Reversible Interactions

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Diversity and Complexity through Reversible Multiple Orthogonal Interactions in Multicomponent Assemblies**

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"Life" in its complexity is not possible without self-organization processes that themselves rely on weak interactions, such as hydrogen bonding, salt bridges, ion–dipole interactions, and metal–ligand coordination, but also on reversible covalent bonds. Indeed, in countless fascinating instances Nature avails itself in an ingenious and efficient manner of the noncovalent interplay of covalently prefabricated building blocks to realize diverse complex biological functions. An outstanding example is the ribosome, a multiprotein and multi-RNA complex conceived to translate the mRNA into proteins.[1] To achieve a similarly high emergence of complex functionality from artificial chemical systems through the interplay of various substructures, one will have to make decisive progress in the development of the thermodynamically controlled synthesis of equilibrating multicomponent assemblies.

Unfortunately, so far there are no quantifiable systematics to describe the complexity level of supramolecular systems in regard to their structural and functional diversity and possibly their associated emergence. However, we may approximate the level of complexity of a structure by the number of its possible permutations based on the number of different components and interactions as well as on the total number of pieces. Such analysis swiftly indicates that the realization of spectacular supramolecular aggregates in the last couple of years, such as Stang's dodecahedron from 50 pieces[2] or Fujita's palladium sphere[3] do not necessarily reflect a mature state of the area. Nearly all systems, even if they are based on multiple components such as Drain's nonakis-porphyrin,[4] so far rely solely on the utilization of just one kind of reversible interaction. High complexity in current supramolecular and equilibrating systems is thus mainly the result of a very large number of reversible interactions of the same kind.[5]

A quintessence of the above analysis is that our tool kit for the construction of multicomponent assemblies needs further development and refinement of reversible orthogonal interactions. Particular attention should be devoted to assure compatibility of all interactions. Analogous to the situation for dynamic combinatorial libraries (DCL),[6] it is imperative to realize that thermodynamic control implies a minimization of the energy G_{total} of the total system. At this juncture, all possible aggregates are linked together in a complex network and influence the total energy in an intricate manner. Thus, it is desirable, aside from the development of novel multicomponent systems, to understand their dynamics and thermodynamics as a function of all determining factors. Actually, those systems appear to be most attractive that use orthogonal interactions for new structural motifs, and not for conceptionally simpler host–guest systems or pending molecular groups,[7] except when this entails the introduction of novel functions.[8]

Some examples, though numerically limited, already describe supramolecular structures that are built on more than two components ($n \geq 3$) as well as on two different weak interactions and reversible bonds. Provisionally, it should suffice to categorize these by the operating interactions: two different metal–ligand interactions,[9–13] metal–ligand coordination + reversible covalent bond,[14,15] metal–ligand coordination + ion–dipole interaction,[7,16] metal–ligand coordination + hydrogen bonding,[17,18] metal–ligand coordination + π–π stacking,[19] reversible covalent bond + ion–dipole interaction,[20] and two different reversible covalent bonds.[21]

Supramolecular multicomponent ($n \geq 4$) self-assemblies, built on more than two different reversible interactions, are still remarkable exceptions,[22] in particular if they form in a quantitative manner. Every additional orthogonal interaction will furthermore open up a multitude of new chances. Using three orthogonal metal–ligand interactions, we realized the quantitative construction of a discrete porphyrin stack (Scheme 1), reminiscent of a superstructure, independent of the sequence of addition of the four components.[23] Most impressive is, however, the work by Stoddart et al. on a Solomon's knot (Scheme 2),[24] because the extraordinary

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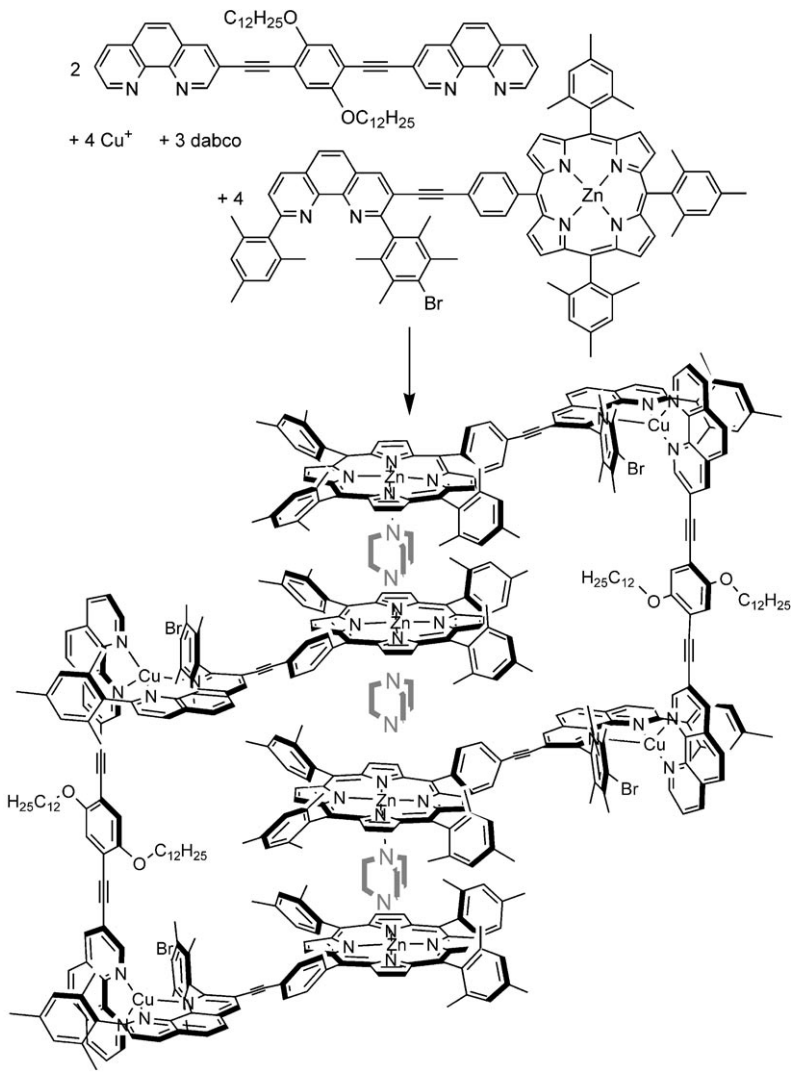

Scheme 1. Quantitative formation of a four-component porphyrin stack constructed by using three different, fully reversible metal–ligand interactions.[23]

topology is realized elegantly by the ingenious utilization of three orthogonal interactions: two different metal–ligand interactions and a reversible imine formation have to work together smoothly to furnish a four-component aggregate.

With the construction of a nanometer-sized four-component macrocycle (Scheme 3) under equilibrating conditions Severin et al.[25] have now demonstrated the utility of a new multiple-orthogonal-assembly tool-kit that will certainly provide new impetus to the field of dynamic combinatorial libraries. A particular element is the utilization of the reversible formation of boronic esters and imines as well as rhenium–ligand interactions. For preparative purposes, moreover, it is very helpful that the thermodynamically controlled reaction is realized at slightly elevated temperature, furnishing kinetically stable products at room temperature.

In light of the fact that living systems constantly exchange building blocks and energy with their environment, our present knowledge on equilibrating artificial multicomponent systems is rudimentary. Therefore, the future will hopefully lead through further efforts to an improved mastery of reversible orthogonal interactions.

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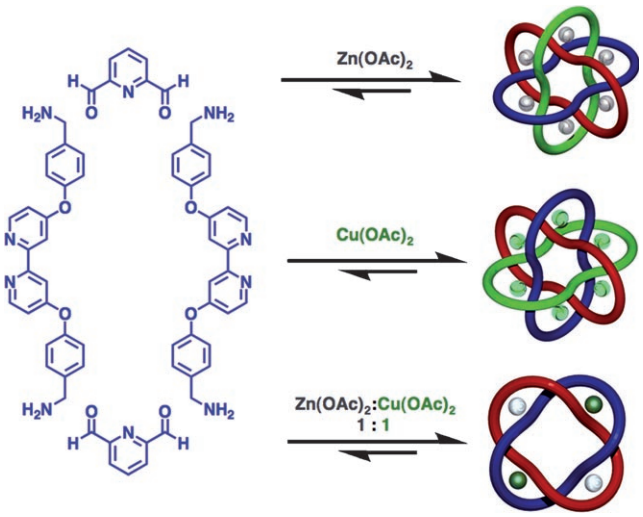
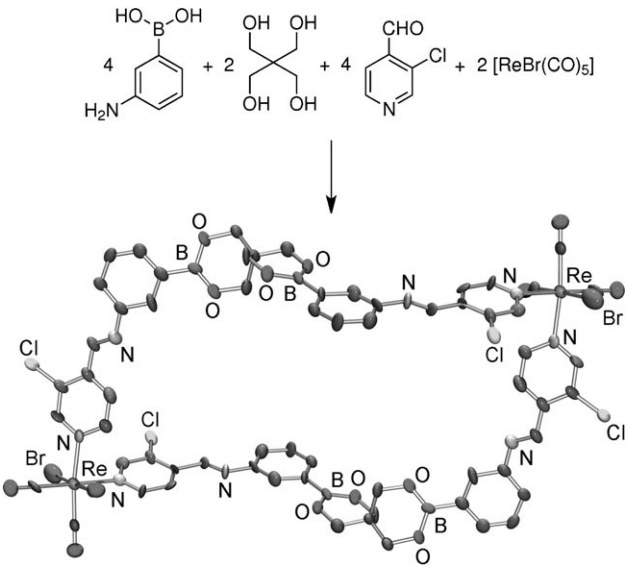


Scheme 2. Stoddart's four-component Solomon's knot generated from a dynamic library by utilizing three different reversible interactions.[24]



Scheme 3. Severin's four-component macrocycle of nanometer-size, generated in a one-pot reaction using three different reversible interactions.[25]

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