Coordination-driven self-assembly of functionalized supramolecular metallacycles

Brian H. Northrop,* Hai-Bo Yang and Peter J. Stang

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Coordination-driven self-assembly that combines rigid ditopic Pt(II) metal acceptors and bis-pyridyl organic donors provides a facile means of synthesizing well-defined metallacycles of predetermined size and geometry. Functionalization of the component acceptor or donor building blocks allows for the preparation of multifunctional supramolecular materials wherein the stoichiometry and position of individual functional moieties can be precisely controlled. The design, self-assembly, and applications of polyfunctional supramolecules incorporating functional moieties with host–guest, photonic, materials, and self-organizational properties is discussed.

1. Self-assembly: an historical perspective

"*The biological example of writing information on a small scale has inspired me to think of something that should be possible. Biology is not simply writing information; it is* doing something *about it. A biological system can be exceedingly small. Many of the cells are very tiny, but they are very active; they manufacture various substances; they walk around; they wiggle; and they do all kinds of marvelous things—all on a very small scale. Also, they store information. Consider the possibility that we too can make a thing very small which does what we want—that we can manufacture an object that maneuvers at that level!*"
Richard P. Feynman
There's Plenty of Room at the Bottom, December 29, 1959.[1]

In the 1860's Friedrich August Kekulé proposed the tetrahedral structure of carbon[2] and solved the structure of benzene,[3] speaking about his reverie of an Ouroboros, a snake seizing its own tail. Amazingly, this was still 30 years before the discovery of electrons. The past 150 years have witnessed tremendous advances in our understanding of structure, reactivity, and synthesis in chemistry. In the intervening years chemists have developed an astounding collection of experimental, theoretical, and analytical tools that have brought with them such previously unthinkable achievements as stereoselective synthesis,[4] femtosecond spectroscopy,[5] *ab initio* computational modeling,[6] force microscopies,[7] and so on. What's even more impressive is that there appears to be no slowing down of this pace of discovery, especially as new and interdisciplinary fields of chemistry are being explored. One such field that has received considerable attention over the past two decades is self-assembly.[8]

It is commonly agreed upon that nature reigns supreme in her ability to wield the powers of self-assembly. A variety of

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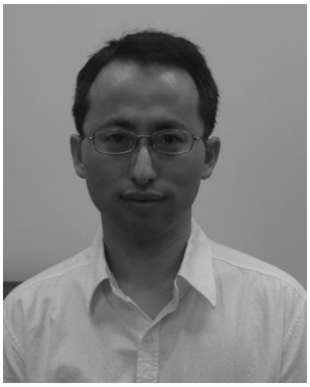
University of Utah Department of Chemistry, 315 So. 1400 E., Salt Lake City, UT, USA. E-mail: b.northrop@utah.edu; Fax: +1 801-581-8433; Tel: +1 801-581-6881

Brian H. Northrop

Brian H. Northrop received his BA degree in Chemistry in 2001 from Middlebury College in Vermont while working with Professor J. Byers. In 2002 he joined the laboratories of Professors K. N. Houk and J. F. Stoddart in the Department of Chemistry and Biochemistry at the University of California, Los Angeles, and obtained his PhD in 2006. Shortly thereafter he moved to Utah and joined the laboratory of Professor P. J. Stang as an NIH postdoctoral fellow where he is conducting research on the self-assembly of metal–organic metallacycles and metallacages focusing on their functionalization, assembly onto surfaces, and ability to act as abiological hosts for the complexation of biologically relevant compounds such as proteins.



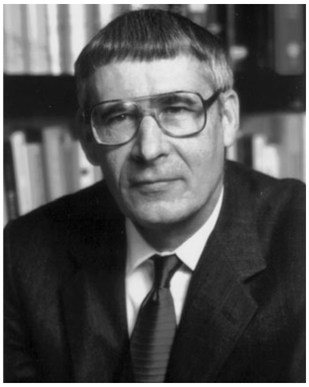
Hai-Bo Yang

Hai-Bo Yang studied chemistry at Beijing Normal University and received his MSc degree in 2001 under the direction of Professor Y. Cheng. In 2004 he obtained his PhD degree at the Institute of Chemistry, Chinese Academy of Sciences in Beijing with Professor M.-X. Wang. Subsequently, he joined the laboratory of Professor P. J. Stang at the University of Utah as a postdoctoral scholar, where he is currently a research assistant. Beginning in the fall of 2008 he will assume the position of Professor at East China Normal University in Shanghai, China. His research interests span many areas of organic, inorganic and supramolecular chemistry, with special emphasis on employing self-assembly to build novel metal–organic architectures.

noncovalent interactions—hydrogen-bonding, charge–charge, donor–acceptor, π–π, van der Waals, *etc.*—allow for the natural formation of highly complex and, often, highly symmetric superstructures. The globular protein actin, for example, self-assembles into filaments that make up the actuating components of muscle cells.[9] Self-assembly leads to the formation of the highly symmetric capsid protein shells of viruses from multiple identical components.[10] Genetic information is stored, retrieved, and transcribed on account of noncovalent self-assembly processes. The quote from Feynman that Hai-Bo Yangopens this section at once pays tribute to the ability of biological systems to perform myriad distinct functions and also proposes that scientists attempt to emulate nature and imagine the world of possibilities that would result from such success.

Shortly after Feynman's speech, significant contributions to the emerging field of chemical nanotechnology were laid down in the pioneering studies[11] of molecular recognition by Lehn, Pederson, Cram, Sauvage, Dietrich, and others in the 1960's and 1970's. The realization that complementary synthetic molecules can be designed such that they recognize each other through noncovalent interactions in a controlled manner soon gave way to the self-assembly of supramolecular structures. Through judicious use of complementary noncovalent interactions, supramolecules of incredible complexity have been prepared. Self-assembly is a thermodynamically driven, dynamic process[12] wherein different molecular building blocks can assemble and disassemble repeatedly until the most exergonically favourable structure is obtained, typically in very high and often quantitative yield. The resultant structures frequently exhibit a high degree of symmetry and would be exceedingly difficult to prepare by traditional, stepwise covalent synthetic means. Molecular self-assembly has resulted in the synthesis of hydrogen bonded rosettes,[13] molecular racks, ladders, and grids,[14] molecular containers,[15] electrically conducting supramolecular helical dendrimers,[16] hybrid metal–organic supramolecular polygons and polyhedra,[17] and mechanically interlocked architectures such as rotaxanes and catenanes,[18] Borromean rings,[19] and suitanes.[20] This is but a short list of examples of the rich and diverse library of supramolecular structures that have been made using self-assembly techniques.

Aside from the relative ease of preparation afforded by self-assembly and the aesthetic value of the resulting structures lies the potential for such systems to be used in a variety of electronic, photonic, magnetic, catalytic, mechanical, and sensor applications. Feynman's "There's Plenty of Room at the Bottom" is often quoted in reference to the emerging field of nanotechnology and the bottom-up paradigm of nanofabrication, and for good reason. The quote above was chosen, however, because it specifically mentions the fact that biological systems aren't simply small abstract representations of information, rather most are *active* systems that are "*doing something about it*". In other words, they are functional. As researchers continue to develop more powerful and selective means of harnessing molecular self-assembly most, if not all, are also working toward developing the functional properties of supramolecular structures. This article presents recent work in the field of functionalized supramolecular metal–organic coordination compounds and discusses some of their potential applications.



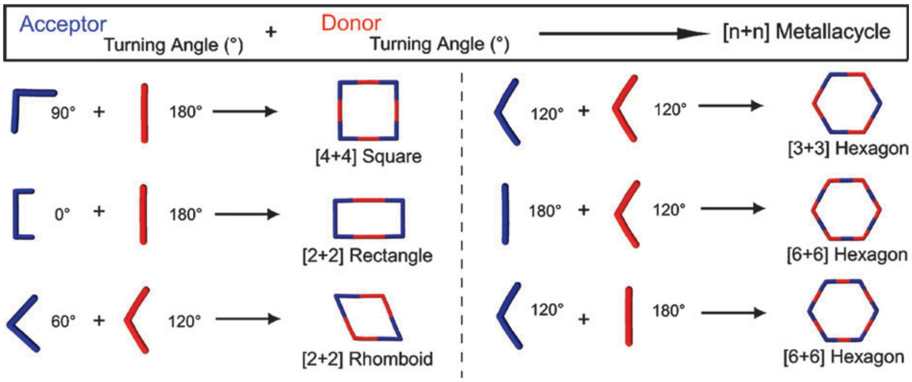
Peter J. Stang

Peter J. Stang is a Distinguished Professor of Chemistry at the University of Utah as well as the Editor of the Journal of the American Chemical Society. *He is a member of the U.S. National Academy of Sciences, the American Academy of Arts and Sciences, and a Foreign Member of the Chinese and Hungarian Academy of Sciences.*

2. Coordination-driven self-assembly

A particularly powerful method for self-assembling large, rigid metal–organic frameworks with well-defined shapes, sizes, and geometries is the directional-bonding approach provided by coordination-driven self-assembly.[17,21–26] Whereas many of the weaker noncovalent interactions are *nondirectional—e.g.* hydrogen-bonding, van der Waals, and solvophobic—dative metal–ligand bonds are highly *directional* and relatively strong. Over the last dozen years, we,[17,21] and the groups of Fujita,[22] Mirkin,[23] Raymond,[24] Lehn,[11,14,25] and others[26] have pioneered the use of the directional-bonding coordination-driven approach to self-assembly. The approach brings together rigid electron-poor metal centers and complementary, rigid electron-rich organic donors to provide a wide variety of discrete two dimensional (2D) and three dimensional (3D) polygonal and polyhedral coordination assemblies, respectively. In particular, electron-poor square planar Pt(II) and Pd(II) metals are often used in conjunction with electron-rich nitrogen-containing moieties such as substituted pyridines and nitriles. While metal–ligand coordination bonds are strong relative to most other noncovalent interactions, they are still kinetically labile. Thus coordination-driven self-assembly is a dynamic process carried out under thermodynamic control, ultimately leading to the most stable supramolecular structure. In order to ensure that the desired suprastructure is obtained, a number of symmetry considerations must be taken into account.

The two most important structural factors that largely dictate the supramolecular structure obtained from coordination-driven self-assembly are the shape and size of individual component building blocks. The shape of donor and/or acceptor building blocks is dominated by the turning angle defined as the angle formed between the two open valencies of a ditopic donor or acceptor. For example, a ditopic linear acceptor will have its two sites of free valence oriented 180° from each other while a ditopic donor such as 3,5-bispyridylbenzene has a turning angle of 120° between its two pyridyl donor sites. Scheme 1 demonstrates how the directional-bonding approach to coordination-driven self-assembly provides a means of synthesizing 2D metallacyclic



Scheme 1 Representation of the coordination-driven self-assembly approach to the construction of 2D metallacycles from rigid, pre-designed di-Pt(II) acceptors (blue) and ditopic organic donors (red).

polygons such as squares, rectangles, rhomboids, triangles, and hexagons.

A natural extension of the directional-bonding approach involves the synthesis of donor and acceptor units with greater than 2 binding sites and non-planar geometries. Through the use of such building blocks a variety of polygonal metallacages[17,21,22,24] have been prepared, including trigonal prisms, truncated tetrahedra, double square, adamantoid, cuboctahedra, and dodecahedra.

3. Coordination compounds as scaffolds for functionalization

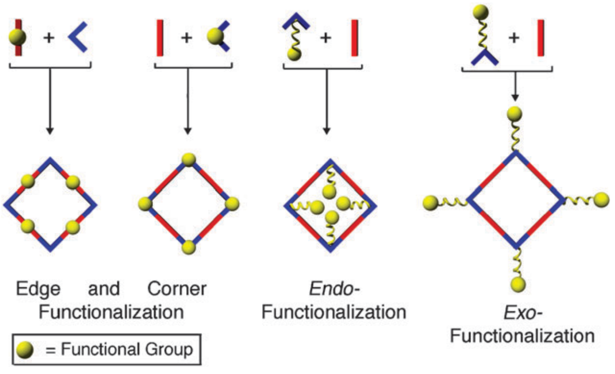
As a result of the requirement that the donor and acceptor components used in the directional-bonding approach be rigid, and thus retain their directionality, their "cores" are largely composed of aromatic and/or acetylenic moieties. Therefore many examples of self-assembled metallacycles and metallacages are, for the most part, unfunctionalized. In hopes to design advanced materials that incorporate, for example, multiple electroactive, photonic, magnetic, or sensor functionalities it becomes highly desirable to be able to exhibit control over the precise location, orientation, and stoichiometry of such functional groups. The structural aspects of rigid, well-defined, supramolecular metal–organic assemblies present unique opportunities for incorporating various functionalities into their architectures.

Large multifunctional molecules have been prepared previously in the form of functionalized polymers[27] and dendrimers.[28] While the design and synthesis of multifunctional polymers allow for a very large number of functional groups to be incorporated into one macromolecule, there is always some degree of polydispersity associated with the synthesis of polymers and it is difficult to obtain a collection of polymers with precisely the same lengths and number of functional groups. Furthermore, most polymer backbones lack structural rigidity and are not structurally well-defined. The synthesis of highly-branched, multifunctional dendrimers affords much greater control over the total number of functional moieties attached to a macromolecule and also avoids the problems associated with polydispersity. Dendrimers, however, typically adopt globular structures and little can be known about the precise position of appended functional groups. The lack of well-defined structures and imprecise positioning of functional groups in polymeric and dendritic macromolecules can present some limits to their use in materials settings.

Attaching or otherwise incorporating functional moieties into/onto self-assembled coordination compounds alleviates many of these problems. The rigid architectures presented by metallacycles and metallacages offer very well-defined scaffolds for the precise positioning of electroactive, host–guest, or other functional groups. Rigid coordination compounds also allow for control over the exact number of functional groups per assembly. Furthermore, the very process of using coordination-driven self-assembly to prepare multifunctional materials significantly reduces synthetic cost in terms of time, materials, and synthetic steps. Self-assembly techniques are very modular and allow for a wide variety of functional moieties to be incorporated into/onto related polygonal metallacycles and polyhedral metallacages.

4. Functionalized metal–organic assemblies

There are, in general, three means of incorporating functionalities into supramolecular metal–organic assemblies: (1) incorporation of a functional moiety into the edge or corner of a building block (edge and corner functionalization, Scheme 2); (2) covalent attachment of a functional moiety to the "inside" of a directional building block with a turning angle $<180^\circ$



Scheme 2 Functional moieties may be incorporated into metal–organic coordination compounds through the use of functionalized edge or corner building blocks or covalent attachment of functional groups *endo*- or *exo*- to the metallacycles or metallacages.

such that it will be positioned within the interior of a resulting self-assembled suprastructure (*endo*-functionalization, Scheme 2); and (3) covalent attachment of a functional moiety to the "outside" of a directional building block with a turning angle ≥ 180° such that it will be positioned on the periphery of a resulting self-assembled suprastructure (*exo*-functionalization, Scheme 2). To date, all three methods have been successfully employed.

5. Edge and corner functionalization

An early example of a functionalized supramolecular metal–organic assembly can be provided by studies done by Drain and Lehn[29] in 1994 wherein a 5,10-bispyridylporphyrin was self-assembled with *cis*- or *trans*-$Pd(NCPh)_2Cl_2$ to afford square-shaped assemblies with two or four porphyrin moieties, respectively. Similar studies that involved the use of derivatized porphyrin units not only as the corners but also as the edges of self-assembled metallacyclic squares were performed by our group.[30] In 2001, Fujita *et al.*[31] used tetrasubstituted Zn porphyrins as the faces of a supramolecular prism. More recently, Hupp *et al.*[32] have used a metallacyclic square containing four Zn porphyrin edges and four $Cl(CO)_3Re(I)$ corners as a host for the complexation of a Mn porphyrin guest. The overall host–guest complex was then shown to function as an efficient epoxidation catalyst. Mirkin and coworkers[33] have also explored the catalytic properties of porphyrin functionalized metal–organic assemblies wherein rectangular complexes of cofacial porphyrins have been shown to function as catalysts for acyl transfer reactions.

The design and synthesis of edge, corner, and/or face functionalized metal–organic supramolecules is by no means limited to the use of porphyrins. Our group has reported the incorporation of a variety of other functional moieties into metallacycles. The preparation of a ferrocenyl phosphine ligand[34] allowed for the formation of supramolecular squares with electroactive ferrocene moieties incorporated into their 90° Pt(II) or Pd(II) metal acceptor corners. Similar syntheses of crown ether and calixarene derivatized phosphines[35] enabled these two host molecules to be built into the corners of supramolecular squares. Over the past four years we have extended this research to other functionalized systems that are able to function in host–guest, photonic, and materials applications.

5.1 Diaza-crown ethers

Beginning with their discovery[36] in 1967, the properties and applications of macrocyclic crown ethers and their derivatives have been extensively explored.[37] Because of their ability to form strong, stable complexes with numerous alkali, alkaline earth, and transition metal cations, as well as their ability to transport such cations, diaza-crown ethers have become one of the most attractive topics in host–guest chemistry. Recently, we have synthesized both flexible pyridine[38] and sodium carboxylate[39] fuctionalized diaza-crown ethers and incorporated them into a variety of discrete supramolecules *via* self-assembly. Combining the diaza-crown ethers with 0°, 60°, and 90° di-Pt(II) acceptors led to the facile formation of a series of geometrically distinct edge and corner functionalized supramolecules, one example of which is shown in Fig. 1A. With the availability of pyridine and carboxylate functionalized macrocycles, both charged[38] and neutral[39] assemblies could be prepared. This work showed for the first time that conformationally flexible, di-subtitued 18 membered diaza-crown ether macrocycles can be incorporated effectively into discrete supramolecular species with Pt(II) metal acceptors.

5.2 Optical sensors

The design and synthesis of optical sensors, especially those that are able to signal the presence of trace amounts of hazardous metals, have proven to be of great interest in modern supramolecular chemistry because of their potential applications in the environmental and the biomedical fields.[40] Supramolecular chemistry is especially useful in the development of sensors. The overall modularity of the supramolecular approach is beneficial given the relative ease with which the necessary requirements of size complementarity, appropriate coordination motifs, and the incorporation of a reliable means of monitoring binding events can be tailored toward specific applications. Along these lines a linear donor containing a phenanthroline moiety in its core was designed.[41] Mixing the phenanthroline functionalized "edge" with a 0° di-Pt(II) acceptor in a 1 : 1 stoichiometric ratio led to the near

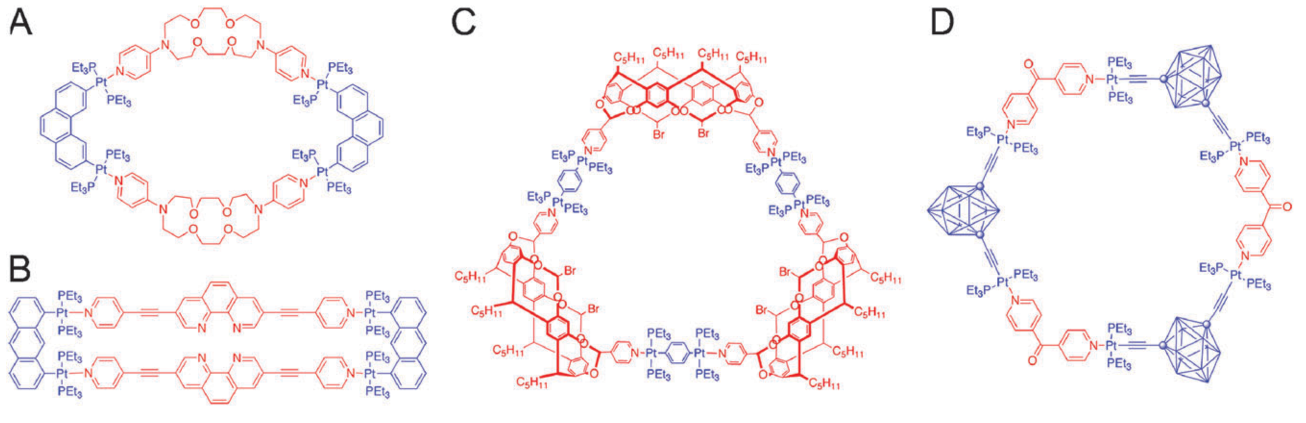


Fig. 1 Representative examples of edge and corner functionalization of 2D metallacycles: (A) an edge functionalized diaza-crown ether supramolecular rhomboid, (B) an edge functionalized phenanthroline rectangle, (C) a corner functionalized cavitand triangle, and (D) a corner functionalized carborane hexagon.

quantitative self-assembly of a supramolecular rectangle (Fig. 1B) that exhibited optical sensing properties towards various hazardous metals. UV-Vis titration studies showed strong complexation of Ni(II), Cd(II), and Cr(III) with the bis-phenanthroline metallacycle. Detection is possible down to micromolar concentrations of each metal.

By employing a similar approach, the combination of a perylene diimide functionalized ligand with 0° or 90° Pt(II) acceptors allowed for the formation of an edge functionalized supramolecular rectangle and rhomboid, respectively.[42] The UV-Vis spectra of the ensembles exhibited displaced and enhanced absorptions relative to the starting, uncoordinated ligands. The size of both assemblies was estimated by MM2 simulations, which showed the compounds to be 3.6 and 4.6 nm in length, respectively.

5.3 Cavitand bowls

Bowl-shaped cavitands have found applications as hosts capable of accommodating a variety of complementary guest molecules or ions.[43] The host–guest properties of cavitands can be varied simply by changing their size and/or depth. Cram and coworkers have demonstrated that the covalent linking of two cavitand bowls in a "rim-to-rim" manner can result in fully closed-shell host molecules.[43] More recently attention has been turned toward noncovalent cavitand assemblies, especially those using metal-directed binding, which can lead to higher order supramolecules that incorporate a greater number of cavitand hosts.[44]

Cavitands offer a unique structure that, if properly functionalized, can be utilized as a corner of supramolecular metallacycles. Diametrically opposed rim substituents of a cavitand bowl project outward at an angle of 60°. In accordance with the directional-bonding approach to coordination-driven self-assembly, the placement of 4-pyridyl or 4-ethynylpyridyl substituents at these positions results in a corner functionalized 60° donor ligand that can be utilized in the construction of multi-cavitand assemblies.[45] The combination of the functionalized cavitand corners with short and long linear di-Pt(II) acceptors led to the formation of four different cavitand functionalized metallacyclic triangles of varying size (Fig. 1C). Likewise, [2 + 2] assemblies were synthesized upon combination of the cavitand functionalized donors with 60° di-Pt(II) acceptors. The six different cavitand functionalized supramolecular assemblies, each with nanoscale cavities in their centers, present a unique series of supramolecular hosts wherein the number and orientation of component cavitand moieties is varied, as is the overall size of each metallacycle, which are capable of selectively incorporating two-fold and three-fold symmetric guests.

5.4 Carboranes

Carboranes are cage cluster molecules that have been explored as components of a variety of materials applications. Their icosahedral symmetry and three-dimensional aromaticity impart a high degree of thermal and chemical stability, which has made them useful as components and templates for applications in, for example, liquid crystalline and nonlinear optical materials.[46] The incorporation of carboranes as functional moieties in supramolecular chemistry has been a desirable goal, with the expectation that the resulting supramolecular assemblies will exhibit properties in addition to those of their parent carborane molecules.

Functionalizing carboranes at their *para* and *meta* positions allows for the synthesis of 180° edge functionalized and 120° corner functionalized building blocks, respectively. With this in mind we have recently reported the synthesis of a carborane functionalized linear bis-pyridyl donor compound as well as linear and 120° carborane functionalized di-Pt(II) acceptors.[47] The linear carborane containing donor was then combined with 0°, 60°, and 90° Pt(II) acceptors, leading to the self-assembly of [2 + 2] rectangular, [3 + 3] triangular, and [4 + 4] square metallacycles, respectively. Moreover, a corner functionalized [3 + 3] hexagon was prepared by mixing the 120° carborane functionalized acceptor and a 120° ditopic bis-pyridyl donor tecton (Fig. 1D). Likewise, the combination of the linear, edge functionalized carborane acceptor unit and a 90° bis-pyridyl donor building block can be used to generate a large, nanoscale supramolecular square. In addition to these examples of pyridyl and Pt(II) substituted carborane building blocks, both *m*- and *p*-carborane dicarboxylates have been prepared[48] and utilized to form neutral rectangular and rhomboidal metallacycles when combined with complimentary ditopic Pt(II) acceptors.

The formation of carborane metallacycles of different shape, size, and charge demonstrates the flexibility and utility of using coordination-driven self-assembly to incorporate multiple carboranes into large supramolecules. Unlike carborods and carborane polymers, where solubility limits the number of carboranes that can be inserted into the large molecules, these edge and corner carborane functionalized assemblies are soluble in common organic solvents. It should therefore be possible to self-assemble supramolecules that incorporate an even greater numbers of carborane cages.

6. *Endo*-functionalization

The growing interest in the design and self-assembly of three dimensional (3D) metallacages has recently brought with it some examples of *endo*-functionalized metal–organic assemblies. Fujita and coworkers have prepared a variety of discrete, *endo*-functionalized $M_{12}L_{24}$ cuboctahedra[49] by combining 12 "naked" Pd(II) ions with 24 bis-pyridyl 120° donor units (Fig. 2). Functionalization of the concave side of the donor units results, upon self-assembly, in *endo*-functionalized cuboctahedra. To date, this method of preparing metal–organic complexes has led to the self-assembly of cuboctahedra functionalized with oligo(ethylene oxide) chains,[49] azobenzene units,[50,51] perfluoroalkyl chains,[52] and polymerizable methyl methacrylate units.[53] Such endohedral functionalized metallacages have been shown to reversibly absorb La(III) ions,[50] provide a means of reversible guest uptake based upon hydrophobic/hydrophilic interactions,[51] solubilize perfluoroalkanes,[52] and increase the efficiency of polymerization reactions,[53] respectively.

At the time of writing there have been no examples of *endo*-functionalization in two dimensional (2D) metallacyclic complexes, likely because simple bond rotations would allow for the functional groups to adopt less sterically imposing *exo*-positions.

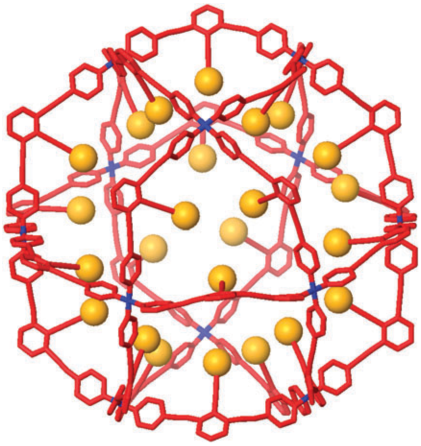


Fig. 2 Representation of *endo*-functionalized coordination cage assemblies prepared by Fujita and coworkers.[49–53] The gold colored spheres projecting inward to the centre of the cage represent functional groups such as oligo(ethylene oxide) chains, perfluoroalkanes, azobenzene units, or polymerizable methyl methacrylate moieties.

7. *Exo*-functionalization

As mentioned previously, self-assembled supramolecular metallacycles and metallacages are capable of providing a well-defined, rigid scaffold whereupon a variety of functional moieties may be precisely positioned and their stoichiometry precisely controlled. Perhaps the most straight-forward realization of the scaffolding properties of discrete metal–organic complexes is through *exo*-functionalization, *e.g.* the covalent attachment of functional moieties to the periphery of supramolecules. In 1998, Diederich *et al.*[54] prepared a metallacyclic rhomboid exohedrally functionalized with two fullerene derivatives. You and Würthner later synthesized[55] supramolecular squares from a 90° di-Pt(II) acceptor and four tetrakisferrocenyl-substituted perylene bis-pyridyl imides, effectively incorporating 16 electroactive ferrocene units into each square. Fujita and coworkers[56] have covalently linked porphyrin, fullerene, and saccharide units to the convex side of 120° bis-pyridyl donors in order to self-assemble *exo*-functionalized $M_{12}L_{24}$ cuboctahedra. Furthermore, the saccharide functionalized assembly was shown capable of selectively interacting with the lectin concanavalin A.

Over the past two years, we have further developed the use of supramolecular metallacycles as scaffolds on which different functional groups can be covalently attached. Taking advantage of the benefits of coordination-driven self-assembly—*i.e.* fewer synthetic steps, near quantitative yields, mild reaction conditions, thermodynamically stable products, and modular assembly protocols—we have prepared a variety of *exo*-functionalized squares, rhomboids, rectangles, triangles, and hexagons that have been functionalized with dendrimers, crown ethers, ferrocene units, and hydrophobic/hydrophilic chains.

7.1 Dendritic functionalized metallacycles

Dendrimers[28] are highly-branched macromolecules composed of several dendritic wedges that extend outward from an internal core. A variety of dendritic structures have been developed and have found applications in such areas as catalysis, light-harvesting, and sensing. Fréchet *et al.*, for example, have developed dendritic materials for use as multichromophoric light-harvesting materials.[57] More recently, Fréchet and coworkers have utilized dendritic materials in a variety of biological applications[58] such as in the treatment of carcinomas in mice.[59] Typically, dendrimers have been prepared *via* convergent and divergent covalent synthetic techniques. Recently, the preparation of dendritic structures with hollow cores has received considerable attention, particularly with respect to their potential uses in drug delivery and transport. For example, Matile *et al.* have used dendritic folate rosettes to study the process of ion transport through lipid bilayers[60] and Percec *et al.* have shown how dendritic dipeptides may self-assemble into extended cylinders with helical pores.[16] Independent from but complimentary to such studies, we have recently developed a new family of dendritic functionalized metallacycles[61,62] utilizing coordination-driven self-assembly, which provides a very simple yet highly effective approach to fine-tune the size and shape of the well-defined cavities within such metallodendrimers.

In an effort to prepare various self-assembled metallodendrimers, the series of dendronized bis-pyridyl donor building blocks **1–4** was synthesized (Fig. 3).[61] Each dendronized donor contains, as a common motif, a 3,5-bis(4-ethynylpyridyl)-1-phenoxy moiety. Fréchet-type dendrons ([G-0]–[G-3]) were then covalently attached to the hydroxyl unit of the 120° ditopic donor, generating the corresponding [G-0]–[G-3] dendronized donors. These dendronized donors were then used to self-assemble a wide range of metallodendrimers of different size, shape, stoichiometry, and generation.

The self-assembly of metallodendrimers with rhomboidal cavities was achieved by the combination of 120° Fréchet-type dendritic donor units and 60° di-Pt(II) acceptor unit **5** in a 1 : 1 stoichiometric ratio (**6a–d**, Scheme 3).[62] Each generation of dendronized donor self-assembled with the di-Pt(II) acceptor in $>96\%$ yield despite the steric bulk imposed upon the resulting rhomboids by the higher generation dendrons. X-Ray quality single crystals of the [G-0] and [G-1] rhomboidal metallodendrimers **6a** and **6b**, respectively, were obtained and their solid state structures were unambiguously established. Both structures feature a well-defined rhombus with an approximately 2.3 × 1.3 nm cavity that embodies the porosity of the crystal.

In addition to rhomboidal metallodendrimers, hexagonal assemblies that are *exo*-functionalized with Fréchet-type dendrons have also been prepared.[61,62] According to the directional-bonding motif, supramolecular hexagons can be prepared by: (1) a combination of three 120° acceptors and three complimentary 120° donors, forming a [3 + 3] hexagon; or (2) combining six 180° building units (donor or acceptor) with six complimentary 120° building units, forming a [6 + 6] hexagon (see Scheme 1). Both self-assembly motifs have been utilized in the construction of metallodendrimers, leading to cavity-cored hexagonal metallodendrimers with core sizes that range from 1.6 nm to 2.9 nm.

Heating [G-0]–[G-3] 120° donors **1–4** with an equimolar amount of 120° di-Pt(II) acceptor **7** resulted in clover-shaped metallodendrimers with hexagonal cavities at their core (**8a–d**, Scheme 3).[61] The structures of each assembly were determined by multinuclear NMR (^{1}H and ^{31}P) and ESI mass

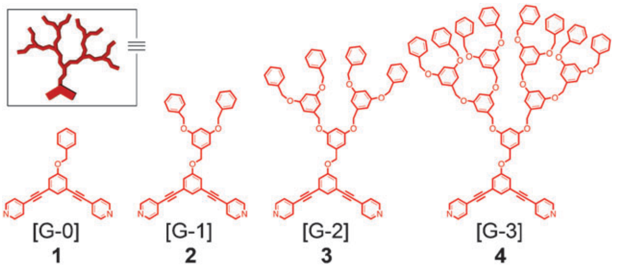
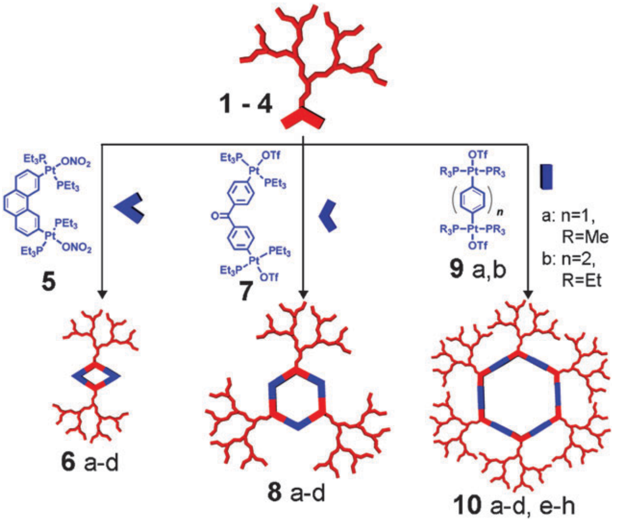


Fig. 3 Chemical structures and schematic representation of [G-0]–[G-3] dendritic 120° bis-pyridyl donors.

spectrometry. MM2 force-field simulations were utilized to determine the structural characteristics of these [3 + 3] hexagonal metallodendrimers and showed that they have a slightly nonplanar hexagonal cavity with an internal radius of approximately 1.6 nm at their core. Furthermore, the outer radius of the largest [G-3] metallodendrimer **8d** was determined to be 2.8 nm, nearly twice the size of the inner radius.

Employing the second protocol for constructing hexagonal dendrimers *via* coordination-driven self-assembly allowed for hexagonal snowflake-shaped metallodendrimers **10a–h** to be prepared by the combination of [G-0]–[G-3] 120° donors **1–4** and both short (monophenyl, **9a**) and long (diphenyl, **9b**) di-Pt(II) linear acceptors as shown in Scheme 3.[62] Multinuclear NMR analysis showed the formation of a single, highly symmetric species for each assembly. The sharp NMR signals in both the ^{31}P and ^{1}H NMR spectra along with the good solubility of these species ruled out the formation of oligomers. ESI-FT-ICR mass spectrometry provided further evidence for the formation of the hexagonal snowflake-shaped metallodendrimers and established their [6 + 6] stoichiometry. It is worth noting that the size of the hexagonal cavities can be controlled by using different sized linear acceptor units. Simulated structures of both [6 + 6] [G-3] assemblies **10d** and **10h** indicate that they have a very similar nonplanar hexagonal cavity at their cores. However, the inner and outer radii of the smaller (monophenyl acceptor) hexagon **10d** are 2.5 and 4.5 nm, respectively, while the inner and outer radii of the larger (diphenyl acceptor) hexagon **10h** are 2.9 and 5.2 nm.



Scheme 3 The self-assembly of [2 + 2] rhomboid, [3 + 3] hexagonal, and [6 + 6] hexagonal dendritic metallacycles.

Using very modular coordination-driven self-assembly techniques we have been able to design and synthesize a wide variety of metallodendrimers. More specifically, 16 different metallodendrimers have been successfully prepared in high yield. The *exo*-functionalized metallacycles all have well-defined cavities and may function as transport vehicles for small, biologically active molecules. The shape, size, number of appended dendrons, and generation of dendron can all be systematically varied using coordination-driven self-assembly techniques.

7.2 Multi-crown ethers

As noted earlier, crown ether macrocycles have garnered considerable research interest as a result of their uses in self-assembly, host–guest complexation, mechanically interlocked systems, and as molecular materials.[20,36,37] As a more recent outgrowth of these investigations, considerable research interest has been turned toward the design and synthesis of macromolecules and supramolecules containing multiple crown ether moieties.[63] Such multi-crown ethers may be used in multi-component host–guest recognition or in the construction of higher-order complexes and assemblies. In this endeavor noncovalent synthetic strategies are again quite useful because of their generally high yield and reduced synthetic cost compared to traditional covalent synthetic strategies.

Along similar lines as those used to prepare supramolecular metallodendrimers, we have provided a simple yet highly efficient approach to the construction, *via* coordination-driven self-assembly, of crown ether derivatized 2D polygons possessing structurally well-defined cavities of varying size and shape.[64,65] The covalent attachment of a dibenzo[24]crown-8 (**DB24C8**) macrocycle to both 120° di-Pt(II) acceptor and 120° bis-pyridyl donor units (Fig. 4) allows for a series of rhomboidal bis-, hexagonal tris-, and hexagonal hexakis-**DB24C8** derivatives to be self-assembled under mild conditions and in quantitative yields when combined with complementary 60°, 120°, and 180° building blocks, respectively.

Upon mixing the 120° crown ether-containing acceptor unit **11** with 60° donor **5** or **14**, for example, a bis-**DB24C8** rhomboid was obtained (Scheme 4).[64] In a complementary

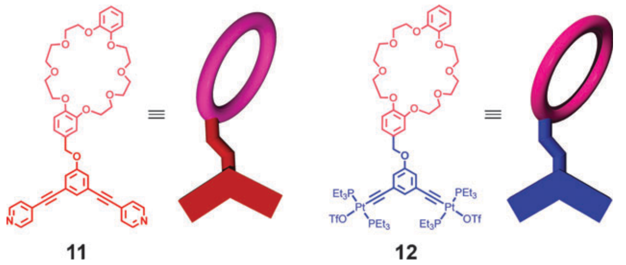
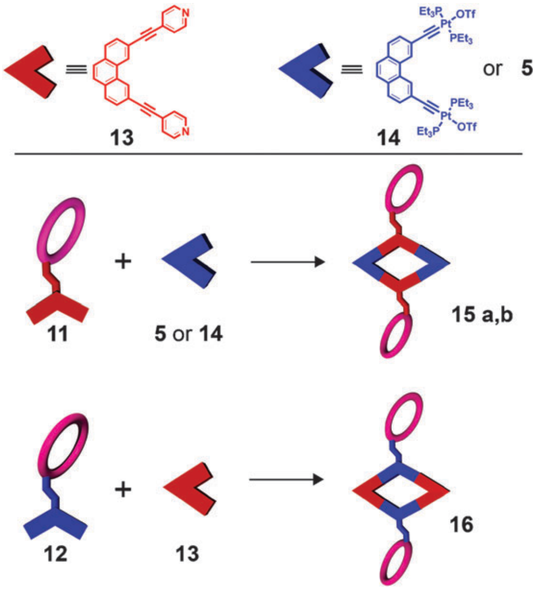


Fig. 4 Chemical structures and schematic representations of a crown ether functionalized donor (**11**) and acceptor (**12**).



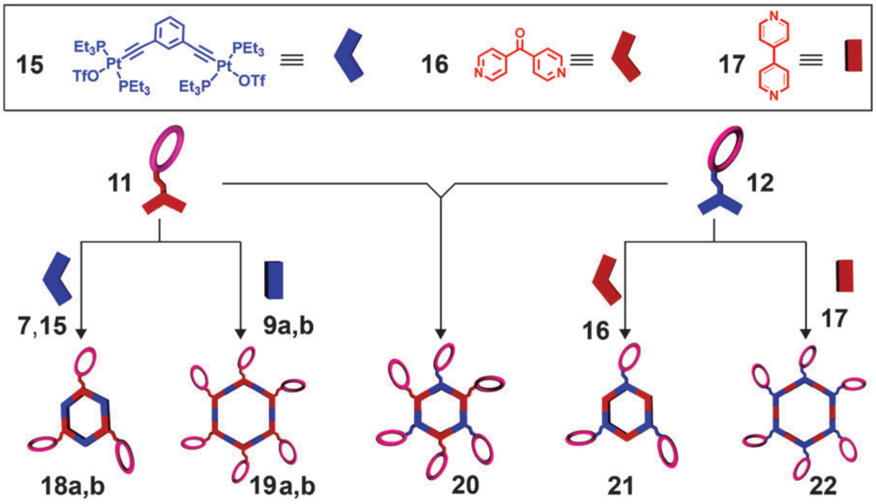
Scheme 4 The self-assembly of metallacyclic rhomboids *exo*-functionalized with pendent **DB24C8** macrocycles.

manner, stirring the 120° crown ether-containing donor **12** with an equimolar amount of the known 60° angular di-Pt(II) acceptor **13** resulted in another type of rhomboidal structure, only here the role of the acceptor and the donor are switched. By using different sized 60° angular di-Pt(II) acceptors, the size of the rhomboidal cavity in the final assemblies can be controlled. Molecular modeling studies show an inner cavity size of 1.6 nm for the smaller rhomboidal bis-**DB24C8** (**15a**) whereas the cavity size of the larger rhomboidal bis-**DB24C8** (**15b**) is 2.0 nm.

Similarly, hexagonal tris-**DB24C8** derivatives were obtained by two complementary strategies (Scheme 5).[64,65] The self-assembly of tris-**DB24C8** derivatives with hexagonal cavities can be achieved by the combination of the 120° **DB24C8** derivatized donor subunit **11** and 120° di-Pt(II) acceptors **7** or **15** in a 1 : 1 stoichiometric ratio. Likewise another type of hexagonal tris-**DB24C8** derivative **21** can also be easily synthesized by mixing the 120° **DB24C8** containing acceptor subunit **12** and di-2-pyridyl ketone (**16**) in a 1 : 1 ratio. The structures of all assemblies are supported by the analysis of multinuclear NMR and ESI mass spectrometry. Molecular modeling studies reveal a smaller internal diameter of 2.3 nm for **21** as compared to 2.9 nm and 3.2 nm for **18a** and **18b**, respectively.

Building further upon these studies, hexagonal metallacycles *exo*-functionalized with six **DB24C8** moieties have been prepared (Scheme 4).[65] The hexakis-**DB24C8** assemblies containing a crown ether moiety covalently attached to each of the vertices of the hexagon were easily prepared *via* coordination-driven self-assembly. The first method investigated for their construction utilized three 120° donor units (**11**) and three 120° acceptor units (**12**), each derivatized with one crown ether moiety, from which the [3 + 3] hexagon **20** can be self-assembled. The synthesis of hexagonal assemblies can also be achieved according to two additional complementary protocols from the combination of six 180° building blocks and six 120° angular subunits. The self-assembly of crown ether derivatized donor **11** with different sized 180° linear acceptors **9a** and **9b** led to the formation of crown ether derivatized hexagons **19a** and **19b**, respectively. Along similar lines, crown ether derivatized acceptor **12** was combined in a 1 : 1 ratio with 180° linear 4,4′-bipyridyl donor **17** demonstrating a complementary method for the preparation of hexagonal hexakis-**DB24C8** assembly **22**.

All hexagonal hexakis-**DB24C8** derivatives (**19a,b**, **20**, and **22**) have been characterized by multinuclear NMR and mass spectrometry (ESI and ESI-TOF). Molecular force-field simulations were used to gain further insight into the structural characteristics of these assemblies. Simulations reveal that the underlying hexagonal structures—the "scaffolds"—all retain their planar and rigid structures even when derivatized with pendent crown ether units, as was the case for dendronized metallacycles. Internal diameters of 3.0, 5.2, 6.2, and 4.5 nm for **20**, **19a**, **19b**, and **22**, respectively, were observed.



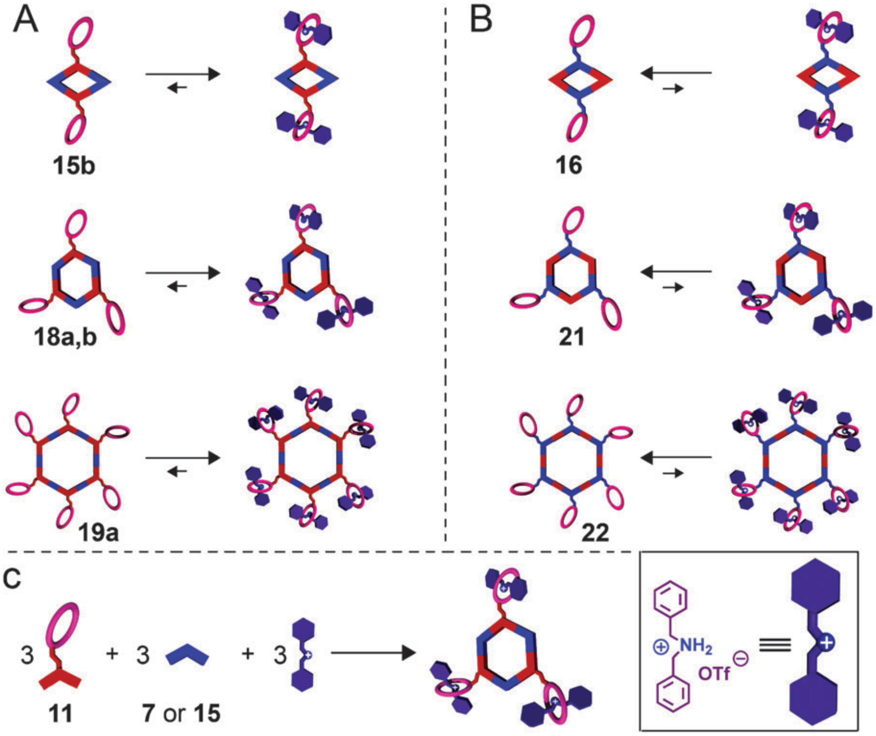
Scheme 5 The self-assembly of [3 + 3] and [6 + 6] hexagonal metallacycles bearing 2 and 3 **DB24C8** host functionalities, respectively, that are covalently linked to both donor (**18–20**) and acceptor (**20–22**) building blocks.

7.3 Poly[2]pseudorotaxanes

Upon the preparation of multi-crown ether metallacycles, it became of immediate interest to investigate the ability of such well-defined, complex structures to act as multi-valent hosts in the formation of poly[2]pseudorotaxanes.[64,65] Through detailed characterization using one-dimensional multinuclear (^{1}H and ^{31}P) and two-dimensional (^{1}H–^{1}H COSY and NOESY) NMR spectroscopies as well as mass spectrometry (ESI-MS) it was established that each multi-crown ether polygon is able to complex two, three, or six dibenzylammonium ions without disrupting the underlying metallacyclic polygons, thus producing a series of different poly[2]pseudorotaxanes (Scheme 6A,B). ^{1}H NMR titration experiments were used to establish thermodynamic binding constants, which ranged from 5.7×10^2 to 2.5×10^4 M^{-1}. The largest binding ability was observed for the complexation of a single dibenzylammonium guest while lower binding constants were obtained upon complexation of additional guests. These values suggest all multiple crown ether derivatives have a similar ability to bind dibenzylammonium guest(s) as does **DB24C8** in nonpolar solvents such as dichloromethane. A general trend of differences in binding ability was observed depending on whether the **DB24C8** host was covalently linked to a 120° bis-pyridyl donor (Scheme 6A) or di-Pt(II) acceptor (Scheme 6B). In particular, the covalent attachment of derivatized crown ether macrocycles to di-Pt(II) acceptor building blocks results in a decrease in binding ability of the resultant rhomboidal and hexagonal multi-crown ether hosts.[65] This reduction in binding ability is likely caused by the loss of electron density upon covalently attaching the electron rich macrocycles to an electron poor acceptor, thus decreasing the electron rich character of the crown ether macrocycles and their ability to bind dibenzylammonium guests.

Molecular force-field simulations were used to gain further insight into the structural characteristics of the exohedrally functionalized poly[2]pseudorotaxanes. Molecular simulations revealed that the addition of dibenzylammonium to **DB24C8** hosts does not disrupt the underlying polygonal scaffolds as ammonium salts are complexed by their pendant **DB24C8** macrocycles. In all cases, the underlying rigid nature of the 2D polygonal cavity is retained while the flexibility of each crown ether is reduced as a result of host–guest complexation.

It is important to note a final means of preparing metallacyclic poly[2]pseudorotaxanes (Scheme 6C) that further demonstrates the power of noncovalent self-assembly and, particularly, orthogonal self-assembly. Simply mixing a 1 : 1 : 1 ratio of the 120° crown ether functionalized donor **11**, a complimentary 120° Pt(II) acceptor (**7** or **15**), and a dibenzylammonium salt results in the spontaneous formation of tris[2]pseudorotaxanes.[64] Spectroscopic characterization of the "one pot" assembled poly[2]pseudorotaxanes matched those of the same assemblies prepared *via* stepwise methods. In this process of construction, however, nine subunits are brought together to spontaneously form discrete, highly symmetric species as directed by multiple noncovalent interactions. These results demonstrate a number of ways that multiple complementary building blocks exhibiting a variety



Scheme 6 Demonstration of the abilities of multi-crown ether metallacycles to act as hosts for dibenzylammonium cations (inset). (A) The formation of poly[2]pseudorotaxanes is thermodynamically favoured when **DB24C8** macrocycles are linked to donor building blocks. (B) Poly[2]psedorotaxane formation is less favoured when the electron rich macrocycles are covalently linked to electron poor di-Pt(II) building blocks. (C) Example of the orthogonality of the self-assembly approach wherein 9 individual subunits are spontaneously brought together in one step.

of orthogonal noncovalent molecular recognition motifs are able to self-assemble into discrete structures according to the specific information encoded within the individual components.

7.4 Multiferrocene complexes

Ferrocene is another molecule that has been of interest to analytical, synthetic, and materials chemists because it is a stable and readily oxidizable organometallic complex that has been incorporated into a variety of functional and multifunctional compounds.[66] With the successful self-assembly of exohedrally functionalized metallodendrimers, multi-crown ethers, and poly[2]pseudorotaxanes the design and synthesis of multi-ferrocenyl metallacycles became of interest. Such multi-redox active compounds may be developed into electroluminescent, information storage, and photochemical devices.[55,67] By synthesizing ferrocene functionalized donor and acceptor building blocks, coordination-driven self-assembly is able to provide a facile and versatile strategy for the preparation of metallacyclic multi-ferrocenyl assemblies that allows precise control over metallacycle shape, size and the distribution of ferrocene moieties.

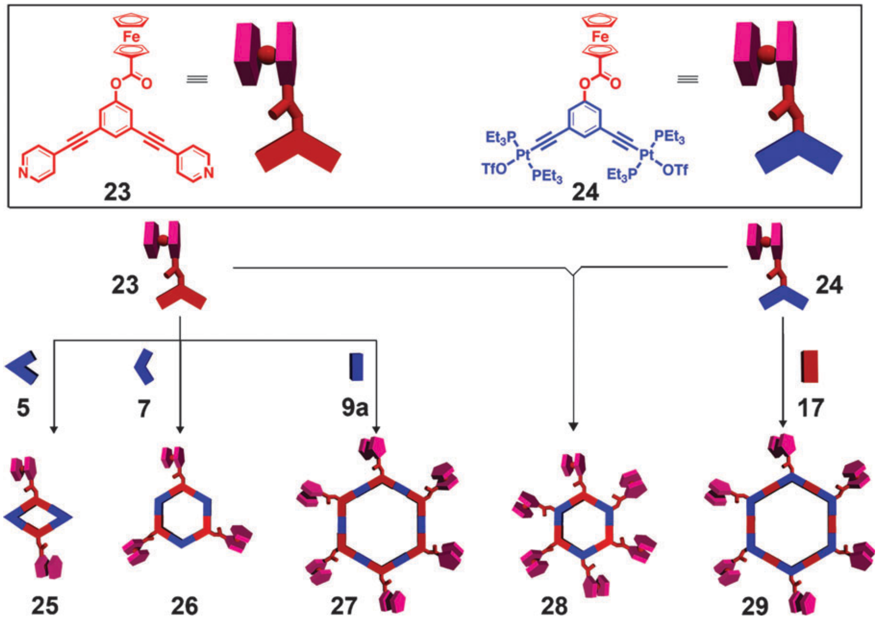
The design and synthesis of *exo*-functionalized multi-ferrocene complexes (Scheme 7) follows that of previously discussed dendritic and crown ether systems. Stirring a 1 : 1 ratio of a ferrocenyl 120° donor precursor[67] (**23**) and 60°, 120°, or 180° di-Pt(II) acceptors (**5**, **7**, or **9a**) resulted in the formation of the [2 + 2] rhomboid **25**, the [3 + 3] hexagon **26**, and the [6 + 6] hexagon **27**, respectively, each with pendant ferrocene groups at donor vertices. Analysis of multinuclear NMR (^{1}H and ^{31}P) and mass spectroscopy (ESI and ESI-TOF) results supported the existence of all multi-ferrocene assemblies. Each multi-ferrocenyl metallacycle contains a well-defined cavity in its center. According to molecular modeling results, these cavities range in size from 2.4 × 1.6 nm for the rhomboid (**25**), to 3.3 × 3.1 nm and 5.3 × 5.1 nm for the different size hexagonal supramolecules (**26** and **27**, respectively).

As is important for their electronic materials properties, electrochemical studies reveal that all of the redox sites attached to complexes **25–27** are stable, independent, electrochemically active, and display 2, 3, and 6 reaction sites, respectively. All heterobimetallic compounds show one-electron reaction responses, with the additional electroactive sites enhancing the magnitude of the current. Furthermore, electrochemical studies were able to reveal that the larger assemblies had lower diffusion coefficients relative to the smaller assemblies.[68]

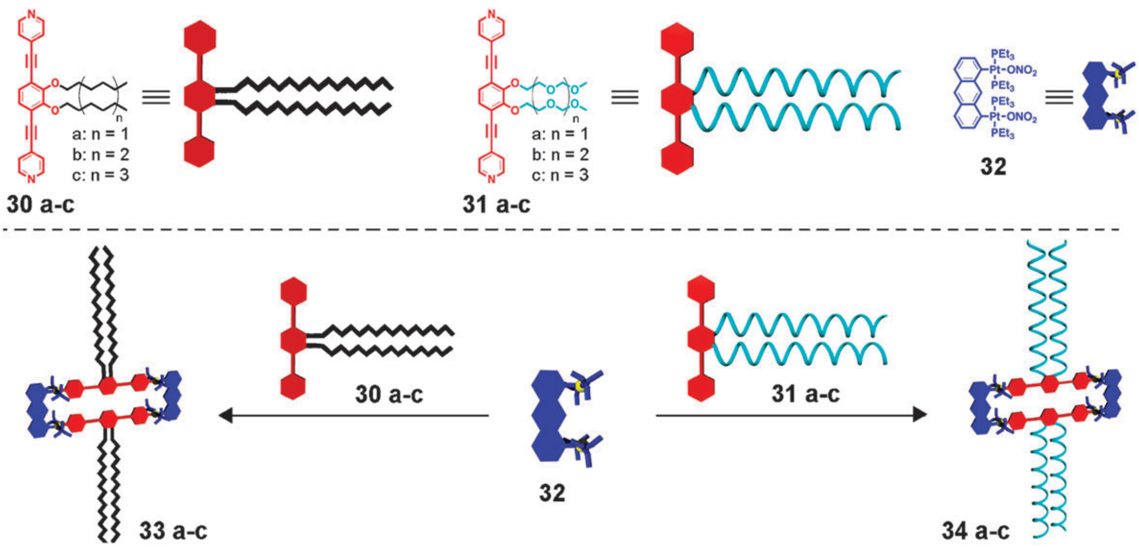
Complementary assemblies have also been prepared using a recently synthesized ferrocenyl 120° di-Pt(II) acceptor **24** (Scheme 7).[69] Using this new functionalized acceptor, two approaches to the preparation of hexakisferrocenyl hexagons have been investigated. Combining three ferrocene functionalized 120° donor units (**23**) and three 120° acceptor units (**24**) results in the formation of [3 + 3] hexakisferrocene hexagon **28**. Alternatively, mixing six 120° ferrocenyl building units and six complementary 180° 4,4′-bipyridyl donors (**17**) in a 1 : 1 ratio results in the larger [6 + 6] hexakisferrocenyl hexagon **29**. Electrochemical studies reveal that the increased size of the hexagonal assemblies has a pronounced effect on their electrochemical properties: a decrease in the diffusion coefficient and increase in the half-wave potential.

7.5 Hydrophobic and hydrophilic rectangles

The self-assembly and self-organization of many biomolecules are heavily influenced by hydrophobic and hydrophilic interactions. Lipid bilayers, micelles, vesicles and the like all take their shapes largely because of the interactions between different hydrophobic and hydrophilic regions of their constituent molecules.[70] Dual character block copolymers, which



Scheme 7 Chemical structures and schematic representation of ferrocene functionalized 120° donor (**23**) and acceptor (**24**) units (inset) along with their self-assembly into *exo*-functionalized ferrocenyl rhomboids and hexagons of varying size and ferrocene stoichiometry.



Scheme 8 Chemical structures and schematic representations of hydrophobic (**30a–c**) and hydrophilic (**31a–c**) functionalized 180° donors and their self-assembly into hydrophobic and hydrophilic supramolecular rectangles of varying size.

represent synthetic analogues of such natural molecules, have been rigorously investigated for their materials properties.[71] There have recently been examples where self-assembly and self-organization involving metallacycles functionalized with hydrophobic chains have been utilized. Lu *et al.*, for example, have prepared alkoxybridged Re(I) supramolecular rectangles that are substituted with long alkyl chains (C_4H_9, C_8H_{17}, and $C_{12}H_{25}$) that, in the presence of increasing water concentrations, induce the supramolecular rectangles to aggregate in solution.[72] This aggregation then leads to enhanced luminescence as well as the ability of the functionalized rectangles to act as probes for photoluminescence quenching.

In order to further study the effects of hydrophilic and hydrophobic interactions on the assembly and organization properties of metallacycles we have prepared[73] a series of hydrophobic and hydrophilic functionalized 180° 1,4-bis-(4-ethynylpyridyl)-2,3-substituted benzenes (Scheme 8). The hydrophobic donors are functionalized with C_6H_{13}, $C_{12}H_{25}$, and $C_{18}H_{37}$ alkyl chains (**30a–c**) whereas the hydrophilic donors are substituted with methyl terminated di-, tetra-, and hexaethyleneglycol units (**31a–c**). Upon combination with the 0° di-Pt(II) acceptor **32** in a 1 : 1 ratio, each donor self-assembles into either hydrophobically functionalized (**33a–c**) or hydrophilically functionalized (**34a–c**) supramolecular rectangles of varying size and affinity for water.[73] All six supramolecular rectangles have been characterized by multinuclear NMR and ESI mass spectroscopies. According to molecular modeling simulations the hydrophobic and hydrophilic chains of each exohedrally functionalized rectangle prefer to wrap around and aggregate in solution (solvent models of both $CHCl_3$ and H_2O were used). With their long chain substituents fully outstretched the rectangles vary in length from 2.9 nm to 5.9 nm.

Further studies of mixed hydrophobic–hydrophilic supramolecular rectangles have been performed and have provided insight into the self-organization properties of these *exo*-functionalized assemblies.[74] Similar length substituents of differing hydrophilicity (*i.e.* C_6H_{13} and diethyleneglycol, $C_{12}H_{25}$ and tetraethyleneglycol, and $C_{18}H_{37}$ and hexaethyleneglycol) were mixed in a 1 : 1 : 2 ratio with the 0° di-Pt(II) acceptor **32**. Such mixtures are able to give rise to purely hydrophobic, amphiphilic, and purely hydrophilic rectangles with a statistical ratio of the three being 1 : 2 : 1, respectively. It was observed through multinuclear (^1H and ^{31}P) and ESI-MS spectroscopies, however, that the complex mixtures self-organized to give a greater than statistical ratio of purely hydrophobic and hydrophilic rectangles at the expense of the formation of amphiphilic rectangles. The extent of self-organization was small for donors bearing shorter hydrophobic and hydrophilic substituents and considerably larger for those with longer functionalities. The observation of such hydrophobic and hydrophilic dictated self-organization phenomena is likely due to a pre-organization and aggregation of like donors, thus biasing the formation of purely hydrophobic or hydrophilic rectangles. The results highlight how the self-assembly and self-organization of functionalized metallacycles may be influenced by the nature of the functionalities themselves.

Conclusions

Chemists continually benefit from an ever growing collection of synthetic protocols that can be utilized and adapted to the preparation of highly complex and functional molecules. Complementary to these synthetic advances are new and more powerful analytical techniques that have allowed for the dynamic electronic, photonic, and other properties of advanced materials to be thoroughly examined. Molecular recognition, dynamic chemistry, and self-assembly are often viewed as being at the forefront of modern materials and molecular device research, and the large, complex molecules and supramolecules prepared by such techniques often demand equally complex analytical techniques. As such, self-assembly is often found at the confluence of many advanced synthetic and analytical techniques. Indeed chemists (as well as biologists, physicists, and materials scientists) have been impressively successful in answering Feynman's call for making "a thing very small which does what we want." As examples we have demonstrated the successful design and synthesis of 2D functionalized metallacycles using high-yielding coordination-driven self-assembly techniques. The supramolecular assemblies described are functionalized with a variety of host–guest (crown ether, cavitand), photonic (optical sensors), materials (carborane, dendritic, ferrocenyl), and self-organizing (hydrophobic/hydrophilic) moieties incorporated onto/into their structures. In particular, we have found that the rigid, highly symmetric structures afforded by coordination-driven self-assembly can act as scaffolds for the precise control of the overall size and geometry of the underlying metallacycles as well as control over functional group stoichiometry and placement. Even greater opportunities in the development of novel molecular materials can be expected when such studies are extended into the 3rd dimension and through the incorporation of addition functional moieties.

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