

# Template-free multicomponent coordination-driven self-assembly of Pd(II)/Pt(II) molecular cages

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Recent years have seen a tremendous increase in the interest for constructing hollowed-out molecular frameworks, for their potential uses. Metal–ligand coordination-driven self-assembly has provided multitudes of opportunities in the formation of molecular architectures of desired shapes and sizes, with the help of the information already coded in the components. This article summarizes the recent developments in the construction of multicomponent molecular cages through this process, with a focus on the decreasing relevance of templates, and use of these systems in catalysis/host–guest chemistry.

## 1. Introduction

As chemists, we can appreciate (perhaps better than others can!) our ignorance of the way the biological multicomponent (molecules and ions) systems self-organise themselves under

the pressure of coded information and subtle electromagnetic forces to serve specific functions. For example, the tomato bushy stunt virus and the rhinovirus incorporate three and four different subunits, respectively, that are held together by selective self-assembly.<sup>1</sup> Similarly, in the proteasome structure of the yeast *Saccharomyces cerevisiae*, seven distinctly different proteins are self-organized in a highly integrated and ordered fashion.<sup>2</sup> Naturally, the investigation of abiological multicomponent systems that can mimic such biological systems

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(in structure or function or both) is appealing to a synthetic chemist.

This fascination led many researchers to find answers to questions about these complex chemical systems, which are mathematically intractable (so far!), by stripping down the problems of weak interactions leading to self-organised systems into manageable (in lab or computers) proportions. It is not just our language that classifies the assembly of more than two components as 'multicomponent', the chemical systems comprising of just three different structural motifs that can interact and self-assemble can really generate a large number of composite systems. But, if your goal is to organize them in a specific manner into a single large assembly exclusively, the challenges are 'multiple' indeed.

Metal-ligand coordination-driven self-assembly has been successfully used in preparing two-component 2D and 3D complexes (with desired shapes and sizes) based on the information coded in individual components.<sup>3</sup> In this field, a few successful attempts have also been made to assemble multiple components in a selective manner. Using topological information, Sauvage *et al.*<sup>4a-d</sup> and Lehn *et al.*<sup>4e</sup> have been able to steer the selective self-assembly of multicomponent pseudorotaxanes. Schmittel *et al.*<sup>5</sup> and Kobayashi *et al.*<sup>6</sup> were successful in exploiting the steric constraints of different components to control the multicomponent selective self-assembly. In fact, Schmittel's group reported the formation of a five-component supramolecular trapezoid and seven-component scalene through integrative self-sorting.<sup>6</sup> However, significant synthetic efforts are necessary for the incorporation of topological or steric information into molecular components.<sup>4-6</sup>

Remarkably, though these achievements are in terms of generating intricate structures, in recent years the attention has shifted to producing more practical and functional hollow 3D architectures using the principles of coordination-driven self-assembly. Although, recently, a few covalent or dative bond assisted hollow organic cages have been reported, these compounds suffer from the limitations (with respect to potential applications) of low stability and/or low solubility.<sup>7</sup> Self-assembled 3D prismatic structures with different types and sizes of cavities have found potential applications in selective guest encapsulation and recognition, cavity induced catalysis and as micro or nano reaction vessels, chemosensing and even storage (gas, fuel *etc.*).<sup>3,8</sup> Therefore, new multicomponent prismatic cage complexes provide a huge incentive for functional studies, because of the opportunities to assemble varied molecular components into a single framework.

Fujita's group, in a pioneering work, demonstrated the template assisted facile and selective self-assembly of 3D trigonal prisms by mixing palladium(II) acceptors with ditopic (acting as pillars) and trioptic pyridyl ligands (acting as roof-floor).<sup>9</sup> Such templates not only help in speeding-up the assembly process, but also guide the selective formation of a single multicomponent cage without other possible by-products. Upon changing the nature and length of the pillars in the assembly they showed various functions of these prismatic complexes, which can be mainly attributed to the weak interactions of various molecular

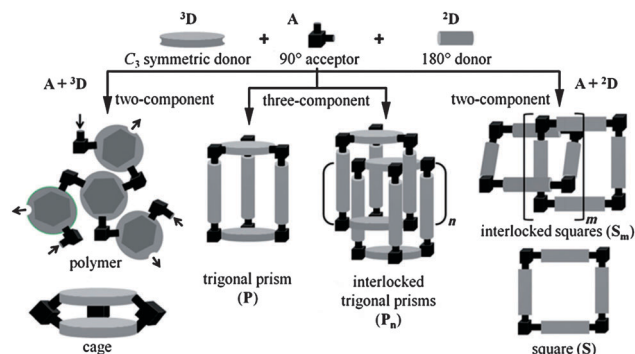
guests with the aromatic roof-floor.<sup>9</sup> However, very recently Stang *et al.*<sup>10</sup> and Mukherjee *et al.*<sup>11</sup> have independently reported a few remarkable examples of multicomponent prismatic structures of varied shapes and sizes without using any templates.

This article intends to provide an overview of the recent progress made by these groups in assembling multiple components into designed prismatic complexes based on Pd(II)/Pt(II) metal-ligand coordination-driven self-assembly and the decreasing importance of templates in such a biology-inspired endeavour. Our recent efforts towards their use for applications are also briefly discussed.

## 2. Entropy, enthalpy, components and templates

Even without going into rigorous mathematical formulations, it can be said that entropy generally plays the role of a spoilsport in the formation of multicomponent assemblies. However, it is also known that entropy will favour smaller compact structures with a minimum number of components rather than the polymeric structures. Generally, the equilibrium systems composed of multiple weakly interacting components depend delicately on this entropy-enthalpy balance, and with sufficient energy incentives derived from carefully chosen donor and acceptor components it is possible to overcome the entropic restrictions. Coordination-driven self-assembly has been hugely successful in this endeavour, taking advantage of the highly directional and predictable nature of metal-ligand coordination bonds. Considering that the energies of metal-ligand bonds (*ca.* 15–50 kcal mol<sup>-1</sup>) lie intermediate between the energies of 'too strong and too directional' organic covalent bonds (*ca.* 60–120 kcal mol<sup>-1</sup>) and the weak interactions (*ca.* 0.5–10 kcal mol<sup>-1</sup>), there are more opportunities for modulating the coordination kinetics of the self-assembly process.<sup>3h</sup> In fact, the resulting kinetic reversibility allows for self-corrections leading to thermodynamically favourable products, replacing any kinetically formed 'undesirable' intermediates. A certain degree of rigidity in the donor and acceptor components is also necessary for building desired 3D architectures. Pd(II)/Pt(II) based acceptors have been widely used because of their regular planar tetra-coordinated geometries. Blocking the *cis* or *trans* sites provides 90° and 180° acceptors. Multi-topic donors of different shapes and sizes can be elaborately designed with organic backbones and pyridyl, imidazole or carboxylate groups as donor sites. Most of these donors are based on symmetry principles and are rigid in nature. However, a certain degree of flexibility (not deviating too much from the symmetry of the backbone) imparted on the donor sites may actually help in overcoming steric problems (at the coordination site) and could be more important in realising the desired multicomponent systems. Although the focus has been on the thermodynamically controlled products, Lusby *et al.* recently showed that through elaborate design it is possible to obtain multicomponent assemblies through kinetically controlled step-wise reactions.<sup>12</sup>

The importance of these choices in selective multicomponent coordination-driven self-assembly becomes clear when we chart

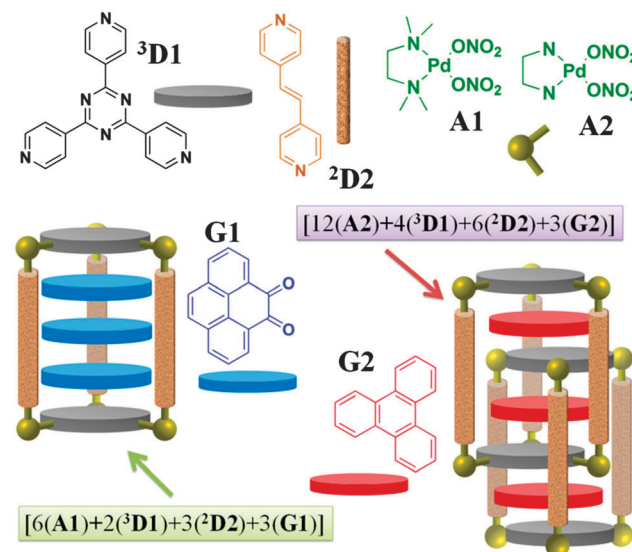


**Scheme 1** Schematic representation of the possible molecular architectures from the self-assembly of a 90° acceptor (**A**) with a linear ditopic donor ( $^2\text{D}$ ) and a  $C_3$ -symmetric tritopic donor ( $^3\text{D}$ ). Adapted with permission from ref. 11b. Copyright 2012 John Wiley and Sons.

out the possibilities of assemblies from just one 90° acceptor (**A**) component and two different donor components. When one of the donor components is taken as a  $C_3$  symmetric tritopic donor ( $^3\text{D}$ , superscript represents the topicity) and the other as a ditopic linear ( $180^\circ$ ) donor ( $^2\text{D}$ ), the resulting reaction mixture may contain one or more of the assemblies as depicted in Scheme 1. If we desire the exclusive formation of the trigonal prismatic cage (**P**, non-interlocked) resulting from the three-component self-assembly of **A**,  $^3\text{D}$  and  $^2\text{D}$  in 6:2:3 ratios, we will need to provide sufficient molecular-level coded information (on the components) for its superior thermodynamic stability. This can be achieved by either modulating the nature of the building units (the components) or the internal cavity of the intended structure.<sup>11b</sup>

The physics of empty space or voids is particularly interesting, with virtual particles bubbling out of nowhere and disappearing without even being seen. The chemistry, however, abhors voids, especially when the empty space is created by relatively friendly molecular entities. Of course, the real dictator in such matters is the energy (minimization!). When entropy is not on our side, which is true for the multicomponent assemblies, the system can be tamed by providing extra incentives. This is particularly important for 3D architectures with void spaces, whereas the 2D multicomponent frameworks are much easier to handle.<sup>6,13</sup> Using templates to construct multicomponent discrete 3D architectures thus proved useful. Templates should in principle be complementary to the assembly, so that working together they can form the desired architecture.

Most of the early attempts made to construct prism shaped multicomponent assemblies relied on this strategy. Fujita *et al.* reported a large number of such systems with 90° acceptors and the tritopic tris(4-pyridyl)-2,4,6-triazine ( $^3\text{D1}$ ) donor used as the roof-floor of the trigonal prisms.<sup>9</sup> The third component, ditopic pillars, dictates the length of the prism. Choosing linear pyridyl donors of various sizes Fujita's group constructed prisms that incorporate different numbers of aromatic (and other molecular units capable of *trans*-annular interactions) guests. Essentially, the roof-floor and the guest molecules form columnar aromatic stacks through  $\pi$ - $\pi$  interactions stabilising the hollow structure.



**Fig. 1** Template-assisted multicomponent assembly of interlocked and non-interlocked trigonal prisms.<sup>9b,g</sup>

These guests are also essential for the formation of the prisms (acting as templates), but can be removed (in some cases) after the assembly process. When the steric requirements are not demanding these cages tend to form triply inter-locked structures (dimers), so that the roof-floor panels form aromatic stacks (Fig. 1). Even these interlocked cages are capable of supporting various guests in their structures extending the stacking interactions. Although some control can be achieved in choosing between the formation of interlocked or non-interlocked cages, this system of trigonal prisms is still limited by the necessity of the presence of suitable templating guest molecules. Fujita *et al.* have recently reviewed these systems and showed their potential use in the understanding of proximity effects on multiple guests bound inside the cages.<sup>14</sup> However, this article concerns with the less explored template-free self-assembled multicomponent structures.

### 3. Neutral donors

For most of the reported (by Fujita *et al.*)<sup>9</sup> three-component assemblies with a 90° acceptor and two different neutral donors, it seems necessary to provide a template for the construction of the cages. The primary reason for this is probably the weak nature of the ligands as donors and the resulting accumulation of high positive charges on the system. In a hollowed-out structure assembled from organic aromatic backbones the cavities are generally hydrophobic (excluding the possibility of incorporating counter-anions in the cavity), so this charge can be dissipated through the inclusion of suitable guests. However, if the roof and floor are constructed through molecular entities that are not highly symmetric and good donors (*i.e.* capable of handling the partial charge generated because of lone-pair donation to the metals, without outside help: donor-acceptor interactions), the charge separation effects may be limited. This logic also leads



to the use of anionic pillars or roof–floor, in combination with neutral donors to avoid the use of templates, which we will discuss in the next section.

### 3.1. Pyridyl donors

In a pioneering paper in *Nature* (1999),<sup>15</sup> Fujita *et al.* reported the three-component assembly of a 90° acceptor [*cis*-(en)M(NO<sub>3</sub>)<sub>2</sub>, M = Pd, **A2** and M = Pt, **A3**] and two different neutral pyridyl-based tritopic donors (**<sup>3</sup>D1** and **<sup>3</sup>D3**). No external templating agents were used and the resulting assemblies [M = Pd, (**P1**)<sub>2</sub> and M = Pt, (**P2**)<sub>2</sub>] were found to be triply interlocked cages (Fig. 2). The interlocked cages were found to be stable in solution as well as in the solid state, and were thoroughly characterized by NMR, ESI-MS and X-Ray structure determination. The stability of these interlocked cage structures was further established by the observation that the 1:2 mixture of the two-component cages [Pd<sub>6</sub>(**<sup>3</sup>D1**)<sub>4</sub>](NO<sub>3</sub>)<sub>12</sub> and [Pd<sub>3</sub>(**<sup>3</sup>D3**)<sub>2</sub>](NO<sub>3</sub>)<sub>6</sub> reorganized in an aqueous solution to form the interlocked cage (**P1**)<sub>2</sub> exclusively. Therefore, it can be argued that this assembly is self-templating in nature, stabilizing itself through interlocking that allows the planar aromatic backbones of the donors to form a columnar structure.

In 2010, Stang's group reported the first template-free construction of tetragonal prisms (Fig. 3) *via* multicomponent

coordination-driven self-assembly using tetratopic neutral roof–floor and ditopic neutral pillars (Fig. 3) of different heights.<sup>10b</sup> Self-assembly of the tetratopic coplanar donor **<sup>4</sup>D4**, linear ditopic donor **<sup>2</sup>D5**/**<sup>2</sup>D2** and acceptor **A4** in 1:2:4 ratios (in CD<sub>2</sub>Cl<sub>2</sub> and CD<sub>3</sub>NO<sub>2</sub>) resulted in single highly symmetrical complexes (as evidenced by <sup>1</sup>H and <sup>31</sup>P NMR) [(PEt<sub>3</sub>)<sub>2</sub>Pt]<sub>8</sub>(**<sup>4</sup>D4**)<sub>2</sub>(**<sup>2</sup>D5**)<sub>4</sub>](OTf)<sub>16</sub> (**P3**) and [(PEt<sub>3</sub>)<sub>2</sub>Pt]<sub>8</sub>(**<sup>4</sup>D4**)<sub>2</sub>(**<sup>2</sup>D2**)<sub>4</sub>](OTf)<sub>16</sub> (**P4**). Also, no two-component complexes were detected by multinuclear NMR. Mass spectra (ESI) of the products provided conclusive evidence for the formation of tetragonal prisms [**P3** shows peaks corresponding to the [M – 4OTf]<sup>4+</sup> and [M – 5OTf]<sup>5+</sup> units at *m/z* = 1786.1 and 1399.3, and **P4** shows a [M – 5OTf]<sup>5+</sup> peak at *m/z* = 1420.1], with good agreements with theoretical isotopic distributions. The authors were unable to crystallize the complexes. However, the energy minimized [MMFF force field] structure of **P3**/**P4** shows that in the roof and the floor, formed by the tetratopic ligand **<sup>4</sup>D4** (Fig. 3), the aromatic rings are not planar. Therefore, the tetratopic ligands do not produce a face like **<sup>3</sup>D1**, so a donor–acceptor type aromatic stacking is not necessary to stabilize the structure. Using simulations the diameters of the two tetragonal prisms were estimated to be 3.61 and 3.65 nm, which are very close to the sizes measured by PGSE NMR (**P3**, 4.2 ± 0.1 nm; **P4**, 4.3 ± 0.1 nm).

Stang's group also reported a hexagonal prism [(PEt<sub>3</sub>)<sub>2</sub>Pt]<sub>6</sub>(**<sup>6</sup>D6**)<sub>2</sub>(**<sup>2</sup>D5**)<sub>6</sub>](PF<sub>6</sub>)<sub>12</sub> (**P5**), self-assembled with the same acceptor (**A4**),

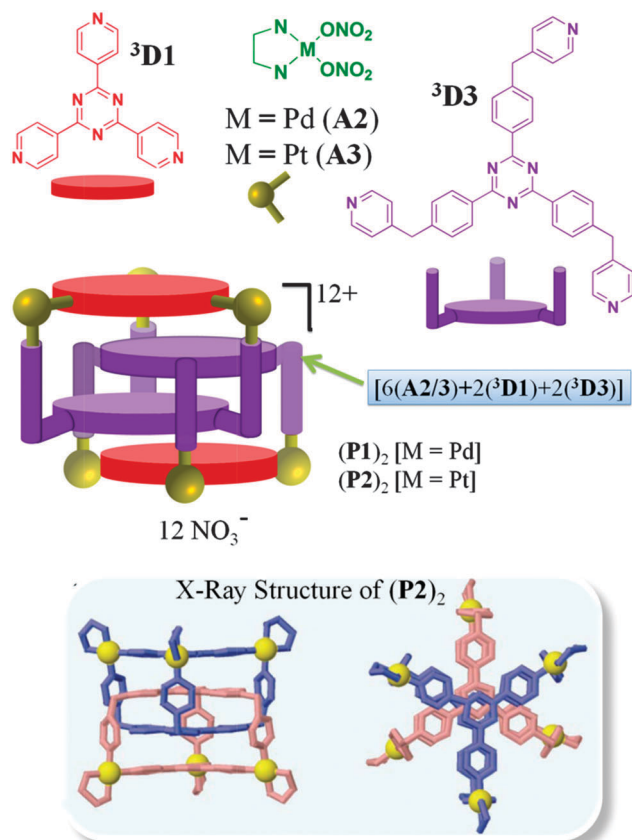


Fig. 2 Formation and structure of interlocked cages through three-component self-assembly of a 90° acceptor and two different tritopic donors. Views of the crystal structure of (**P2**)<sub>2</sub> are adapted with permission from ref. 15. Copyright 1999 Nature Publishing Group.

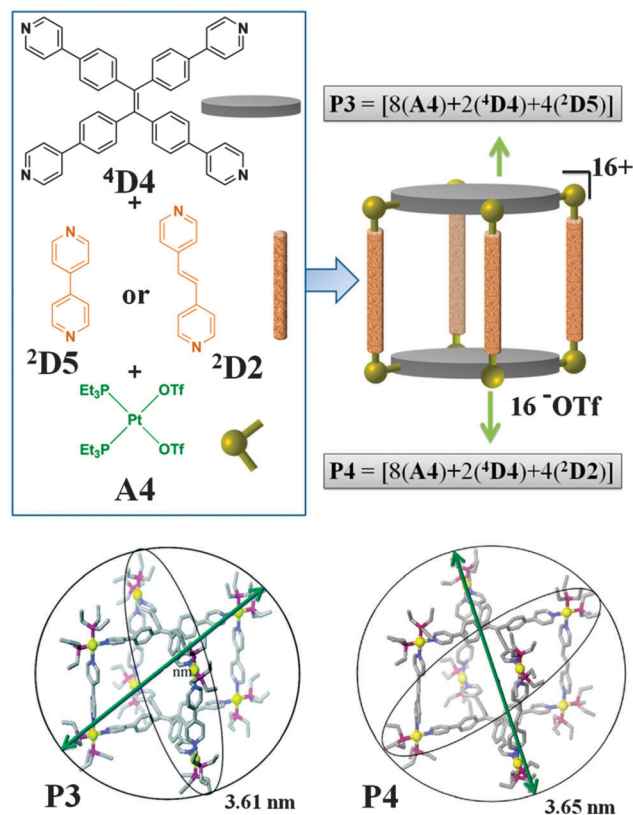


Fig. 3 Formation and structures (simulated) of tetragonal prisms through three-component self-assembly of a 90° acceptor, a tetratopic donor and linear 180° donors. The simulated structures are adapted with permission from ref. 10b. Copyright 2010 American Chemical Society.

hexakis[4-(4-pyridyl)-phenyl]benzene (**6D6**) as the roof-floor and 4,4'-bipyridyl (**2D5**) pillars [in a 12 : 2 : 6 ratio in an acetone–water mixture (9 : 1)].<sup>10a</sup> Again, no template was necessary for this multicomponent prism. Although no crystal structures were reported for this study, the authors showed convincing evidence for formation of a single multicomponent product though multinuclear NMR and ESI-MS also provided further evidence for the formation of the hexagonal prism [ $m/z = 2751.2 [M - 4PF_6^-]^{4+}$  and  $2171.5 [M - 5PF_6^-]^{5+}$ ].

### 3.2. Imidazole donors

Although poly-pyridyl donors with rigid backbones have been widely used with Pd(II)/Pt(II) metal ions, Mukherjee's group has been involved in developing new molecular architectures using the poly-imidazole donors. Imidazole-based ligands are commonly found in the active sites of various biomolecules. Also, as donors imidazole moieties are known to have a better coordinating ability compared to the pyridyl donors, providing energy incentives to otherwise unfavourable structures. When one of the imidazole ring's nitrogen atoms is linked to a rigid backbone, the remaining is free and thus the donating nitrogen atom can have various dispositions with respect to the backbone. Therefore, the architectural properties of poly-imidazole ligands become much more interesting. This is because a five-member ring structure means non-alignment of the donor nitrogen with the backbone and at least two orientations are possible even when the ring remains in the same plane of the aromatic backbone. A little structural flexibility at the donor sites may facilitate the self-sorting or self-organization of complex and high-nuclearity multicomponent structures without external help (template).

Using a *cis*-blocked Pd(II) acceptor (**A1**) with 1,2,4,5-tetrakis(1-imidazolyl)benzene (**4D7**) and pyridyl-based ditopic pillars of different lengths (**2D5** and **2D2**), a Pd<sub>8</sub> molecular swing  $[(\text{tmen})\text{Pd}]_8(\text{4D7})_2(\text{2D5})_4(\text{NO}_3)_{16}(\text{H}_2\text{O})_{25}$  (**P6**), and a Pd<sub>6</sub> molecular boat  $[(\text{tmen})\text{Pd}]_6(\text{4D7})_2(\text{2D2})_2(\text{NO}_3)_{12}(\text{H}_2\text{O})_{20}$  (**P7**) were constructed *via* a three-component self-assembly process.<sup>11c</sup> Two tetraimidazole linkers acting as rectangular panels form a chair like structure, the ends of which are linked *via* the pillars (Fig. 4). Now, when a long enough pillar [*trans*-1,2-bis-(4-pyridyl)ethylene, **2D2**] is used, it can span the length between the ends of the rectangular panels to form a boat-like structure. But with a shorter pillar (4,4'-bipyridyl, **2D5**) it requires a bridge [another *cis*-blocked Pd(II) acceptor] to reach the other end of the chair, giving the overall Pd<sub>8</sub> structure a swing-like shape. Both the complex structures were formed *via* self-sorting without the assistance of any templates, and with no traces of two-component assemblies which are generally expected in the given situations. Both the structures are not expected to form, especially if the rectangular panel consists of 4-pyridyl donors. In that case, a trifacial prism should be the preferred structure. However, as explained earlier the tetra-imidazole donor is flexible in nature, and the dispositions of the donor-sites can be slightly out of the plane of the aromatic backbone. In this situation, the self-sorting process finds a different route and

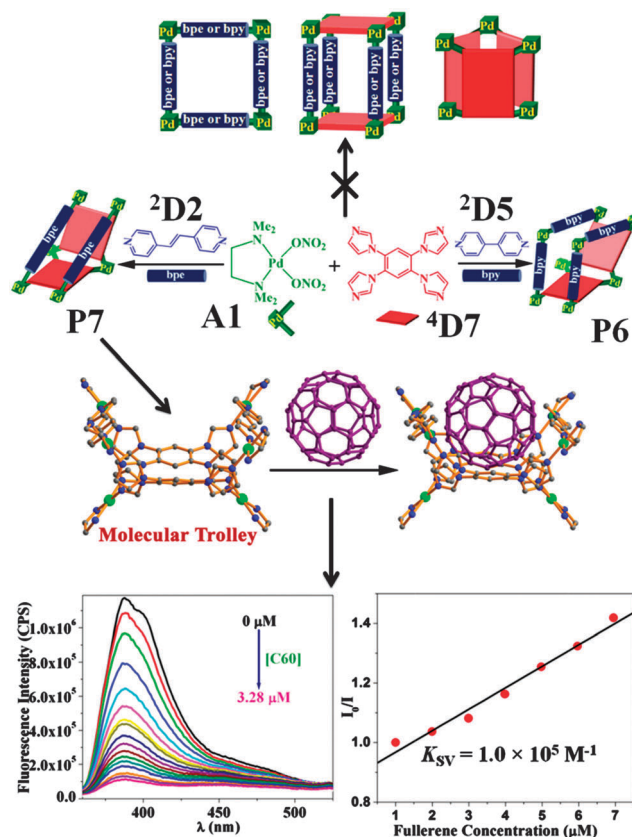


Fig. 4 Formation, structures and application ( $C_{60}$  sensing) of unusual cages self-assembled through three-component reactions of a 90° acceptor, a tetra-topic imidazole based donor and linear 180° donors. Adapted with permission from ref. 11c. Copyright 2012 Royal Society of Chemistry.

the architectural preference changes in an unexpected way to form previously unknown types of multicomponent assemblies.

The same group followed this work by replacing the ditopic pillar like linkers with another imidazole based tritopic ligand (**3D8**). This changed the bridging structure (Fig. 5) for the two rectangular panels forming an unusual three-component cage,  $[(\text{tmen})\text{Pd}]_7(\text{4D7})_2(\text{3D8})_2(\text{NO}_3)_{14}(\text{H}_2\text{O})_{20}$  (**P8**), with two rectangular and two trigonal faces with seven *cis*-blocked Pd(II) acceptors.<sup>11d</sup> This Pd<sub>7</sub> cage took the multicomponent directional self-assembly to the next level of complexity. The cage forms *via* the self-sorting process of three components, although the two-component cage (with trigonal faces, already reported by the same group) or trifacial barrel (with rectangular faces) is generally expected.

Given our limitations in the understanding of the natural biological multicomponent assemblies (which are governed by much subtler forces), we believe that this kind of new architectures and self-sorting processes with semi-flexible linkers should point to the right direction to build a better set of experimental and theoretical tools to tackle such problems. It is also possible to find new applications of such hollow architectures. Both the complexes **P6** and **P7** have large internal cavities and concave aromatic surfaces, suitable for interacting with spherical or convex guests like the fullerene  $C_{60}$ . The diameters of the internal cavities of these two complexes are

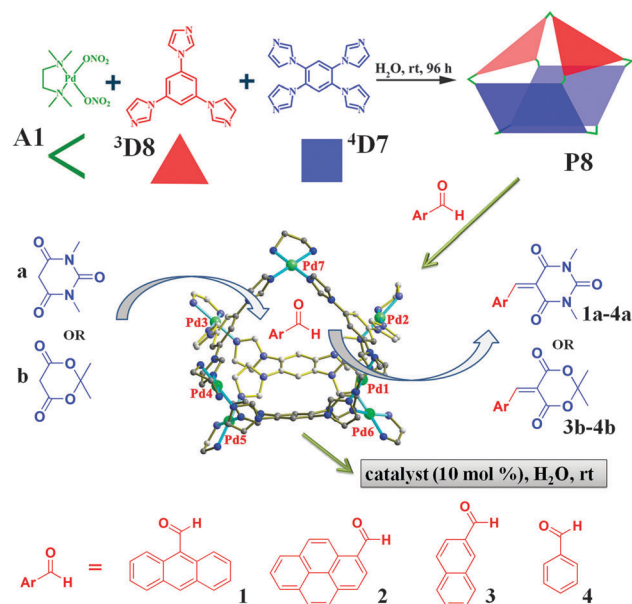


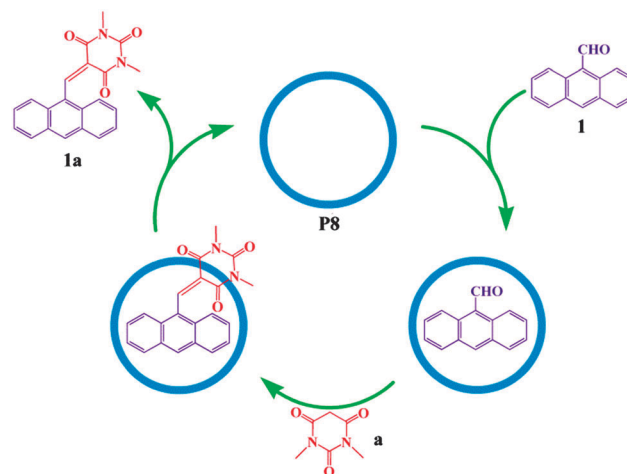
Fig. 5 Formation, structure and application (catalyst for Knoevenagel condensation in aqueous medium) of a cage self-assembled through three-component reactions of a 90° acceptor, a tetratopic and a tritopic imidazole based donor. Adapted with permission from ref. 11d. Copyright 2012 Royal Society of Chemistry.

also larger than the van der Waals radius of C<sub>60</sub>. These assemblies are electron-rich and also show strong fluorescence emissions at  $\lambda = 388$  nm (**P6**) and 429 nm (**P7**) in CH<sub>3</sub>CN–CH<sub>3</sub>OH (1 : 1). Fluorescence titrations with a C<sub>60</sub> solution in toluene (at 298 K) showed rapid depletion (Fig. 4) of emission intensity of both the assemblies upon gradual increment of C<sub>60</sub>, suggesting the formation of charge-transfer type complexes between the bowl shaped hosts **P6** or **P7** and C<sub>60</sub> in solution. Linear Stern–Volmer plots were obtained from the fluorescence quenching titrations and the Stern–Volmer binding constants ( $K_{SV}$ ) were estimated to be  $1.0 \times 10^5$  M<sup>−1</sup> (**P6**) and  $1.6 \times 10^6$  M<sup>−1</sup> (**P7**). The high  $K_{SV}$  values for both the assemblies with C<sub>60</sub> indicated the propensity of these assemblies to form host–guest complexes with C<sub>60</sub> in solution.<sup>11c</sup>

The Pd<sub>7</sub> cage was employed as a nano-reactor for catalytic Knoevenagel condensations (Fig. 5) of a series of aromatic aldehydes with 1,3-dimethylbarbituric acid (**a**) and Meldrum's acid (**b**) in 'green' aqueous media (Table 1). The cavity of the cage is hydrophobic and the walls of the cage allow the aromatic aldehyde guests to sit inside the cage, in aqueous medium. Addition of active methylene compounds in this mixture allows for the Knoevenagel condensation reactions with aldehyde groups protruding outside the cage, and once the product is formed, the cage can no longer support the sterically demanding product, which comes out of the solution as a precipitate (water insoluble). The cage can then take up a new aldehyde guest, and the process becomes catalytic (Scheme 2). Consistent with this mechanism the larger aromatic aldehydes (9-anthracene aldehyde, 1-pyrene aldehyde *etc.*) showed the maximum increase in yields of Knoevenagel products in water, compared to the non-catalytic reactions.<sup>11d</sup>

Table 1 Yields of the Knoevenagel condensations of aromatic aldehydes and active methylene compounds in the presence and absence of cage **P8**

| ArCHO | Active methylene compounds | Reaction time | Product (% yield) |                   |
|-------|----------------------------|---------------|-------------------|-------------------|
|       |                            |               | With <b>P8</b>    | Without <b>P8</b> |
|       | <b>a</b>                   | 72 h          | <b>1a</b> (35)    | <b>1a</b> (5)     |
|       | <b>a</b>                   | 3 h           | <b>2a</b> (33)    | <b>2a</b> (2)     |
|       | <b>a</b>                   | 75 min        | <b>3a</b> (77)    | <b>3a</b> (25)    |
|       | <b>b</b>                   | 8 h 30 min    | <b>3b</b> (51)    | <b>3b</b> (21)    |
|       | <b>a</b>                   | 4 min         | <b>4a</b> (69)    | <b>4a</b> (64)    |
|       | <b>b</b>                   | 6 h           | <b>4b</b> (58)    | <b>4b</b> (45)    |



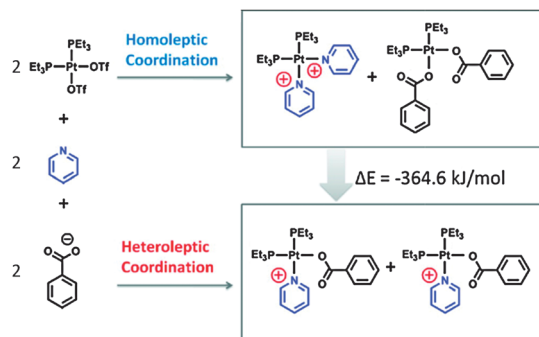
Scheme 2 Catalytic cycle for the Knoevenagel condensation reaction in the aqueous medium in the presence of the cage **P8**.

## 4. Neutral and anionic donors

Anionic oxygen donors are generally unsuitable for the formation of polynuclear Pd(II)/Pt(II) structures of a particular shape and size, due to the unfavourable hard–soft interactions. However, Stang and Mukherjee have recently reported several new multicomponent systems with 90° acceptors, neutral pyridyl donors and anionic carboxylates of various denticities. The systems developed from the two groups are complementary to each other, in the sense that, while Stang's group employed the anionic ligands as pillars, Mukherjee's group used them as roof–floor of the multicomponent prisms.

Stang and co-workers showed a simple computational justification (Scheme 3) for using neutral and anionic donors together to form multicomponent systems, by demonstrating that the heteroleptic coordination mode (one pyridyl donor and



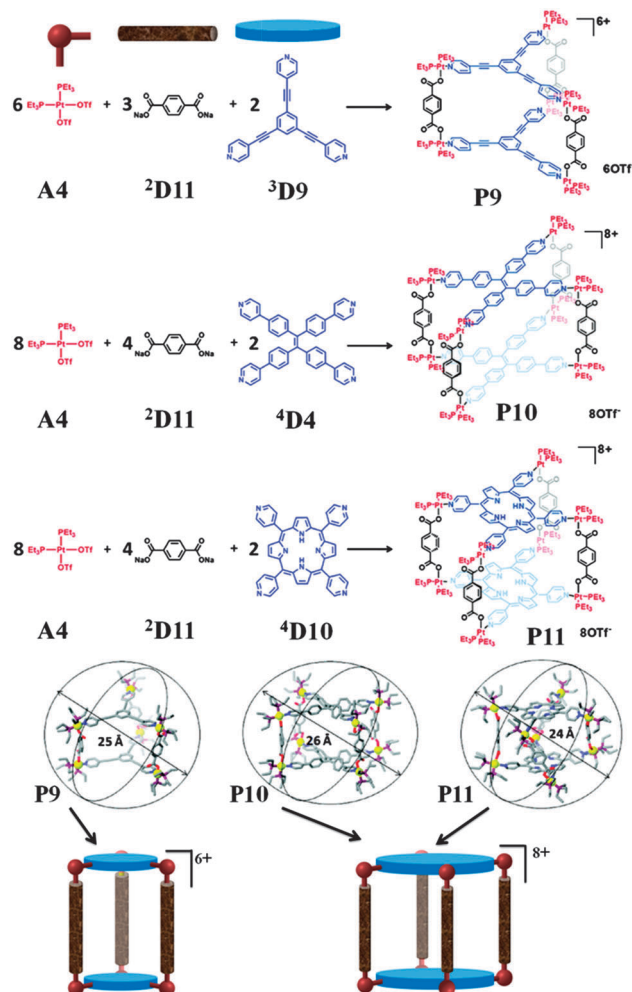


**Scheme 3** Representation of the selective self-assembly of *cis*-Pt(PEt<sub>3</sub>)<sub>2</sub>(OTf)<sub>2</sub> with carboxylate and pyridyl moieties due to the lower energy of the heteroleptic system. Reprinted with permission from ref. 10c. Copyright 2010 American Chemical Society.

one carboxylate donor linked to the acceptor) is much more energetically favourable than the homoleptic coordination mode (acceptor with either two pyridyl or two carboxylate donors).<sup>10c</sup> Experimentally, appropriate stoichiometric mixtures of the acceptor **A4**, the tri- (**<sup>3</sup>D9**) or tetra-pyridyl (**<sup>4</sup>D4** and **<sup>4</sup>D10**) donors and terephthalate (**<sup>2</sup>D11**, a linear pillar-like dicarboxylate) produced single products (tri- or tetragonal prisms) through self-assembly (Fig. 6). Subsequently, the same group reported another series of hexagonal prisms with a symmetric hexapyridyl donor and different dicarboxylate pillars (Fig. 7), with the same acceptor.<sup>10a</sup> The prisms were all characterized by multinuclear NMR [<sup>31</sup>P, <sup>1</sup>H], and ESI-MS provided further evidence for the formation of the selective multicomponent systems. Although, no crystal structures could be obtained, the authors used computational simulations (MMFF force field) to generate the energy minimized structures. The dimensions of the structures matched nicely with those obtained from PGSE NMR analysis.

Both computational analysis and experimental findings showed that the unexpected multicomponent assemblies form selectively, driven by the intrinsic information coded in the components without the helping hand of any templating motifs. Therefore, the different electronic properties of the anionic and the neutral donors play a major role in allowing the heteroleptic coordination, guided by the charge separation effects.

Mukherjee's group reported a trigonal prism (**P15**) formed by the acceptor **A1**, trimesate anion (**<sup>3</sup>D14**, forming the roof and the floor) and 4,4'-bipyridyl (**<sup>2</sup>D5** as the pillars).<sup>11a</sup> No templating agents were found to be necessary for the multicomponent architecture. But, a small amount of the molecular square (two-component byproduct) was isolated. However, unlike Stang's prisms, this trigonal prism could be isolated by fractional crystallization and single crystals could be grown, giving better and direct structural evidence for the assembly (in addition to the spectroscopic confirmations). The prism, however, still carries a large void space. Therefore, when a suitable guest like trimesic acid (**G3**) is added to the reaction mixture, the prism forms exclusively (no two-component products) incorporating two guest molecules per prism. This stable host-guest complex



**Fig. 6** Three-component self-assembly of a 90° acceptor, a tri-/tetrapic neutral donor and a ditopic anionic donor. Adapted with permission from ref. 10c. Copyright 2010 American Chemical Society.

was thoroughly investigated using NMR spectroscopy (HSQC, DOSY), which revealed that the guest aromatic molecules stack parallel to the roof-floor through  $\pi$ - $\pi$  stacking. Therefore, the prism **P15** does not form exclusively without a suitable guest, and the fact that it can still be isolated in large yields from the three-component reaction mixture shows that the guest is probably not templating its formation. However, the guest certainly does help to stabilize the large molecular cage like structure. This prism is thus very important in understanding the subtle forces responsible for the selective formation of multicomponent systems and deserves further probing through theoretical and experimental methods.

For further investigation, Mukherjee's group decided to investigate the effects of changes in the neutral pillar length and the steric effects arising from the *cis*-blocking ligands on the acceptor component, for the trigonal prismatic systems with the same roof and floor (trimesate anion, **<sup>3</sup>D14**).<sup>11b</sup> This study revealed (Fig. 8) that replacing the bulky tetramethylethylenediamine (tmen) blocker with a far less sterically demanding ethylenediamine (en) results in the exclusive formation of triply

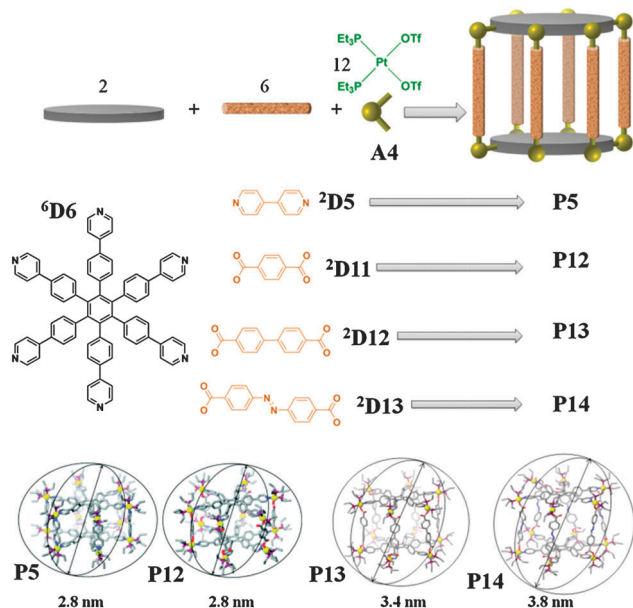


Fig. 7 Three-component self-assembly (with simulated structures) of a 90° acceptor, a hexatopic neutral donor and ditopic anionic donors. The simulated structures are adapted with permission from ref. 10a. Copyright 2010 American Chemical Society.

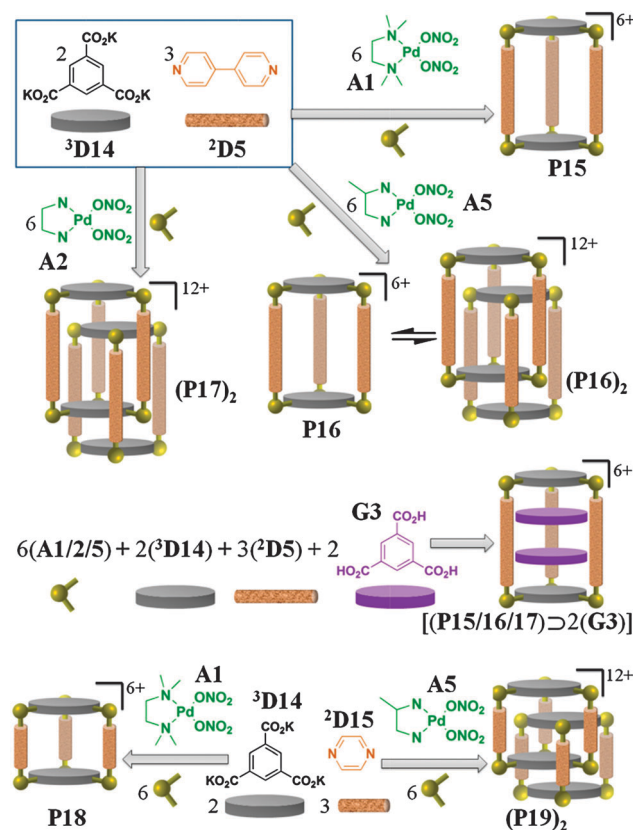


Fig. 8 Schematic representation of a three-component self-assembly with various 90° acceptors, ditopic neutral linear donors and tritopic anionic donors.<sup>11a,b</sup>

interlocked trigonal prisms  $[(P17)_2]$ . However, upon introducing guest molecules like trimesic acid (G3), the product that exclusively formed was the single prism with two guest molecules stacked inside the molecular architecture through  $\pi$ - $\pi$  interactions. Therefore, when tmen is used the sterical disposition of the methyl groups on the acceptor disrupts the formation of the intercalated locked cages (which is highly sterically demanding), and without any guest molecules this leads to the “incomplete” formation of the single prism (which forms exclusively with the help of the guest molecules). This study was the first to reveal such subtle effects of the steric influences on the formation of this kind of multicomponent assemblies. These effects were further shown by using a propane-1,2-diamine (pn) blocked acceptor, which along with 4,4'-bipyridyl generated both the interlocked and non-interlocked prisms, in the absence of any guests  $[P16 \text{ and } (P16)_2]$ . In solution, the amount of the non-interlocked prism decreases as the temperature is decreased, and in the solid state the interlocked prism is the sole product (as revealed by single crystal and powder XRD studies). Again, upon introduction of the guest molecules in the system the non-interlocked prism with two guest molecules was the only product. The blocker pn can be viewed as very similar to en, with only being slightly more bulky a little further away from the coordinating sites. Therefore, the equilibrium in solution between the intercalated and non-intercalated prisms shows how these kinds of small changes really affect the overall reaction pathway.

However, when the pillar length is shortened by using pyrazine ( $^2D15$ ) instead of 4,4'-bipyridyl (Fig. 8), with the pn based acceptor only the triply interlocked prisms formed  $[(P19)_2]$  and with the tmen based acceptor the exclusive product was the non-intercalated prism (P18).

## 5. Conclusions and outlook

Herein, we have highlighted the continuing success story of the metal-ligand [with the discussions limited to Pd(II)/Pt(II) based systems] coordination-driven self-assembly process, in pursuit of higher complexities involving self-organising multicomponent systems. In its early days, the problems associated with the selective assembly of multiple components were overcome through the use of templating agents and steric constraints. For the formation of desired multicomponent hollow prismatic structures, templates have been elegantly and effectively utilized by Fujita's group. Although this useful strategy is not the central theme of this review, it must be noted that in many cases, templates are only used to speed up the formation of the final assemblies and could be removed without affecting the stability of the assembled products. However, recently it has become clear that ‘order out of chaos’ can be achieved through a better understanding of the subtle energy requirements for the selective self-assembly, utilizing specific coded information on the components of the assembly itself and thus avoiding the templates altogether (which may be desirable for certain applications of the architectures). In this, the borderline systems



with different multicomponent assemblies, for example the interlocked and non-interlocked cages in equilibrium, provide the opportunities for better understanding and thus modulating the components with specific coded information for reaching the targeted assembly. Therefore, we hope that the importance of the template-free constructions of the multicomponent systems discussed in this article would be duly recognized, especially with the realization of the potential applications of such systems. The journey that started as a curiosity of natural biological processes has quickly evolved in finding a range of practical applications.

This bio-inspired adventure of molecular engineers, however, is still in its infancy. Although these early successful results point to a paradigm shift in the venture, still the underlying principles of complex structure formation are elusive enough to come to clear and logical conclusions. A quick look at all of the systems discussed here shows that the individual components as well as the final assemblies are based on high symmetries and their interactions with each other remain true to these pre-encoded guiding symmetries. But in the biological world, the symmetries or rather the asymmetries of various components are used in a much more complex manner. Biology also utilizes assemblies of huge numbers of components, the functions of which are thus much more fine-tunable. The synthetic analogues developed so far lack this kind of programmabilities. That goal would require continued investigations of complex self-sorting systems.

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