were cleanly reacted to the five-component supramolecular pentagon **P2** (Scheme 3a, step-II) after heating to reflux for 2 h in CH_2Cl_2 (see ESI†). The characterisation and purity of the pentametallacycle **P2** was verified from ESI-MS, ^{1}H-NMR, ^{1}H–^{1}H 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 [Zn$_2$Cu$_3$(**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 $D = 3.8 \times 10^{-10}$ m^2 s^{-1} in the DOSY NMR provided evidence for its purity (see ESI,† Fig. S33 and S44).

A comparison among the ^{1}H-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 CD_2Cl_2, as evidenced by ESI-MS (*m*/*z* = 1093.2, 1403.1 and 1920.6 Da for [Zn$_2$Cu$_3$(**8**)$_2$(**9**)(**11**)$_2$] (OTf)$_n^{(7-n)+}$ with *n* = 2, 3 and 4, respectively), ^{1}H-NMR (Fig. 1d), DOSY NMR ($D = 3.2 \times 10^{-10}$ m^2 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 Zn^{2+}) 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 completive (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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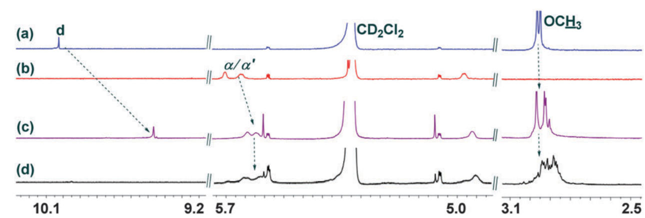

Fig. 1 Partial ^{1}H NMR spectrum for comparison (400 MHz, CD_2Cl_2, 298 K) of (a) **T**, (b) **A**, (c) **P2** and (d) **P1**.

Notes and references

‡ In the ^{1}H-NMR spectrum (see ESI†), we observed additional signals representing the free ligand **1** (*ca.* 30%) and [Cu(**1**)](PF$_6$) (*ca.* 25%). Thus, the mixture contains **C2** : **C4** : **1** : [Cu(**1**)](PF$_6$) = 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.

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