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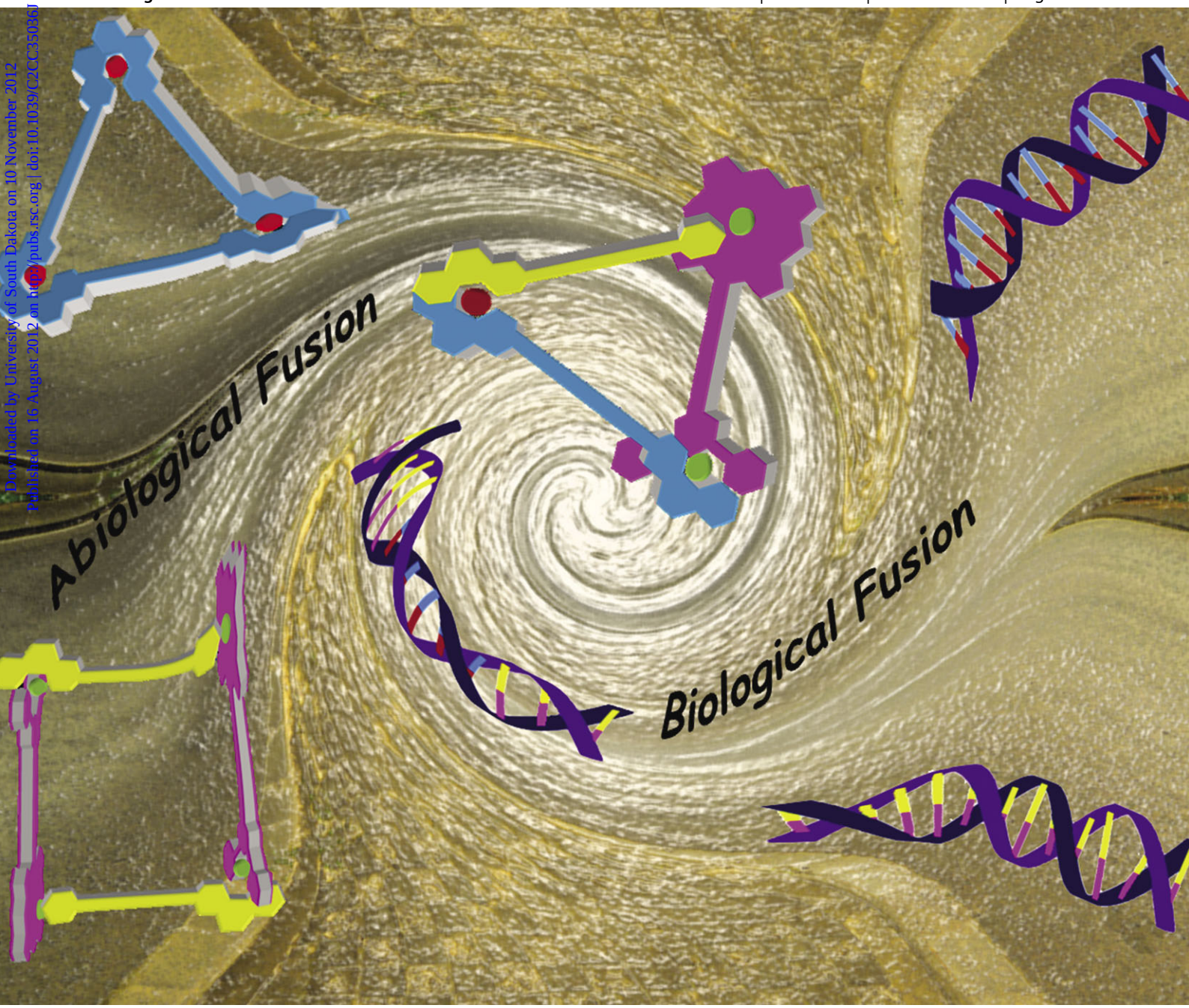

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Michael Schmittel *et al.*

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Spontaneous and catalytic fusion of supramolecules†

Manik Lal Saha, Susnata Pramanik and Michael Schmittel*

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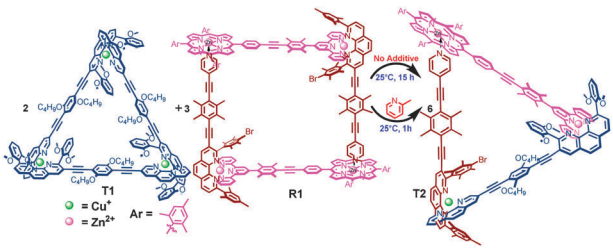
Using principles of *completive* and *integrative self-sorting*, a clean supramolecule-to-supramolecule transformation is realised that involves fusion of a 3-component rectangle and a 2-component equilateral triangle into a 5-component scalene triangle. While the spontaneous process takes 15 h at 25 °C, the catalytic transformation is completed within 1 h.

Gene shuffling, *i.e.* combination of dissimilar genes to create novel and improved recombinant genes, is one of the key mechanisms through which new genes emerge in Nature.[1] In fact, *gene shuffling* is a highly effective mechanism for innovation because it can generate new genes with structures and functions drastically different from those of the parental progenitors. Similarly, the use of an *evolutionary mechanism* may allow us to design and fabricate intricate new aggregates starting from simple self-assemblies, *i.e.* eventually from libraries of supramolecular assemblies. However, such a protocol inherently demands, in contrast to the typical bottom-up approach, a clean supramolecule-to-supramolecule transformation[2] with at least two distinct self-assemblies merging into a new assembly *via* shuffling of their components, a process described only once to date. In an example reported by Stang *et al.*[3] two homoleptic 2-component architectures merge into a heteroleptic 3-component system upon heating. While this reaction may be considered somewhat analogous to gene shuffling, biological processes usually occur under conditions that are tightly regulated, often by enzymatic action. In order to account for regulation, we report herein not only on the spontaneous but also catalytic fusion of two supramolecular assemblies (Scheme 1). Explicitly, the two distinct and dynamic supramolecules **T1** and **R1** endure spontaneous and catalytic reshuffling of their components upon mixing and evolve as the 5-component scalene triangle **T2**, a rare topology.[4] Clearly, the diversity and complexity of **T2** are much increased due to the enlarged number of different components and reversible orthogonal interactions.[5]

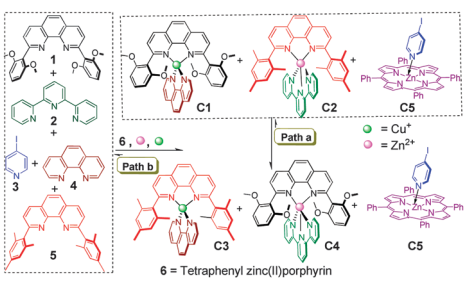
At the start, using an approach based on *completive*[4] and *integrative* self-sorting,[6,7] we decided to preassemble the



Scheme 1 Clean supramolecular fusion of **T1** and **R1**.

mononuclear cornerstones in 'disfavoured' combinations, *e.g.* in **T1** and **R1**. Upon mixing, both aggregates should be strongly biased to reshuffle their components and reassemble in their thermodynamically 'favoured' pair, as allocated in **T2**. In order to set up the high-fidelity self-sorting required in Scheme 1, we first interrogated path a in Scheme 2. To check for alternative combinations, we prepared separately the pure complexes **C1** = [Cu(**1**)(**4**)](PF$_6$) and **C2** = [Zn(**2**)(**5**)](OTf)$_2$ using the HETPHEN[8] and HETTAP[9] complexation approach. Upon their mixing in a 1 : 1 ratio in MeCN at 25 °C, clean formation of **C3** = [Cu(**4**)(**5**)](PF$_6$) and **C4** = [Zn(**1**)(**2**)](OTf)$_2$ is observed after *ca.* 30 min (Scheme 2, path a), as evidenced by ^{1}H-NMR analysis (Fig. S5, ESI†). The ease of component shuffling indicates that the kinetic barrier for such a process is not too high. As expected, the thermodynamically driven self-sorting is similar to one of the free components,[4c] as shown in path b (Scheme 2). Component exchange of **C1** and **C2** is equally successful in the presence of the preassembled pyridine–zinc porphyrin complex **C5** = [(**3**)(**6**)] (Scheme 2, path a). Re-assembly of the 8-component library to **C3–C5** is thus warranted irrespective of the preassembled state of ligands **1–5**, two metals (Cu^+ and Zn^{2+}) and zinc porphyrin **6**.

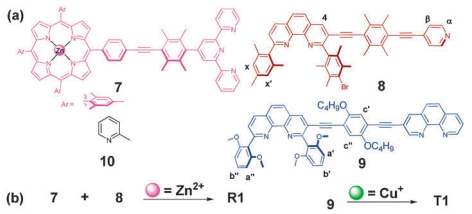
The flawless error correction between two heteroleptic complexes, as represented above, encouraged us to engineer a supramolecule-to-supramolecule fusion (Scheme 1). In order



Scheme 2 Reshuffling of 3^{2,3,3}-fold(8) *completive* library.[4c]

Center of Micro and Nanochemistry and Engineering, Organische Chemie I, Universität Siegen, Adolf-Reichwein-Str. 2, D-57068 Siegen, Germany. E-mail: schmittel@chemie.uni-siegen.de; Tel: +49 271740-4356

† Electronic supplementary information (ESI) available: Experimental procedures and spectroscopic data for ligand **7** and all complex (**T1**, **T2**, **R1**) assemblies. See DOI: 10.1039/c2cc35036j



Scheme 3 (a) Chemical structures of ligands **7–10**. (b) Synthesis of rectangle **R1** and equilateral triangle **T1**.

to establish positional control, we installed the ligands **2** and **6** as termini of the new porphyrin–terpyridine hybrid **7**, readily accessible *via* Sonogashira cross-coupling. Along known procedures, the coordination units of **3** and **5** were combined within the phenanthroline–pyridine hybrid **8**[4c] and the complexing properties of **1** and **4** in the unsymmetrical bisphenanthroline **9**.[4b] For all ligands, spacers were chosen to render the building blocks **7–9** unequal in length (Scheme 3a).

In a first experiment, ligands **7** and **8** as well as $Zn(OTf)_2$ were mixed in a 1 : 1 : 1 ratio and refluxed for 1 h in MeCN–DCM (1 : 8) (Scheme 3b). The reaction mixture was characterised without any further purification by ^{1}H-NMR, ^{1}H–^{1}H COSY, diffusion-ordered spectroscopy (DOSY), elemental analysis, and electrospray ionisation mass spectrometry (ESI-MS). All spectroscopic data confirm clean formation and integrity of rectangle **R1** (Fig. S25, ESI†), a discrete 3-component nanostructure. ^{1}H-NMR shows a diagnostic upfield shift of the mesityl protons in **R1** (x, x', δ = 6.30 ppm) as compared to those in free **8** (δ = 6.92 ppm).[4c] In light of the HETTAP concept, an intimate π–π stacking between the mesityl groups of **8** and the terpyridine of **7** is responsible for such a shift in the ^{1}H-NMR of **R1**.[9] Furthermore, the pyridine protons (α, β) of **8** in **R1** experience upfield shifts from 8.61 to 3.41 ppm and from 7.38 to 5.62 ppm, respectively, that are diagnostic for pyridine protons upon axial coordination to a zinc porphyrin.[8b] ^{1}H-NMR peak assignments were corroborated by COSY experiments (Fig. S11, ESI†). The ESI-MS of **R1** further substantiates the structure by showing signals m/z = 1011.7 and 1399.0 (Fig. S19, ESI†) corresponding to $[Zn_2(\mathbf{7})_2(\mathbf{8})_2]^{4+}$ and $[Zn_2(\mathbf{7})_2(\mathbf{8})_2](OTf)^{3+}$, respectively. Finally, exclusive formation of **R1** was confirmed by a single diffusion coefficient in the DOSY NMR (Fig. S14, ESI†).

In another experiment, we studied the coordination behaviour of ligand **9** and $[Cu(CH_3CN)_4]PF_6$ when mixed in a 1 : 1 ratio and refluxed for 1 h in MeCN–DCM (4 : 1) to furnish a clear red solution of **T1** (Scheme 3b and Fig. S26 in ESI†). The product was characterised by ESI-MS, ^{1}H-NMR, DOSY, and elemental analysis. The ESI-MS spectrum exhibits two major peaks at m/z = 962.0, 1515.7 for $[Cu_3(\mathbf{9})_3]^{3+}$, $[Cu_3(\mathbf{9})_3](PF_6)^{2+}$ in full accord with assembly **T1** (Fig. S20, ESI†). The experimental isotopic splitting pattern of the major peak is in full agreement with its calculated splitting pattern. Importantly, no other peak was noticed in the spectral region between 150 and 2000 Da. ^{1}H-NMR and DOSY NMR further support the assignment. Exclusive formation of **T1** in solution was confirmed by a single diffusion coefficient in the DOSY NMR. To substantiate the clean self-assembly process, we carefully interrogated the ^{1}H-NMR of **T1**. It is complicated due to the existence of two diastereomers in a 1 : 3 ratio, as a result of three stereogenic cornerstones of the type $[Cu(\mathbf{9}_{phen})(\mathbf{9}_{phenAr2})]^+$.[10] Notably, the c'-H and c''-H (Scheme 3) appear as 4 singlets with a ratio 1 : 1 : 1 : 1. Apparently, in one of the diastereomers all 3 ligands show up in a single set due to its C_3 symmetry (*P*,*P*,*P*), while in the second isomer (*P*,*P*,*M*) the protons emerge as three distinct sets (1 : 1 : 1) (Fig. S27, ESI†). Other valuable information arises from the ^{1}H-NMR signals of the OMe protons belonging to ligand **9**. All four OMe protons of ligand **9** in **T1** appear as separate singlets due to their diastereotopicity caused by the stereogenic $[Cu(\mathbf{9}_{phen})(\mathbf{9}_{phenAr2})]^+$ units.[10]

The collected spectroscopic evidence convincingly establishes the integrity of both **T1** and **R1** in solution. **T1** and **R1** are thermodynamically favoured over any larger structures because they constitute discrete entities at the lowest possible entropic costs while realising maximum site occupancy.

Finally, in order to test our concept presented in Scheme 1, **T1** and **R1** were mixed in a 2 : 3 ratio and kept under NMR surveillance for 15 h at 25 °C. The progress of the reaction was monitored in 0.5 h intervals (Fig. S9, ESI†) and may be best judged by characteristic resonances of **R1** (ligand **8**, 4-H, and x, x') and **T1** (ligand **9**, b', b''). They reveal that the spectrum gradually becomes simpler, with full convergence into a single set after 15 h. Additionally, a single diffusion coefficient obtained in the DOSY provides unambiguous evidence for the clean formation of a single product, identified as **T2** below.

In order to examine the connectivity of the ligands in the putative **T2**, we paid special attention to several characteristic proton resonances in the ^{1}H-NMR. For example, the 0.44 and 0.52 ppm downfield shifts of b' and b''-H (from 6.52–6.38 ppm in **T1** to 6.96 and 6.90 ppm in **T2**) are indicative of a HETTAP complex between **7** and **9** (Scheme 1 and Fig. 1). In contrast to **R1**, the pyridine β-proton in **T2** experiences a slight downfield shift of 0.26 ppm (from 5.62 to 5.88 ppm), indicating the survival of the pyridine–zinc porphyrin interaction in solution. Similar to **T1**, the suggested structure requires that **T2** is chiral, due to the stereogenic $[Cu(\mathbf{9}_{phen})(\mathbf{8}_{phenAr2})]^+$ unit.[4c,10] As a result, the mesityl protons x and x'-H of ligand **8** being enantiotropic in **R1** become diastereotopic in **T2**. This is corroborated by the existence of two singlets at 6.15 and 5.97 ppm in **T2**. The 0.15 and 0.33 ppm upfield shift (from 6.30 ppm in **R1**) of the two mesityl protons (x and x') in **T2** also supports the presence of a $[Cu(\mathbf{9}_{phen})(\mathbf{8}_{phenAr2})]^+$ HETPHEN coordination center. As further support, four singlets for the diastereotopic methoxy protons (OMe) appear at 2.73–2.83 ppm, a range typical for HETTAP complexes.[4a]

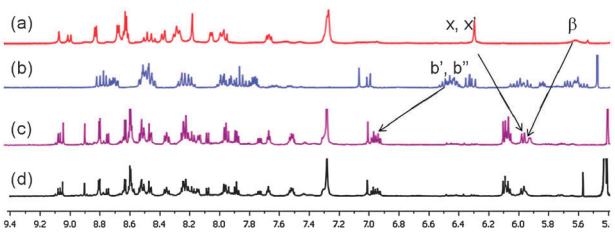


Fig. 1 Comparison of partial ^{1}H-NMR spectra of (a) **R1** (CD_2Cl_2), (b) **T1** (CD_3CN), (c) **T1** : **R1** (2 : 3) (CD_3CN : CD_2Cl_2 = 4 : 1) after 16 h at 25 °C, and (d) **T1** : **R1** (2 : 3) (CD_3CN : CD_2Cl_2 = 4 : 1) with **10** (10 mol% with respect to **R1**) after 1.5 h at 25 °C.

The fusion was additionally followed by ESI-MS. Upon mixing **T1** and **R1**, initially only the starting materials are observable in the ESI-MS spectra (Fig. S21, ESI†). However, over time they convert to **T2**. Finally, after 15 h, the ESI-MS spectrum exhibits no more signals corresponding to **T1** or **R1**, but only peaks being in full agreement with the newly formed triangle **T2** (Fig. S22, ESI†). For example, the signals at m/z = 995.7 and 1565.6 Da represent $[ZnCu(\mathbf{7})(\mathbf{8})(\mathbf{9})]^{3+}$ and $[ZnCu(\mathbf{7})(\mathbf{8})(\mathbf{9})](PF_6)^{2+}$, respectively. The experimental isotopic splitting of all major peaks agrees with the calculated one.

Existence of the $[Cu(\mathbf{9}_{phen})(\mathbf{8}_{phenAr2})]^{+}$ unit in one of the metal corners of **T2** was also interrogated by differential pulse voltammetry (DPV) probing the Cu^{+} oxidation wave. A single oxidation wave at 0.70 V_{SCE} in **T2** (Fig. S24, ESI†) confirms the presence of only one type of copper(I) complex, pointing persuasively to the formation of $[Cu(\mathbf{9}_{phen})(\mathbf{8}_{phenAr2})]^{+}$.[4c] A combination of ESI-MS, ^{1}H-NMR, DPV, DOSY, and elemental analysis thus unambiguously provides evidence for the clean formation of scalene triangle **T2**.

All attempts to obtain single crystals of **T2** met with failure. Fortunately, MM^{+} force field computations on **T2** provide some insight into the scalene triangular structure. Taking the metal–metal distance as a measure, the three metal corners of **T2** are separated by 1.70, 1.86, and 1.95 nm in the energy minimised structure (Fig. S28, ESI†), nicely illustrating the geometrically scalene arrangement of **T2**.

In an effort to accelerate the process we anticipated that labilisation of metal–ligand bonds[11] may shorten the time of the fusion. We envisaged 2-methylpyridine (**10**) to be a suitable candidate because the methyl group should prevent any strong binding to the zinc porphyrin unit of **7**.[12] Indeed, in a control experiment, 10 mol% of **10** (related to the initial amount of **R1**) was added to a 2 : 3 mixture of **T1** and **R1** at 25 °C and the reaction monitored by NMR. To our delight, the transformation was effected in *ca.* 1 h, as suggested by diagnostic shifts in the NMR signals (Fig. 1). Clearly, the spectrum in Fig. 1c resembles very much the spectrum in Fig. 1d. To further prove the integrity of **T2** generated in the catalytic process, we measured its ESI-MS. We only observe peaks for **T2**, indicating that **10** does not lead to destruction of the triangular assembly (Fig. S23, ESI†).

The above fusion of supramolecules comprises several distinct chemical events, including (i) self-correction under thermodynamic control; (ii) favoured pair-selection due to high-fidelity self-sorting; and (iii) acceleration of a supramolecular fusion reaction *via* labilisation of the metal–ligand bonds.

In conclusion, the present strategy based on *completive* and *integrative* self-sorting describes a viable means for constructing topologically demanding supramolecules starting from simpler supramolecular aggregates. As a demonstration we describe herein the shuffling and recombination of components from the 2-component equilateral triangle **T1** and 3-component rectangle **R1** to the 5-component scalene triangle **T2**. To the best of our knowledge, the fabrication of a clean multicomponent ($n > 3$) assembly by just mixing two assemblies in appropriate stoichiometry is without precedence. Furthermore, the supramolecular fusion is readily catalysed.

In our view, a supramolecular fusion is more valuable than a bottom-up self-assembly of all constituents, as both precursor supramolecules already represent sophisticated chemical information. While **T1** is fully defined by the length of one side, description of **R1** requires two inputs and that of **T2** at least three inputs, *i.e.* three different lengths. The fusion thus not only involves a first step toward evolution of supramolecular architectures but equally to higher information content.[5c]

Looking more on molecular details, the reported example has clearly some analogy to *gene-shuffling*, chiefly to *indel* mutations (Fig. S29, ESI†)[1b] because **T2** forms by insertion and deletion of subunits that are delivered by **T1** and **R1**. Efforts to extend this strategy to multi-stage adaptive assemblies are underway in our laboratory.

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