

Self-Organization in Coordination-Driven Self-Assembly

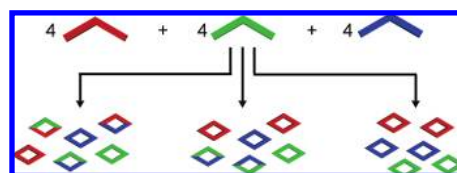
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CON SPECTUS

Self-assembly allows for the preparation of highly complex molecular and supramolecular systems from relatively simple starting materials. Typically, self-assembled supramolecules are constructed by combining complementary pairs of two highly symmetric molecular components, thus limiting the chances of forming unwanted side products. Combining asymmetric molecular components or multiple complementary sets of molecules in one complex mixture can produce myriad different ordered and disordered supramolecular assemblies. Alternatively, spontaneous self-organization phenomena can promote the formation of specific product(s) out of a collection of multiple possibilities. Self-organization processes are common throughout much of nature and are especially common in biological systems. Recently, researchers have studied self-organized self-assembly in purely synthetic systems.



This Account describes our investigations of self-organization in the coordination-driven self-assembly of platinum(II)-based metallocsupramolecules. The modularity of the coordination-driven approach to self-assembly has allowed us to systematically study a wide variety of different factors that can control the extent of supramolecular self-organization. In particular, we have evaluated the effects of the symmetry and polarity of ambidentate donor subunits, differences in geometrical parameters (e.g., the size, angularity, and dimensionality) of Pt(II)-based acceptors and organic donors, the influence of temperature and solvent, and the effects of intermolecular steric interactions and hydrophobic interactions on self-organization.

Our studies have shown that the extent of self-organization in the coordination-driven self-assembly of both 2D polygons and 3D polyhedra ranges from no organization (a statistical mixture of multiple products) to amplified organization (wherein a particular product or products are favored over others) and all the way to the absolute self-organization of discrete supramolecular assemblies. In many cases, inputs such as dipolar interactions, steric interactions, and differences in the geometric parameters of subunits, used either alone or as multiple factors simultaneously, can achieve absolute self-organization of discrete supramolecules. We have also observed instances where self-organization is not absolute and varies in its deviation from statistical results. Steric interactions are particularly useful control factors for driving such amplified self-organization because they can be subtly tuned through small structural variations.

Having the ability to fully understand and control the self-organization of complex mixtures into specific synthetic supramolecules can provide a better understanding of analogous processes in biological systems. Furthermore, self-organization may allow for the facile synthesis of complex multifunctional, multicomponent systems from simply mixing a collection of much simpler, judiciously designed individual molecular components.

Introduction

Chemists have developed an extensive collection of protocols for making compounds with desirable properties or functions. It is often the case, however, that complex molecules require equally complex synthesis, which can be costly in terms of

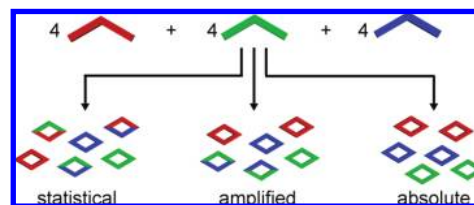
time, materials, atom economy, and yield. Natural systems, on the other hand, are capable of synthesizing molecular and supramolecular systems of impressive complexity and functionality in high yield with relative ease. For example, while it may take a biochemist a few days to prepare a 100

amino acid polypeptide, a bacterial cell can carry out the same feat on the order of seconds.¹ Some enzymes have evolved to be so efficient that their catalysis is limited² only by the rate of diffusion ($k_{\text{cat}}/k_{\text{m}} \approx 10^8$), a target so far unattained in synthetic systems. In general, biological systems are able to perform complex tasks by taking advantage of reversible noncovalent interactions to dictate their structural, physical, and functional properties. Inspired by Nature, chemists have developed myriad ways of utilizing noncovalent interactions to direct the spontaneous self-assembly³ of supramolecular systems⁴ in manners similar to the same phenomena that occur throughout Nature. Self-assembly protocols can considerably reduce synthetic costs and often lead to the formation of a single thermodynamic product in high yield.

Supramolecular chemistry takes advantage of the fact that complementary molecular subunits can be specifically designed such that they selectively recognize each other and spontaneously assemble into well-defined suprastructures. In the 1960s, Lehn, Cram, and Pederson provided early examples of self-assembling supramolecular systems in their studies⁵ of cation binding cryptand and crown ether compounds. In the intervening years, researchers have designed and synthesized complementary pairs of molecular subunits that are capable of utilizing the noncovalent information stored within their structural and electronic properties to spontaneously self-assemble into a preferred supramolecule(s). It is often advantageous to limit the number of potential supramolecular products by combining, for example, only one hydrogen bond donor with one hydrogen bond acceptor or one metal acceptor with one organic donor, etc., and by using highly symmetric molecular inputs. Such a protocol has the clear advantage of reducing the complexity of the system and promoting the efficient, high yielding assembly of a singular product. There are, however, several merits to exploring considerably more complex self-assembling systems that either contain multiple molecular subunits or are able to produce multiple different products. Not only do such complex mixtures more closely resemble biological systems, but they also open the possibility for self-organization⁶ phenomena.

Self-organization⁶ is the selective and spontaneous formation of one or more well-ordered structures from within a complex mixture that could otherwise form a much greater number of structures. Self-organization phenomena occur throughout Nature across all length scales^{3b} from the creation of galaxies to the formation of hydrogen atoms. Mammalian cells can be considered highly complex self-organized structures composed of multiple biomolecules brought together by noncovalent self-assembly. In the 1990s, the research groups

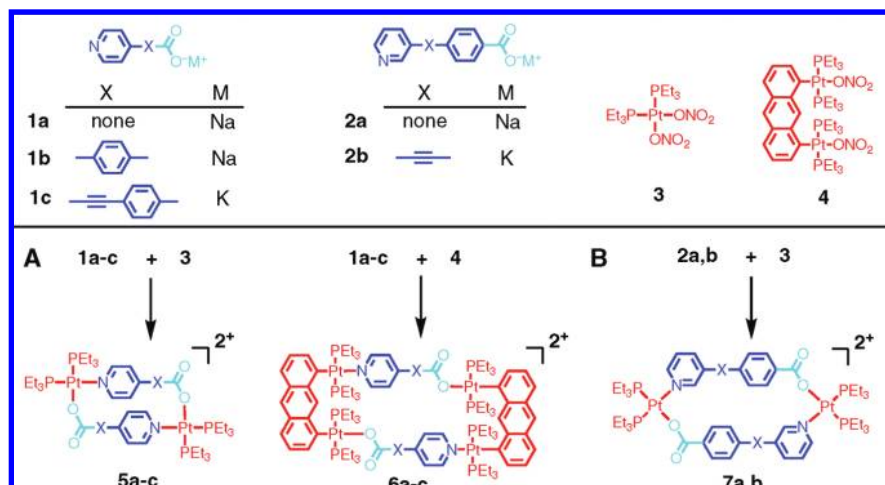
SCHEME 1. Schematic Representation of the Differing Extents of Self-Organization Phenomena That Can Occur within a Complex Mixture of Subunits: Statistical (No Organization); Amplified (Partial Organization); Absolute (Exclusive Organization)



of Lehn,⁷ Raymond,⁸ and Albrecht⁹ developed and explored the self-organization of supramolecular helicates. Lehn et al. demonstrated⁷ that mixtures of oligobipyridine strands containing between 2 and 5 bipyridine units will, in the presence of Cu^{I} ions, self-organize into double helicates exclusively composed of oligobipyridine strands of the same length (i.e., 2:2, 3:3, 4:4, 5:5). By preparing a number of biscatecholamide ligands separated by *o*- C_6H_4 , *p*- C_6H_4 , and 4,4'-biphenyl spacers, Raymond et al. showed⁸ that the addition of Ga^{III} ions prompted the facile self-organization of triple helices composed exclusively of identical ligands. Albrecht and co-workers observed^{9a} that the extent of self-organization of alkyl-bridged bis-catechol ligands into discrete triple helicates in the presence of Ti^{IV} and alkali metal carbonates could be controlled by the nature of the alkali metal (Li^+ , Na^+ , or K^+). In each of these helicate self-organizing systems, metal cations are utilized as "external effectors" that trigger the spontaneous ordering of individual components. The use of reversible metal–ligand coordination interactions allows for a dynamic¹⁰ self-assembly process to take place: supramolecular complexes are assembled and disassembled continuously as the most thermodynamically favorable collection of supramolecules is obtained, at which point no thermodynamic driving forces exist to promote further changes in the system as a whole, though dynamic exchange can still occur.

In each of the previous examples of self-organization, the end results represent the exclusive formation of self-organized structures. This situation can be referred to as absolute self-organization. It is also possible that self-organization is not absolute. As shown schematically in Scheme 1, the self-organization of complementary angular components can range from essentially no organization, resulting in a statistical mixture of different supramolecules, to amplified organization, where some supramolecules are formed in greater ratios than others, to absolute self-organization and the exclusive formation of discrete supramolecules. Where a specific complex mixture of molecular components falls on this spectrum of self-organization depends on a number of factors such as the

SCHEME 2. Chemical Structures of Ambidentate Pyridyl/Carboxylate Donors and Their Self-Assembly into 2D Supramolecular Structures



solvent or temperature as well as the properties or structures of individual components. Over the past decade, studies by Stack,¹¹ Davis,¹² Raymond,¹³ Severin,¹⁴ Isaacs,¹⁵ Barboiu,¹⁶ and Nistchke¹⁷ have explored a wide range of complex synthetic mixtures that undergo varying degrees of self-organization. Isaacs et al. have performed^{15b} an extensive exploration of multiple different complementary hydrogen bond donors and acceptors and showed that the temperature, concentration, association constants of complementary pairs, and presence of competitors all play a part in determining the extent of self-organization phenomena. While the self-organization of hydrogen-bonded systems^{12,15} and various coordination complexes^{7–9,11,13,14,16,17} such as helicates and grids have been studied over the past decade, there have been few studies¹⁸ of self-organization in the coordination-driven self-assembly of closed metallosupramolecular systems.

Recently, we have investigated^{19–27} self-organization processes in coordination-driven self-assembly.^{28,29} Specifically, we have focused on the use of square-planar platinum(II) metal acceptors and electron-rich pyridyl donors to direct the self-assembly of 2D polygons and 3D polyhedra via the directional-bonding approach.²⁸ By employing rigid acceptor and donor subunits, coordination-driven self-assembly protocols can be used to selectively prepare predesigned metallosupramolecules under mild conditions in nearly quantitative isolated yields. The directional-bonding approach allows for precise control over the geometric factors that largely determine which supramolecular structure(s) form. Combining multiple complementary Pt(II) acceptors and pyridyl donors, rather than simply one of each, allows for the prospect of self-organization in the self-assembly of discrete closed supramolecules to be investigated. The extensive library of individual molecular subunits of varying size, geometry, and physical proper-

ties that have been prepared, and the modularity of the coordination-driven approach, enables the self-organization of a large variety of 2D^{19–21,23–27} and 3D^{22,24} supramolecules to be studied. The results of these studies help to elucidate the details of self-organization phenomena and contribute to our knowledge of how similar organization processes occur in natural and biological systems.

Absolute Self-Organization

Complex mixtures of multiple subunits can be driven to absolute self-organized self-assembly when the information encoded within individual molecular subunits is detailed enough. This information can manifest itself electronically (e.g., dipolar interactions) as well as structurally (e.g., subunits differing in size, geometry, or dimensionality). We have investigated the effects of each of these variables to assess their ability to influence the absolute self-organization of multiple Pt(II) acceptor and pyridyl donor subunits into discrete, organized supramolecules.

As shown in Scheme 2A, three unsymmetrical bidentate ligands of varying size (**1a–c**) were synthesized bearing two different binding sites: one pyridyl and the other a carboxylate anion.¹⁹ Mixing the unsymmetrical ligands with 90° monoplatinum acceptor **3** or 0° molecular “clip” **4** results in the exclusive formation of discrete supramolecular rhomboids and rectangles, respectively. The asymmetric ligands can potentially form two isomeric products during self-assembly: one with the bidentate ligands oriented in the same direction and another with the ligands oriented in opposite directions. In the absence of a driving bias between these isomeric pairs, a statistical mixture of the different isomers in a 1:1 ratio would be expected. Experimentally, it was found that only isomers **5a–c** and **6a–c**, with alternating ligand orientations,

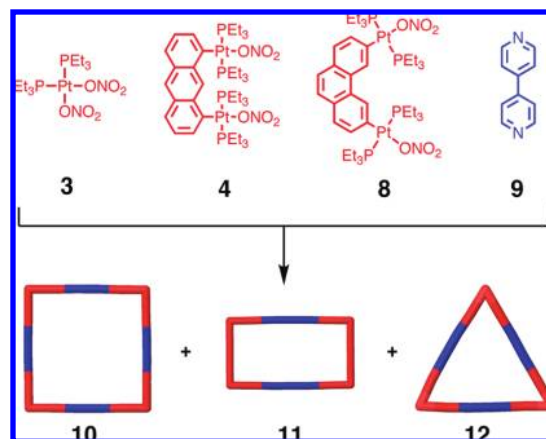
form as determined by ^{31}P and ^1H NMR, ESI mass spectrometry, and X-ray crystallography.¹⁹ Absolute self-organization is primarily driven by the enthalpic benefit of separating the cationic Pt–N centers. An additional factor lies in the more favorable geometry and decreased geometric strain that results from having ligands coordinated in an alternating fashion, creating identical coordination environments at each Pt center. Combined, these influences select for the thermodynamically preferred species during self-assembly, whereby only **5a–c** and **6a–c** are generated.

The charge separation strategy has been recently expanded²⁰ by incorporating flexible unsymmetrical pyridyl–carboxylate ligands (**2a,b**), wherein the pyridyl moieties are substituted at the 3-position rather than the 4-position (Scheme 2B). As before, the different charge state of pyridyl and carboxylate binding sites of ligands **2a,b** promote absolute selection of isomers **7a,b**, which adopt a head-to-tail motif in accordance with the preference for maximum charge separation. Similar results have been observed by Mukherjee and co-workers in their study of self-selection in the [3 + 3] self-assembly of a single isomer of heterobimetallic $\text{Pd}_3\text{–Fe}_3$ triangles via the coordination of an ambidentate 3-nicotinate ligand with a palladium acceptor,^{30,31} as well as the self-selection of [4 + 4] supramolecular squares using a 4-nicotinate bidentate donor.³²

Building on the selective self-assembly of a single supramolecule, the absolute self-organization of multiple different supramolecular assemblies from a complex mixture of various molecular subunits is both more interesting and more challenging. We have recently found that by manipulating the intrinsic geometric parameters of molecular subunits (e.g., the angle, size, and relative orientation of coordination centers), absolute self-organization can be obtained without introducing any external effectors and the process can be applied to a diverse set of coordinative supramolecules.

The first such example involves the absolute self-organization of multiple organoplatinum acceptors **3**, **4**, and **8**, which differ in the angle between their labile NO_3^- ligands, in combination with 4,4'-bipyridyl donor **9** (Scheme 3).²¹ It has been previously reported that each of these individual organoplatinum acceptors is capable of forming ordered supramolecular polygons (square, rectangular, and triangular, respectively) via self-assembly with the linear donor **9**. When all four molecular subunits are combined in one mixture, the self-assembly of like acceptors with donor **9** is in competition with a multitude of nonidentical acceptor–donor combinations, possibly resulting in disordered aggregates. Indeed, mixing **3**, **4**, **8**, and **9** in a 1:1:1:3 ratio initially (1–3 days) results in a highly dis-

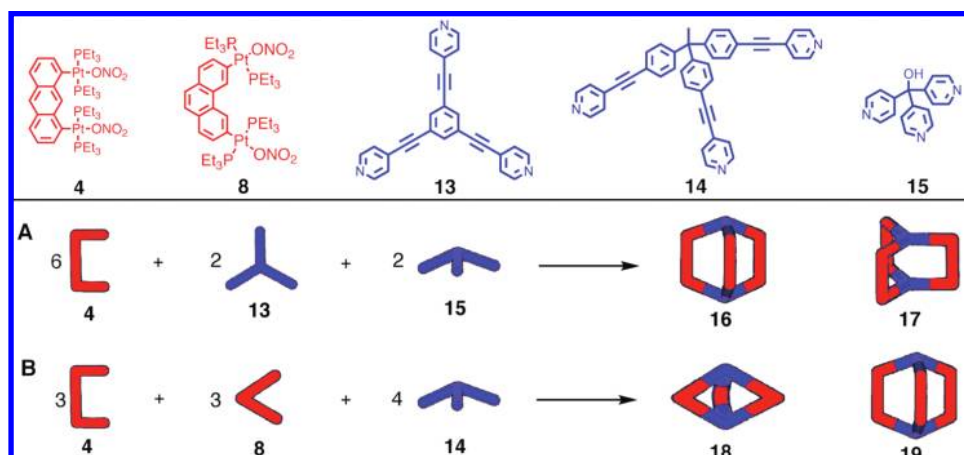
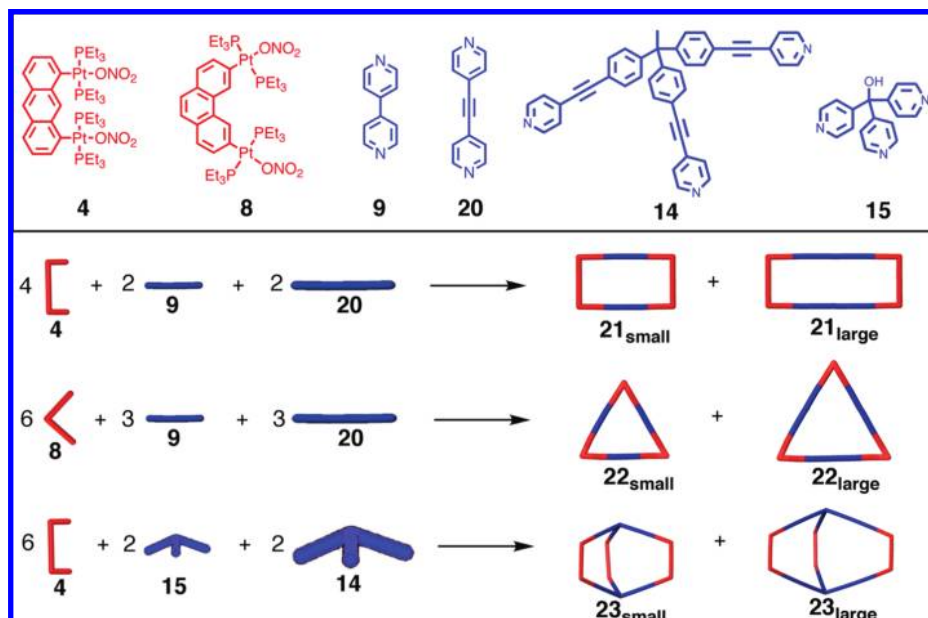
SCHEME 3. Geometric Self-Organization Wherein a Mixture of Three Pt(II)-Based Acceptors (**3**, **4**, and **8**) and Linear Bis-pyridyl Donor **9** Self-Organize Exclusively into Supramolecular Structures **10–12** with No Mixed Acceptor Assemblies



ordered mixture of supramolecular structures likely formed from the random combination of various subunits. For comparison, each individual self-assembly can be accomplished under 6 h. After 5–6 days, however, NMR and ESI-MS studies reveal that only the three discrete square, rectangular, and triangular supramolecules **10–12**, respectively, are formed in the fully equilibrated mixtures; each spectroscopically identical to their individually self-assembled species.²¹

During the self-organization described above, the angular differences of organoplatinum acceptors **3**, **4**, and **8** constitute the major driving force inducing the selective generation of discrete supramolecular polygons. Indeed, the thermodynamic stability of different products also plays a significant role in this angle-directing self-organization process. Disordered oligomeric species can be randomly formed from the combination of various subunits. Compared with closed discrete supramolecules formed from acceptors of the same angle, however, these disordered species are found to be thermodynamically (entropically and enthalpically) less favored.²¹ The dynamic nature of the kinetically labile Pt–N coordination bonds allows for the individual components of the oligomeric structures to be continuously exchanged as the mixture progressively self-organizes toward the thermodynamically most favored products. A recent study by Fujita et al. suggests³³ that once the most stable species is formed it is considerably less likely to undergo further ligand exchange, thus retaining its supramolecular structure.

Self-organization of 3-D metallacages was studied²² by combining planar and pyramidal tritopic donors **13** and **15**, respectively, with molecular clip **4** in a 1:1:3 ratio as shown in Scheme 4A. Self-organized self-assembly allows for the absolute formation of only two discrete supramolecular polyhedra (**16** and **17**) from the equilibrated mixture; no mixed

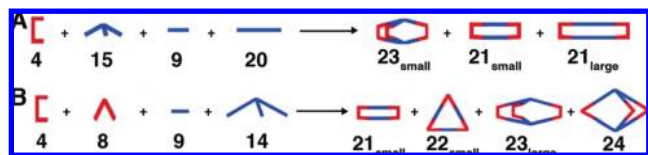
SCHEME 4. The Absolute Self-Organization of 3D Supramolecular Trigonal Prism Structures **16**–**19** as Driven by Differences in the Size and Geometry of Individual Subunits

SCHEME 5. Demonstration of the Use of Different Sized Molecular Components as a Means To Drive Self-Organization of 2D and 3D Metallocsupramolecules


ligand supramolecules were observed spectroscopically.²² Similarly, mixing molecular clip **4** and 60° acceptor **8** with nonplanar donor **15** results in the analogous trigonal prism species **18** and **19** (Scheme 4B). In these systems, the major driving forces directing self-organization are the geometric features of the molecular subunits, the different angles between donors **13**–**15** and between acceptors **4** and **8**.

In addition to angular influences, we have found that another geometric feature, size, is able to drive the absolute self-organization of both 2D supramolecular polygons and 3D polyhedra.²³ As shown in Scheme 5, two ditopic (**9**, **20**) or tritopic (**14**, **15**) pyridyl donors, solely varying in their size, can simultaneously self-assemble with molecular clip **4** or 60° acceptor **8**. As monitored by ³¹P{¹H} and ¹H NMR spectroscopy,

these mixtures of acceptors and donors initially combine randomly with each other, resulting in the formation of highly disordered oligomeric species. After 24–65 h of heating at 60–65 °C, equilibrium is reached as indicated by the disappearance of disordered species, the sharpening of signals corresponding to supramolecular polygons (**21** and **22**) and polyhedra (**23**), and the fact that no further spectroscopic changes are observed. NMR and ESI-MS analysis reveal the absolute self-organization of the complex mixtures into discrete supramolecular structures as driven by differences in the size of individual donor subunits. Similar results have been reported by Raymond and co-workers⁸ in their studies of ligand self-recognition in the self-assembly of triple-stranded helicates.

SCHEME 6. Simultaneous Use of Three Different Geometric Parameters (Angle, Size, And Dimensionality) To Drive the Self-Organization of Multiple Discrete 2D and 3D Supramolecules from within Complex Mixtures



More recently, a third basic geometric feature, dimensionality, has been shown capable of directing absolute self-organization.²⁴ Subunits of differing dimensionality can be used to self-assemble a diverse range of both 2D and 3D supramolecular polygons and polyhedra based on the varying numbers of binding sites of donors and acceptors and their directionality. For example, as shown in Scheme 6A, ditopic ligands **9** and **20** and tritopic ligand **15** were mixed with molecular clip **4** in a 2:2:2:7 ratio in an aqueous acetone solution (1:1) and heated at 65–70 °C. In keeping with previous observations in simpler systems, random combinations of different subunits were initially observed and were directly characterized by ESI mass spectrometry. After 24 h of heating, however, the complex mixture of four subunits reached equilibrium and resulted in the formation of different sized 2D rectangles as well as a 3D triangular prism through the self-correction of randomly formed oligomeric species resulting in absolute self-organization.²⁴

In contrast with the majority of previously discussed examples, which explored self-organization as driven predominantly by one specific structural or electronic feature, this study demonstrates the simultaneous integration of multiple different structural driving forces. In particular, different subunits of varying angle, size, and dimensionality were all utilized to control the absolute self-organization of various metallosupramolecular structures in one mixture. In order to systematically investigate the use of multiple driving forces simultaneously, nine different self-organizing systems, wherein two or more different structural driving features have been encoded within component donors or donors and acceptors, have been carried out.²⁴ Two representative examples of these complex systems are shown in Scheme 6. Despite the higher complexity and the increased number of possible disordered byproducts in these systems, discrete supramolecules are still selectively and predominantly formed within each mixture. In Scheme 6B, for example, the molecular clip **4** and 60° acceptor **8**, which vary in their coordination angles, were combined with linear bipyridyl donor **9** and pyramidal donor **14**, which vary in both their size and shape. Upon heating at 60 °C for 96 h in a mixed aqueous acetone solution (1:1),

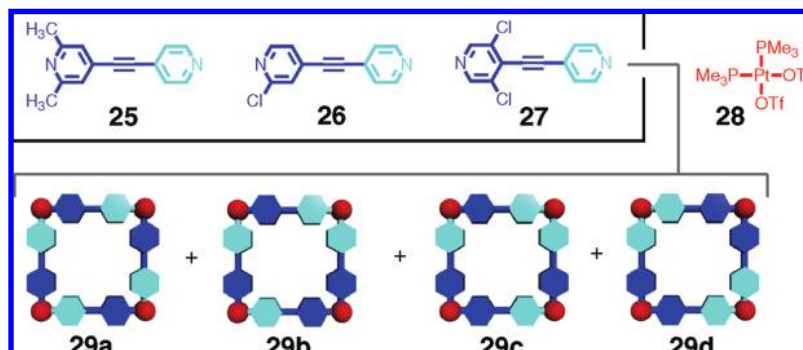
only four discrete supramolecular structures were formed: 2D rectangle **21_{small}** and triangle **22_{small}**, along with the 3D trigonal prisms **23_{large}** and **24**. No mixed, disordered, or random aggregates were observed.²⁴

Aside from differences in the molecular subunits themselves, the absolute self-organization of platinum-based metallosupramolecules also depends on experimental parameters such as the reaction temperature and the nature of the solvent.²⁴ In general, as expected, lower reaction temperatures significantly decrease the rate of the self-organization process. For example, the self-organization shown in Scheme 6B requires 24 h to reach equilibrium at 65–70 °C, while at 45–50 °C, it requires 120 h, and at room temperature, essentially no self-organization occurs after 20 days. The choice of solvent is also influential.²⁴ Almost every example introduced so far undergoes self-organization in an aqueous acetone (1:1) mixture. Carrying out the same experiments in a less polar solvent such as CH₂Cl₂ results in no self-organization, likely because the less polar CH₂Cl₂ is not as able to stabilize the charged metallosupramolecular products or the various oligomeric precursors that precede them. Solvent systems with a high dielectric, such as the 1:1 acetone/H₂O mixture, allow the self-organization of these complex species to take place. This observation is supported by the fact that decreasing the dielectric of the solvent by carrying out the self-assembly shown in Scheme 6A in a 20:1 ratio of acetone/H₂O essentially abolishes the self-organization process.²⁴

Factors other than dipolar interactions and geometric differences can also influence absolute self-organization. Stack et al.¹¹ and Davis et al.¹² have both used chirality as a parameter to dictate self-organization. Stack demonstrated that the chirality of a rigid, racemic bispyridyl diiminocyclohexane derivative is capable of controlling absolute self-organization upon coordination with metal cations such as Cu^I. Davis has found that (D,L)-5'-silyl-2',3'-O-isopropylidene guanosine subunits prefer to undergo the absolute self-organization of homochiral aggregates in the presence of Ba²⁺ but give statistical mixtures of products when K⁺ is used.

Nonabsolute Self-Organization

As mentioned previously, and exemplified by the above discussion of the work of Davis et al., not all self-organization processes are absolute and where a particular mixture of components lies on the self-organization spectrum is dependent on the specific influences that govern their assembly. For example, our group has recently investigated²⁵ the use of steric interactions as a driving force for self-organized self-

SCHEME 7. Chemical Structures of Unsymmetrical Bispyridyl Donors **25–27** and Schematic Representation of the Four Different Supramolecular Squares (**29a–d**) That Can Be Formed upon Their Self-Assembly with Pt(II) Acceptor **28**

assembly and found that steric interactions are able to drive a system from being statistical to absolute.

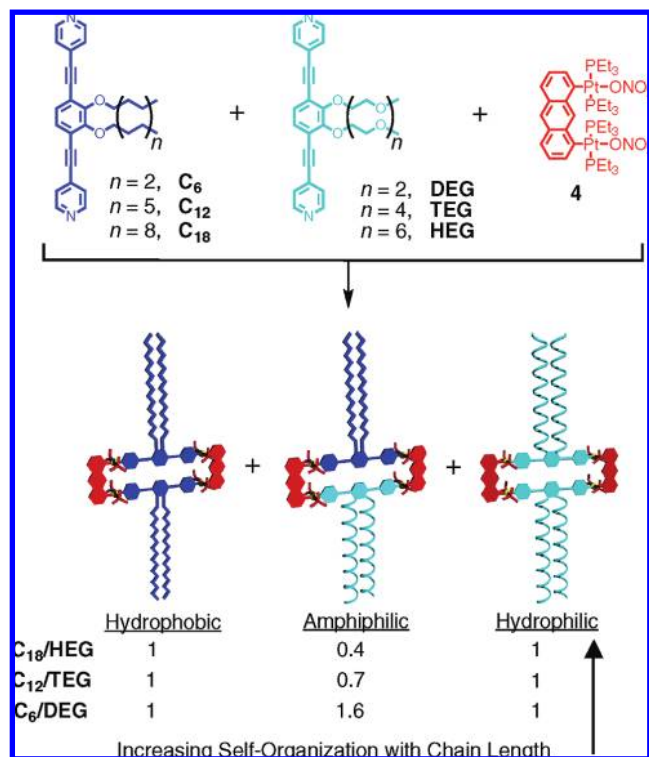
Three unsymmetric bis(4-pyridyl)acetylene ligands were prepared with one of the two pyridyl moieties substituted with 2,6-dimethyl-, 2-chloro-, and 3,5-dichloro- substituents (**25–27**, Scheme 7).²⁵ Each of the linear donor components was then mixed in a 1:1 ratio with 90° Pt(II) acceptor **28** in order to self-assemble supramolecular squares. The asymmetry of the linear donors allows for up to four different supramolecular squares to be generated depending on the relative orientations of each squares' constituent donors (**29a–d**). The different sizes and substitution patterns of unsymmetrical donors **25–27** result in different steric interactions between pyridyl groups coordinated to the same Pt(II) acceptor. These differences in steric interactions lead to varying degrees of self-organization.

In the absence of any interligand effects, isomeric supramolecular squares **29a–d** would be formed in a statistical ratio of 1:4:2:1, respectively. When 3,5-dichloro-4-(4-ethynylpyridyl)pyridine ligand **27** was mixed with 90° Pt(II) acceptor **28** in CD₃NO₂, careful analysis of the symmetry and splitting of signals in the ¹H and ³¹P NMR spectra of the resulting equilibrated mixture of squares indicated a near statistical mixture of products with no self-organization. Substitution of the β positions of one of the pyridyl groups with chlorine atoms places these substituents too far from the Pt–N coordination site to effect self-organization. NMR spectroscopic analysis of a 1:1 mixture of **26** and **28** in CD₃NO₂ indicated that isomer **29a** was the most dominant species in solution. Isomers **29b** and **29c** were also formed as minor products, while no evidence of isomer **29d** could be observed. These results indicate that a single chlorine atom substituted at the α position of one pyridine moiety is sufficient to achieve amplified self-organization. Mixing Pt(II) acceptor **28** with 2,6-dimethyl-4-(4-ethynylpyridyl)pyridine (**25**) in CD₃NO₂ resulted in the exclusive formation of isomer **29a**, indicating that bis-α-

methyl substituents are able to drive absolute self-organization in this system. The relative energies of each series of supramolecular squares were evaluated using molecular force field modeling, further revealing the steric effects that governed the degree of self-organization in each system.²⁵ Similar results have been observed by Albrecht and co-workers⁹ in their studies of ligand self-recognition in the self-assembly of triple-stranded helicates. In Albrecht's work, small variations in the geometry and size of bis-catechole ligands were able to drive self-organization of helicates from purely statistical mixtures to absolute self-organization.

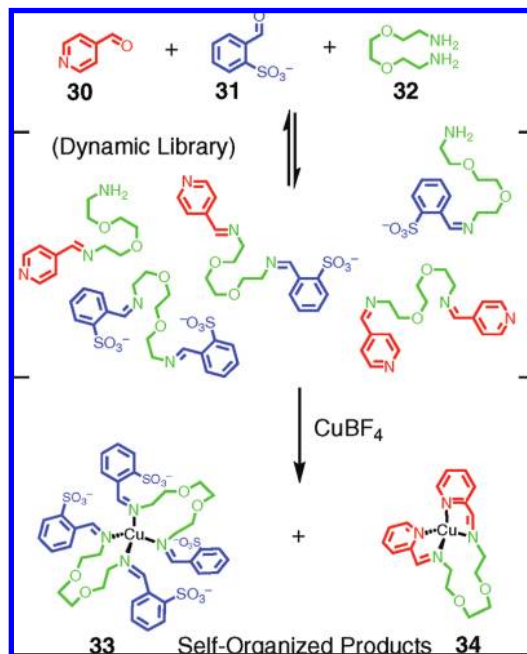
Amplified self-organization has also been reported in the self-assembly of supramolecular triangles.²⁶ Mixing 2,6-diazaanthracene with 60° dilatinum(II) acceptor **8** can lead to the formation of two diastereotopic supramolecular triangles, one symmetric and one asymmetric, that differ in the relative orientation of their component diazaanthracene donors. Statistically, the different supramolecular triangles should be formed in a ratio of 1:2 in favor of the asymmetric diastereomer. Experimentally, however, it was found that the symmetric diastereomer is favored by roughly 10:1 indicating the amplified, though not absolute, formation of the statistically less favored diastereomer.²⁶ In this example, preference for the symmetric diastereomer arises because a symmetric arrangement of the diazaanthracene donors leads to a significantly more favorable triangle geometry than if one of the donors is oriented opposite the others. In this case, geometric strain promotes self-organization.

Recently, linear donors functionalized with long chain alkane or ethylene glycol substituents have been used to investigate potential "second-order" effects on self-organization.²⁷ The factors influencing self-organization discussed so far have been essentially limited to differences in the geometry, size, dimensionality, sterics, or electronic structure of the component donors or acceptors. In studying second-order effects, a series of donors functionalized at their core with long

SCHEME 8. The Amplified Self-Organization of Functionalized Donors into Hydrophobic, Amphiphilic, and Hydrophilic Rectangles

hydrophobic (C₆H₁₃, C₁₂H₂₅, or C₁₈H₃₇) or hydrophilic (di(ethylene glycol), tetra(ethylene glycol), or hexa(ethylene glycol)) chains were prepared (Scheme 8). The geometry, length, and dimensionality of each donor was kept constant and the long chain alkane or ethylene glycol functionalities were far removed from the nitrogen coordination sites. In this manner, the functional moieties had no steric, kinetic, or thermodynamic influence over the otherwise identical donors and any self-organization phenomena would arise from purely second-order effects of the functional groups.

Each individual functionalized donor, when mixed with diplatinum(II) molecular clip **4** in a 1:1 ratio, self-assembles into hydrophobic or hydrophilic rectangles. Mixtures of **4** with donors bearing different side chains, **C₆/DEG**, **C₁₂/TEG**, and **C₁₈/HEG**, were then used to investigate the possibility of self-organization. In the absence of any second-order effects, each mixture should produce hydrophobic, amphiphilic, and hydrophilic supramolecular rectangles in a statistical 1:2:1 ratio. Analysis and integration of ³¹P NMR spectroscopic signals for each mixture revealed increasingly amplified self-organization as the lengths of the hydrophobic and hydrophilic chains were increased.²⁷ The equilibrated **C₆/DEG** mixture, for example, resulted in a ratio of 1:1.6:1 for hydrophobic, amphiphilic, and hydrophilic rectangles, respectively. This ratio changed to 1:0.7:1 in the **C₁₂/TEG** mixture, and finally to 1:0.4:1 in the

SCHEME 9. Representative Example of the Work of Nitschke and Co-workers Wherein Metal–Ligand Coordination Is Used To Collapse a Dynamic Library of Interconverting Imines into Self-Organized Supramolecular Complexes

C₁₈/HEG mixture. High-resolution ESI-MS studies further supported the trend toward greater amplified self-organization with increasing chain length. Additional experiments with mixtures of **4** and **C₆/C₁₈** and **DEG/TEG** indicated that self-organization is likely promoted by the aggregation of like-philicity donors prior to self-assembly, thus biasing the formation of rectangles with identical donors.²⁷ The driving force for aggregation increases with increasing chain length, accounting for the trend in amplified self-organization.

Self-Organization of Dynamic Covalent Libraries

Nitschke and co-workers have explored¹⁷ self-organization phenomena that take advantage of the dynamic nature of both metal–ligand coordination and reversible imine bond formation. A representative example is shown in Scheme 9, where a dynamic combinatorial library of multiple imine condensation products is generated upon mixing **30**, **31**, and **32**. The subsequent addition of CuBF₄ to this rapidly equilibrating complex mixture results in the collapse of the dynamic covalent library and the exclusive, self-organized formation of metallo-organic supramolecules **33** and **34**.^{17a} Self-organization in this example is highly efficient because (a) dynamically reversible coordination and imine bond formation are inherently self-correcting, and (b) the two different sets of self-assembling subunits are noninterfering. Nitschke and co-work-

ers have investigated similar self-organization phenomena in the formation of Cu^I-coordinated double and triple helicates^{17c} and have demonstrated the use of two different metals, Cu^I and Fe^{II}, to induce a dynamic combinatorial library of 11 structures to self-organize into only two discrete metallo-organic supramolecules.^{17b} The efficiency and selectivity of self-organization could be correlated with the electronic nature of the substituted amine subunits, which were studied using Hammett σ_{para} values,^{17d} and on the coordination geometries of the metal ions used. Lehn and co-workers have also investigated the effects of combining dynamic imine formation and metal coordination to drive self-organization in constitutional dynamic systems.³⁴ The results of these studies represent an elegant use of multiple dynamic combinatorial interactions to achieve self-organization from within complex mixtures.

Conclusion

Recent years have witnessed tremendously rapid developments in molecular self-assembly and supramolecular chemistry. The self-organization of asymmetric molecular components or highly complex mixtures of multiple subunits into well-defined supramolecular structures represents an extension of the development of self-assembly that more closely resembles natural systems. While modern chemical laboratories allow for reactions to be carried out in exceedingly controlled environments, biological systems are forced to develop, survive, and reproduce in the significantly more chaotic natural world, yet they do so with aplomb. Systematic investigations of the factors that influence and control self-organization phenomena in abiological systems, such as 2D and 3D metallosupramolecules, contribute to an increased understanding of analogous processes in Nature as well as to the future development of functional multicomponent systems.

The results presented in this Account demonstrate a variety of control factors that can be used to drive self-organization in coordination-driven self-assembly. The absolute self-organization of discrete supramolecules can be achieved using inputs such as dipolar interactions, steric interactions, and differences in the geometric parameters of subunits. Absolute self-organization can be directed by a single control factor or multiple factors used simultaneously. We have also observed instances where self-organization is not absolute and varies in its deviation from statistical results. Steric interactions are particularly useful control factors for driving such amplified self-organization because they can be subtly tuned through small structural variations, allowing for the degree of amplified organization to be continuously controlled. Functional groups

attached to otherwise identical subunits have been shown to influence self-organization through "second order" effects. For example, hydrophobic interactions, which play a significant role in the self-assembly and self-organization of biological systems, can have an effect on the extent of abiological self-organization. All together these studies outline a range of influences that can drive a complex mixture of Pt(II)-based acceptors and pyridyl donors from assembling into a purely statistical collection of products to a collection where certain products are more favored and all the way to the absolute self-organization of particular supramolecular structures. Future investigations of self-organization that combine various self-assembly protocols will continue to build upon these results. An ultimate goal of this research would be to have the ability to prepare highly functional systems (catalysts, supramolecular motors, light-harvesting assemblies, etc.) simply by mixing a variety of molecular subunits that then self-organize into the desired complex assemblies according to the information and control factors built into their structures.

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FOOTNOTES

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