

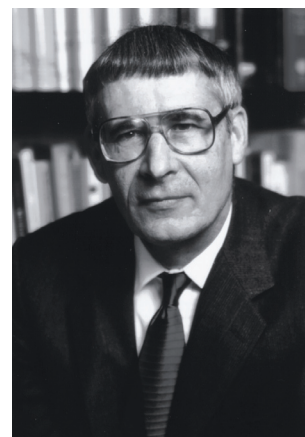
Supramolecular Co-ordination: Predesigned Metallacycles and Metallacages *via* Self-Assembly

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About the Author

Peter Stang was born in Nürnberg Germany, in 1941, became a naturalized US citizen in 1962 and gained his BS in Chemistry from DePaul University in Chicago (Magna Cum Laude) in 1963. He obtained his Ph.D. with Andrew Streitwieser at UC-Berkeley in 1966 and was a postdoctoral fellow with Paul Schleyer, then Lecturer, at Princeton University prior to moving to Utah in 1969. He has remained there since and, since 1992, is Distinguished Professor in Chemistry. His academic appointments include serving as Department Chairperson and Dean of the College of Science. Over the past 40 years, he has made numerous, seminal contributions to diverse areas of physical organic and synthetic chemistry. His pioneering achievements include the first preparation of vinyl triflates in the late 1960s and 1970s, and then several major advances in supramolecular chemistry, self-assembly and organometallic chemistry from the 1990s to the present, including the design and preparation of exquisitely complex assemblies. He has authored or co-authored some 500 publications with 11 in the first six months of this year; they include six monographs and numerous reviews.



His record of service to the chemical community includes participation in numerous national and international panels and committees, *e.g.* Pacifichem (2000-), serving as Associate Editor (1981-2002) and then Editor-in Chief of the *Journal of the American Chemical Society* (2002-present). He has mentored 43 postdoctoral associates, 31 PhD students, and 7 MS students. His previous recognitions include the F.A. Cotton Medal for Excellence in Chemical Research (2010), the Fred Basolo Medal for Outstanding Research in Inorganic Chemistry (2009), the ACS Award for Creative Research and Applications of Iodine Chemistry (2007), the Linus Pauling Medal (2006), as well as numerous others. He is a member of the US National Academy of Sciences (2000) and the American Academy of Arts and Sciences (2002), a Foreign Member of the Hungarian Academy of Sciences (2007), and a Foreign Member, Chinese Academy of Sciences (2006).

The inclusion of this article in Volume 75 is at the invitation of the editor whose very successful collaboration began in October 1981, almost exactly 30 years ago.

Self-assembly is a widely used, but by no means universally agreed upon, concept and process. It generally refers to the spontaneous association of appropriate complementary molecular sub-units to form more complex, larger ensembles according to the specific information encoded within their structures. It generally involves weak interactions such as hydrophilic-hydrophobic effects, van der Waals forces, π - π -stacking, dipolar interactions, hydrogen bonding, *etc.* It involves reversible reactions and is primarily controlled by thermodynamics. As a consequence, most self-assembly processes are self-correcting or self-healing; an incorrectly formed bond can readily dissociate and re-associate correctly and, therefore, afford essentially quantitative or very high product yields. Numerous biological processes such as nucleic acid assembly and tertiary structure, ribosomes, microtubules, protein folding, *etc.*, occur via self-assembly that are important in all living organisms from simple viruses to humans.

Nature, of course, has had billions of years to evolve elegant, deceptively simple, efficient protocols for the

self-assembly of complex, sophisticated *supramolecules*, generally under mild conditions. Just as an example, the protein coat of all viruses surrounding their nucleic acid, consists of self-assembled spherical capsids in the shape of either an icosahedron or a dodecahedron.¹

One may ask a simple question. *Can one use self-assembly and weak interactions in the laboratory to prepare complex nanoscale molecules with well-defined shapes, dimensions and sizes?* Many attempts to mimic nature's elegant self-assembly processes with hydrogen bonds generally met with limited success, particularly in the formation of large, three-dimensional assemblies, with pre-defined shapes and sizes. This is due to the lack of directionality of the weaker interactions and the necessity of accurately positioning dozens of these interactions in order to obtain functional assemblies. In contrast, the use of metals, and dative metal-ligand interactions, circumvents these challenges. Dative bonds are highly directional due to *d*-orbital involvement and their geometry. Moreover, third row metal ligand bonds have energies in the range

of 15-25 kcal/mol, much less than covalent bonds (*ca.* 60-120 kcal/mol) but stronger than the weak interactions used by biology (*ca.* 0.5-10 kcal/mol). Furthermore, by virtue of its higher bond strength, one dative metal-ligand bond can replace several hydrogen bonds in the self-assembly process. That is why we and others, as described below, have used various transition metals and metal-ligand interactions for the abiological self-assembly of nanoscale species with pre-designed, well-defined shapes and sizes.

After almost a quarter of a century of active research in classical physical-organic chemistry,² including a most enjoyable and productive collaboration with Brian Halton (now Editor of *Chemistry in New Zealand*) in the area of alkylidenecyclopropenes,³ in the early 1990s, I became interested and involved in self-assembly. In particular, my interest is in the rational design and co-ordination-driven self-assembly of two-dimensional (2D) metallacycles and three-dimensional (3D) metallacages. Pioneering work, primarily by Lehn and Sauvage,⁴ demonstrated the advantages and usefulness of co-ordination-driven self-assembly in the formation of infinite helicates, grids, ladders, racks and related species.⁵ Subsequently, the co-ordination-driven self-assembly of rationally pre-designed metallacycles and metallacages at the nanoscale has become a very active area of research.⁶ Five major strategies have been developed and are in wide use for the ready formation of these species⁶, *viz.* i) our *directional bonding* approach;⁷ ii) Raymond's *symmetry interaction* method;⁸ iii) Fujita's *molecular paneling* procedure;⁹ iv) Mirkin's *weak link* approach;¹⁰ and v) Cotton's use of *dimetallic building blocks*.¹¹ Herein, I shall summarize and briefly describe our contributions to this field.

Our initial efforts involved the self-assembly of 2D polygons and, in particular, molecular squares,¹² a consequence and outgrowth of our related previous work on covalent iodonium- based squares.¹³ This was followed by the self-assembly^{7a} of various triangles, rectangles, rhomboids and hexagons as illustrated in Fig. 1. Chiral self-assembled supramolecular species were also prepared.¹⁴ More recently, dendrimer, ferrocene, crown ether, and poly[2]pseudorotaxane functionalized systems have been assembled,¹⁵ as shown in Fig. 2. All of the new compounds were characterized by multi-nuclear NMR, electrospray mass spectrometry, including isotope distributions and, where possible, X-ray structural analysis.

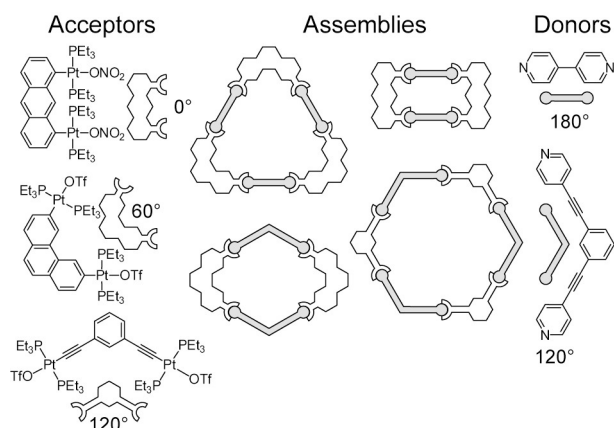


Fig 1. Representative self-assembled polygons.

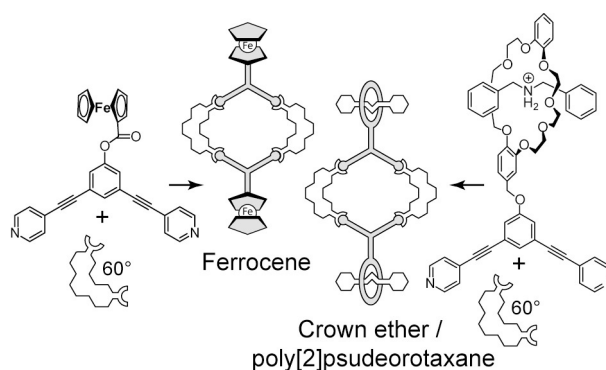


Fig 2. Functionalized self-assembled polygons.

Self-organization is the spontaneous, selective formation of one or more well-ordered ensembles from a complex mixture. It occurs throughout Nature from molecules to galaxies and depends, among other factors, on self-recognition and self-selection. Self-organization is an important phenomenon in biological systems and biological self-assembly. Hence, we investigated self-organization in co-ordination-driven self-assembly.¹⁶ A wide variety of complex mixtures of sub-units undergoes self-organized self-assembly into discrete supramolecules based upon the information encoded within the individual building unit.¹⁶

Depositing metallocupramolecular compounds on solid supports is a very important step in exploring their materials properties and potential applications in devices. Surfaces afford a means of uniformly aligning and ordering such metallacycles as well as increasing their coherence and addressability. Hence, in a collaborative study with Professor Li-Jun Wan (Institute of Chemistry of the Chinese Academy of Sciences in Beijing), we examined, using scanning tunneling microscopy (STM), surface confinement of self-assembled metallacycles and metallacages.¹⁷ Both 2D squares as well as rectangles and 3D trigonal bipyramidal and prisms form intact assemblies and ordered adlayers on highly oriented pyrolytic graphite (HOPG) or Au(111) surfaces,¹⁷ as illustrated in Fig. 3.

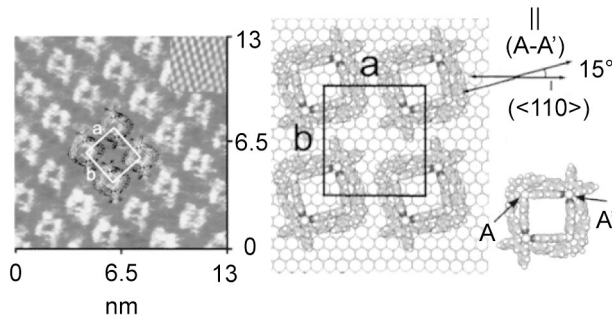


Fig 3. Surface-confined squares adsorbed on a Au surface.

An important and fascinating part of abiological co-ordination-driven self-assembly is the formation of 3D supramolecular cages and polyhedra. 3D self-assembly is more complex and challenging than 2D self-assembly but inherently more interesting. These systems may be self-assembled via either an edge/corner or face-directed approach.^{6,7b} The former involves designing building units that make up the corners or edges of a polyhedra or 3D cage and connecting these with appropriate con-

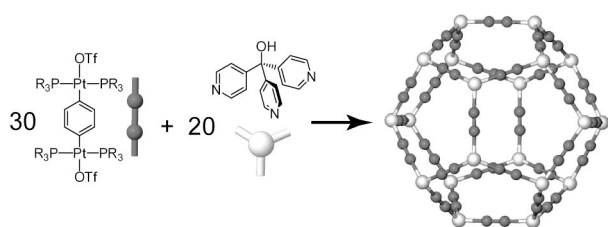


Fig 4. Self-assembly of a dodecahedron.

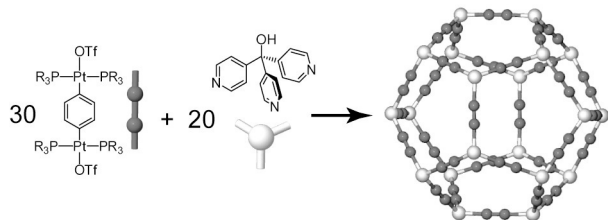


Fig 5. Self-assembly of a cuboctahedron.

necting units. The latter, which is similar to Fujita's molecular paneling method, involves making the face of a polyhedron or 3D cage and connecting these with appropriate connectors. We have used the edge/corner directed approach to self-assemble dodecahedra,¹⁸ as illustrated in Fig. 4, as well as a variety of diverse 3D cages.¹⁹ Similarly, we employed the face-directed approach to self-assemble cuboctahedra,²⁰ as shown in Fig. 5, in addition to various molecular prisms.²¹

Fujita and co-workers,²² have used self-assembled 3D cages as *molecular flasks* for the encapsulation of guests in order to study unusual reactions and unique chemical phenomena. Likewise, Raymond and co-workers²³ have investigated metallacages as supramolecular catalysts. Similarly, we have recently demonstrated²⁴ the encapsulation of 1,3,5-triphenylbenzene in a truncated tetrahedra as shown in Figure 6.

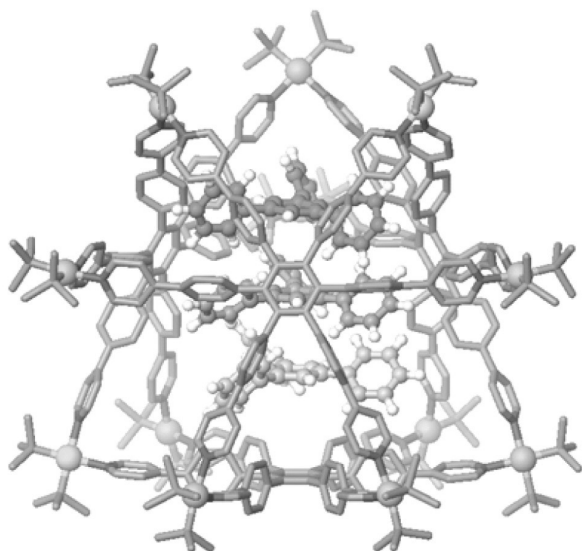


Fig 6. Structure of a truncated tetrahedron encapsulating three 1,3,5-triphenylbenzene molecules.

Most recently, we have examined both the photophysical properties²⁵ as well as the biological activity²⁶ of self-assembled supramolecular species. Both we²⁶ and Therrien and co-workers²⁷ have demonstrated that self-assembled ruthenium supramolecular species possess novel anti-tumor activity and, hence, are part of a new class of emerg-

ing metal-based potential drugs.²⁸ The *in vitro* activity in human cancer cells^{26a} of a Ru-based molecular cage is comparable, or better, than that of cisplatin, one of the most widely used anti-tumor drugs.

Finally, these self-assembled, pre-designed co-ordination-based metallacages have influenced the development and are related to metal-organic frameworks (MOF), that are currently very topical due to their potential use in gas (H_2 , CO_2 , etc.) uptake and storage and other potential applications.²⁹

In summary, co-ordination-based self-assembly is a very active area of contemporary chemistry and an important part of abiological self-assembly. The first two decades were primarily devoted to developing and understanding the process of co-ordination-based self-assembly, along with the challenges of proper characterization. More recently, applications have started to emerge. The future in this area will likely focus on a) multi-component (more than two building units), more complex self-assembly; b) further understanding of the self-assembly processes and c) applications in the materials science and the biochemical and biomedical areas.

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