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**Construction, Substitution, and  
Sorting of Metallo-organic  
Structures via Subcomponent  
Self-Assembly**

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**ABSTRACT**

Subcomponent self-assembly allows the construction of complex architectures from simple building blocks via formation of covalent bonds around metal templates. Since both covalent and coordinative bonds are formed reversibly, a wealth of rearrangement reactions is possible involving substitution at both intraligand (often C=N) and metal–ligand (N → metal) bonds. If the possibilities latent within a set of subcomponents and metal ions are understood, one may also select specific structures from among dynamic libraries of products. The parallel preparation of structures from “nonorthogonal” mixtures of subcomponents is also possible, as is the direction of subcomponents to specific sites within product structures.

**1. Introduction**

Self-assembly is the fundamental technique employed by Nature to construct the elegant and intricate molecular machinery from which life is built. In recent years self-assembly has been harnessed to create materials<sup>1–3</sup> and prototypes of functional molecular machines.<sup>4–13</sup> In order to create molecular devices of real economic value, further mastery is required over the basic techniques of self-assembly.

Jonathan Nitschke was born in 1973 in Syracuse, NY. He received his Bachelor's degree in Chemistry from Williams College in 1995 and his Ph.D. degree from the University of California—Berkeley in 2001 under the supervision of T. Don Tilley. He then undertook postdoctoral studies with Jean-Marie Lehn (Strasbourg) under the auspices of a U.S. NSF fellowship, and in 2003 he started his independent career as a *maitre-assistant* (fixed-term lecturer) in the Organic Chemistry Department of the University of Geneva. In August 2006 he was the first recipient of the European Young Chemist Award.

Over the course of the past 3 years we have developed and employed the technique of *subcomponent self-assembly* toward the creation of increasingly complex structures. This technique, itself a subset of metallo-organic self-assembly,<sup>14–20</sup> involves the simultaneous formation of covalent (carbon–heteroatom) and dative (heteroatom–metal) bonds, bringing both ligand and complex into being at the same time. The roots of subcomponent self-assembly lie in the template synthesis of Busch.<sup>21</sup> Recently, other researchers have employed this method to synthesize a wealth of structures, including macrocycles,<sup>22,23</sup> helicates,<sup>24–27</sup> rotaxanes,<sup>28</sup> catenanes,<sup>29</sup> grids,<sup>30–32</sup> and a Borromean link.<sup>33</sup>

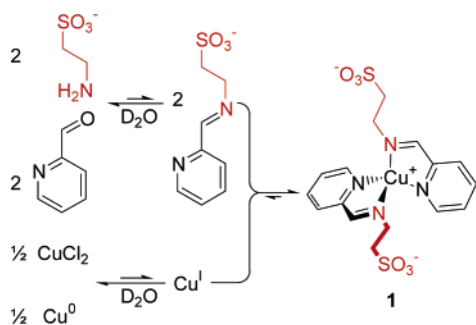
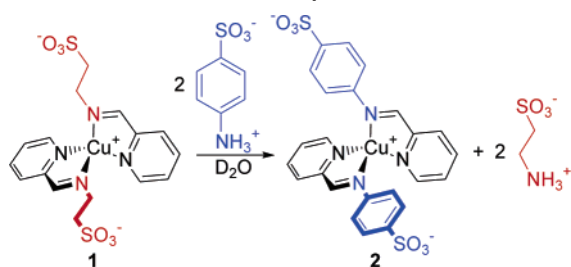
Initial proof-of-concept experiments in our laboratories established the utility of a subcomponent self-assembly based upon copper(I) coordination and imine bond formation, most usefully in aqueous solution.<sup>34</sup> We subsequently developed our research program along three main lines, seeking responses to a series of questions.

Our first line of research deals with *construction*: What architectures might be created using this methodology? Are there structures that are readily accessible using subcomponent self-assembly that are difficult or impossible to create otherwise? Can this method be used to generate topological complexity?

Our second line of inquiry treats the *substitution* and *reconfiguration* chemistry of these complexes on both dynamic covalent<sup>35</sup> (C=N) and coordinative (N → metal) levels: What driving forces may be harnessed to effect the transformation of one structure into another, cleanly and in high yield? Can one address the two different levels, coordinative and covalent, independently? Is it possible to preferentially substitute a single subcomponent within a structure or a mixture that contains several different possible sites of attack?

Our third line of investigation delves into the possibility of utilizing this methodology in *sorting* complex mixtures using the techniques and ideas of dynamic combinatorial chemistry.<sup>36–42</sup> Is it possible to direct given subcompo-

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**Scheme 1. Mutual Stabilization of Imines and Cu<sup>I</sup> in Aqueous Solution**

**Scheme 2. Subcomponent Substitution Driven by Differences in Acidity**


nents into specific places within assemblies? Can one observe the clean formation of two distinct structures from a common pool of ligand subcomponents? May the coordinative preferences of two different metal ions be used to induce different sets of ligand subcomponents to assemble around each metal?

**1.1. Aqueous Cu(I).** The first study we undertook<sup>34</sup> validated the use of subcomponent self-assembly using aqueous copper(I) as well as taking initial steps in the directions of *construction*, *substitution*, and *sorting*.

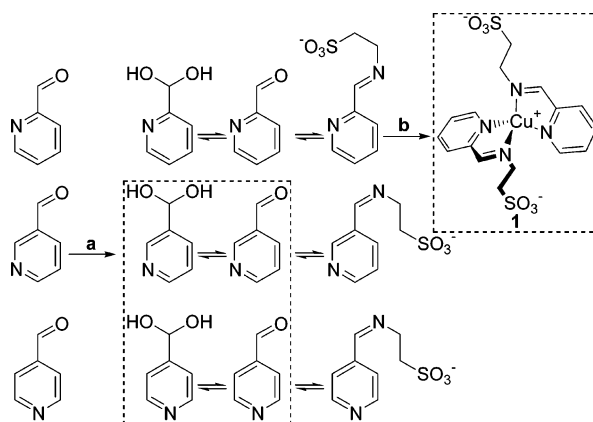
In aqueous solution Cu<sup>I</sup> is frequently observed to disproportionate to Cu<sup>II</sup> and copper metal, and imines are in most cases the minority species when amines and carbonyl compounds are mixed in water.<sup>43</sup> When imines and copper(I) are present in the same solution, however, this pattern of stability reverses. Imines are excellent ligands for Cu<sup>I</sup>, stabilizing the metal in this oxidation state, and metal coordination can prevent imines from hydrolyzing. We were thus able to prepare complex **1** from the precursors shown at the left in Scheme 1.<sup>34</sup>

Although thermodynamically stable in aqueous solution, complex **1** nonetheless readily underwent covalent imine substitution in the presence of sulfanilic acid to form **2** (Scheme 2).

This reaction occurred with greater than 95% selectivity. The driving force behind this imine exchange may be understood in terms of the difference in acidity between sulfanilic acid ( $pK_a = 3.2$ ) and taurine ( $pK_a = 9.1$ ), which favors displacement of the protonated form of the weaker acid (taurine) from **1** and incorporation of the deprotonated form of the stronger acid (sulfanilic acid) during the formation of **2**.<sup>34</sup>

A sorting effect could also be induced during the synthesis of **1**. Addition of copper(I) to the library of three

isomeric pyridine carbaldehydes shown in Scheme 3 selects only the 2-isomer, collapsing the library down into the products outlined below.

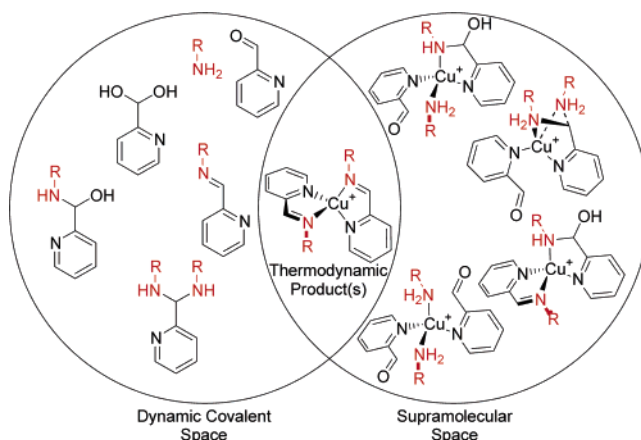
**Scheme 3. Cu<sup>I</sup>-Mediated Selection of Pyridine-2-carboxaldehyde from Among a Library of Its Isomers<sup>a</sup>**


<sup>a</sup> (a) Taurine, sodium bicarbonate, D<sub>2</sub>O. (b) Cu<sub>2</sub>O. The compounds remaining after the addition of Cu<sub>2</sub>O are outlined.

Conceptually, one may imagine two different spaces within the flask wherein **1** self-assembles: a dynamic covalent<sup>35</sup> space and a supramolecular<sup>14</sup> space (Figure 1). The dynamic covalent space consists of all of the different possible ligand structures that could self-assemble from a given set of ligand subcomponents, and the supramolecular space consists of all possible metal complexes of these possible ligands.

Certain ligand structures are more likely to be favored and others not present at all (“virtual”).<sup>38</sup> Likewise, certain metal complexes are thermodynamically more stable than others. Since dynamic interconversion is possible on both covalent and supramolecular levels, both ligand and metal preferences act in concert to amplify a limited subset of structures out of the dynamic library of all possible structures.

Due to the strong preference of copper(I) for imine ligands, the set of observed structures is often much smaller than the set of possible structures, such as those containing aminated or hemiaminal ligands. Copper(I)/imine systems are thus particularly fruitful for use in



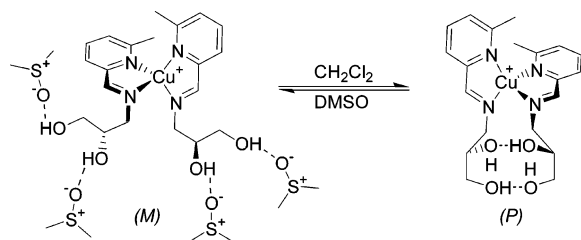
**FIGURE 1.** Intersection of dynamic covalent and supramolecular spaces during subcomponent self-assembly.

subcomponent self-assembly. We are very interested in deciphering the selection rules that dictate the products observed under a given set of conditions with the goal of being able to understand and exploit the basic “programming language” that might enable formation of complex structures based on simple starting materials.

**1.2. Chirality.** The copper(I) centers of **1** and **2** are chiral. The proximity of another chiral center gives diastereomers, differentiating the energies of the *P* and *M* metal-based stereocenters of the mononuclear complex.

Initial investigations<sup>44</sup> revealed that (*S*)-3-amino-propane-1,2-diol may be used to synthesize a mononuclear complex similar to **1** (Scheme 4). In dimethyl sulfoxide (DMSO) solution, circular dichroism (CD) and NMR spectra indicated that one diastereomer is present in 20% excess over the other. In dichloromethane solution, however, only one diastereomer was observed by NMR. The CD spectrum indicated, however, that it had the opposite chirality at copper than the one favored in DMSO!

**Scheme 4. Postulated Structures of a Mononuclear Complex Containing a Chiral Amine Subcomponent in DMSO (left, *M* Predominating) and CH<sub>2</sub>Cl<sub>2</sub> (right, *P* Exclusively)**



In dichloromethane, the hydroxyl groups appeared to be strongly associated with each other, rigidifying the structure and leading to efficient chiral induction. In contrast, DMSO would be expected to interact strongly with the hydroxyl groups, acting as a hydrogen-bond acceptor (Scheme 4, left). The effect should be to pull the hydroxyl groups out into the solvent medium. One of the two diastereomers should allow for more energetically favorable interactions between the hydroxyl groups and the solvent, leading to the observed diastereoselectivity.

This interpretation is also supported by the results of a study correlating the observed diastereomeric excess with the Kamlet–Taft  $\beta$  parameter,<sup>45</sup> a measure of the hydrogen-bond acceptor strength. A linear free energy relationship was found to exist between  $\beta$  and the diastereomeric excess for those solvents having  $\alpha$  (hydrogen-bond donor strength) = 0.<sup>44</sup>

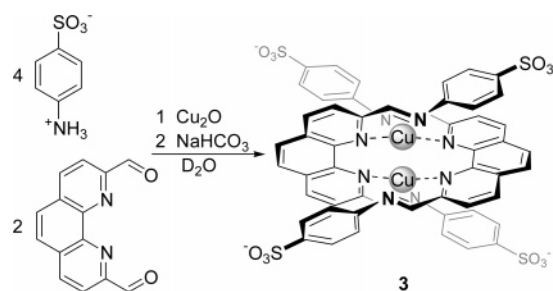
## 2. Construction

Following our preparation of mononuclear complexes **1** and **2**, we sought to employ subcomponent self-assembly to prepare polynuclear assemblies of greater structural complexity. Some of the architectures that proved accessible are described below.

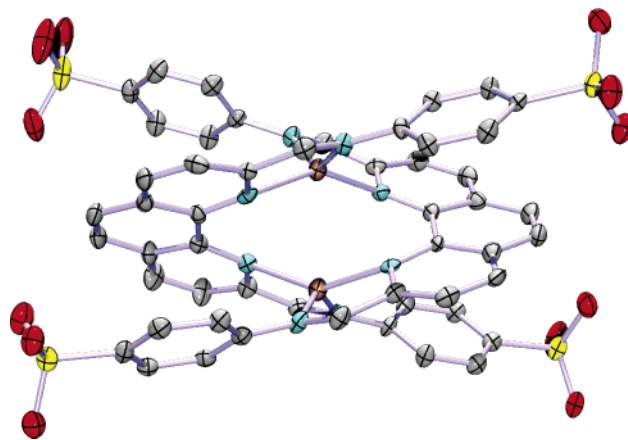
**2.1. Dicopper Helicates.** The reaction of sulfanilic acid with phenanthroline-2,9-dicarbaldehyde, copper(I) oxide,

and sodium bicarbonate gave a quantitative yield of the anionic double helicate **3**, as shown in Scheme 5.<sup>27</sup>

**Scheme 5. Construction of Double-Helicate **3** from Subcomponents**



In the crystal, the copper(I) centers of **3** adopt a flattened tetrahedral geometry (Figure 2) in very similar fashion to what has been observed in related structures.<sup>46,47</sup> The deep green color of such complexes has been noted<sup>46</sup> to be extremely unusual for copper(I), being more frequently associated with copper(II). The color is associated with a local minimum in the UV–visible spectrum of **3** at 560 nm, between higher-energy absorptions associated with  $\pi$ – $\pi^*$  transitions and a broad absorption centered around 690 nm. We suspect this latter feature to be associated with one or more metal-to-ligand charge-transfer transitions. The 2.73 Å distance between the copper centers might allow a photoexcited state in which the additional positive charge is delocalized across both copper ions, as seen in other dicopper(I) structures.<sup>48</sup> Theoretical investigations are underway.


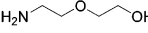

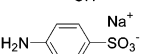
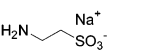

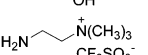
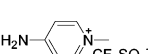


**FIGURE 2.** ORTEP diagram of dianionic **3**.

In addition to sulfanilic acid, numerous other primary amines could be used to construct helicates. The conditions under which different amines were incorporated into these helicates were investigated. Table 1 summarizes the selection rules discovered.

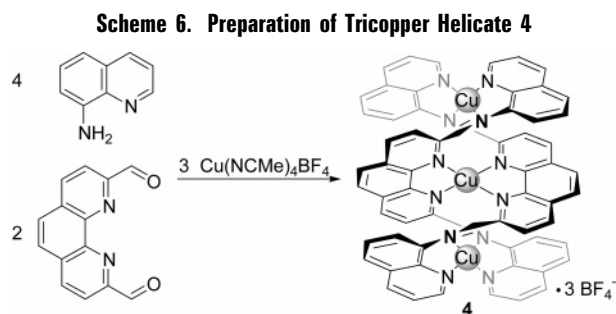
Water was preferred to acetonitrile as the solvent, allowing moderately hindered and anionic amines to self-assemble. Acetonitrile is a much better ligand for copper(I) than water, making it more difficult for hindered ligands (such as the one formed from serinol, third entry in Table 1) to form complexes in competition with the solvent. More hindered amines as well as cationic amines were

**Table 1. Helicate Formation Selection Rules in Water and Acetonitrile**

Amine	Helicate in H <sub>2</sub> O	Helicate in MeCN
	Yes	Yes
	Yes	Yes
	Yes	No
	Yes	No
	Yes	No
	No	No
	No	No
	No	No

not incorporated in either solvent, which we attribute to steric and Coulombic repulsion, respectively.

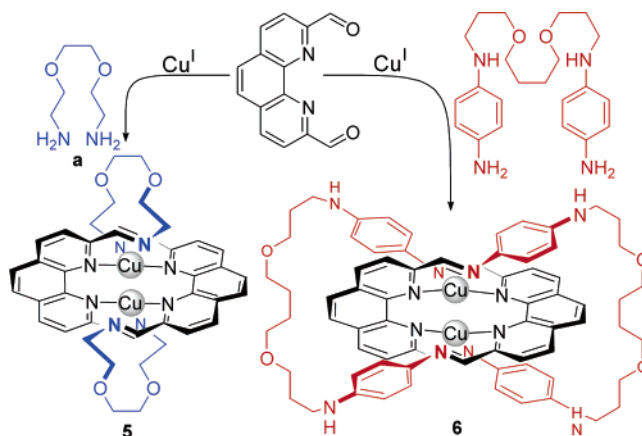
**2.2. Tricopper Helicates.** Tricopper helicates could also be synthesized using a simple modification of the dicopper helicate preparation.<sup>44</sup> When three equivalents of copper(I) were employed and 8-aminoquinoline was used in place of an aniline, tricopper double-helicate **4** was formed as the unique product (Scheme 6).



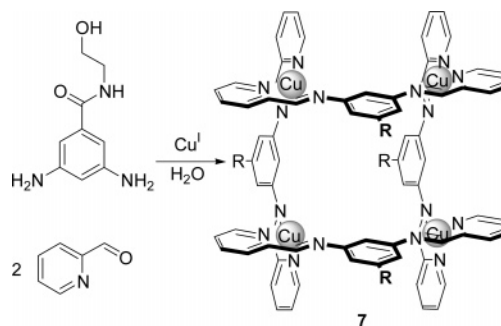
**2.3. Catenanes and Macrocycles.** When short, flexible diamine **a** was used as a subcomponent in helicate formation, as shown on the left side of Scheme 7, only one topological isomer of product was observed: twisted macrocycle **5**. This diamine is not long enough to loop around the phenanthroline to form a catenated structure.<sup>44</sup>

When a longer diamine that contained rigid phenylene segments was used, as shown in Scheme 7 at right, formation of such macrocyclic structures became energetically disfavored. The orientation of the rigid phenylene groups readily allowed the flexible chains to bridge across the backs of the phenanthroline groups, giving rise to the catenated structure **6**. This interpenetration of two identical macrocycles was the only observed product.<sup>44</sup>

Unlike the original Sauvage catenanes,<sup>49</sup> catenate **6** is helically chiral in addition to possessing the possibility of becoming topologically chiral through incorporation of an asymmetrical dianiline. Investigations of both kinds of chirality in catenanes similar to **4** are currently underway.

**Scheme 7. Selection of a Macrocyclic (5) or Catenated (6) Topology On the Basis of the Rigidity and Length of the Subcomponents Employed**

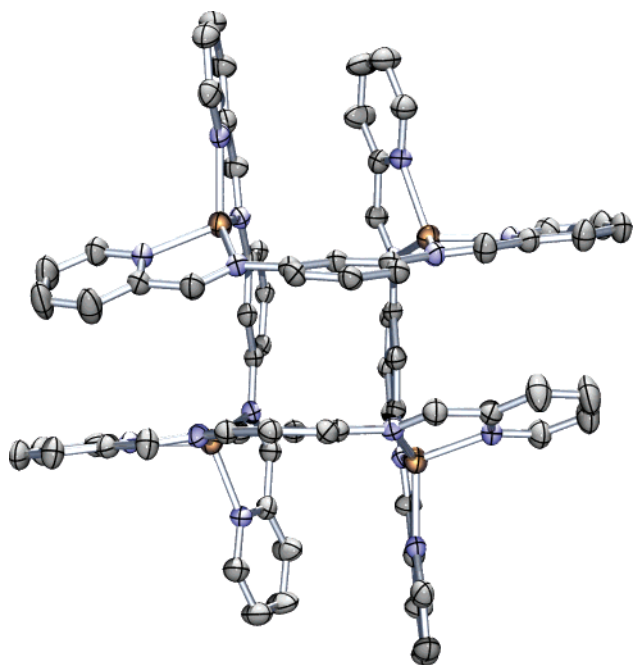
**2.4. [2 × 2] Tetracopper(I) Grid.** The aqueous reaction of Cu<sup>I</sup>, pyridine-2-carbaldehyde, and a water-soluble *m*-phenylenediamine resulted in the quantitative formation of the tetracopper(I) grid complex **7** shown in Scheme 8.<sup>31</sup>

**Scheme 8. Self-Assembly of [2 × 2] Grid Complex 7 That Forms Only in Water Among All Solvents Tried (R = -CONHCH<sub>2</sub>CH<sub>2</sub>OH)**

The crystal structure of the grid (Figure 3) suggested the presence of strain, an unusual feature for a quantitatively self-assembled structure. Intriguingly, no grid was observed to form in any solvent except water. We hypothesize that the hydrophobic effect plays an essential role in the self-assembly process, causing ligands and metal ions to wrap together into a compact structure in which the hydrophobic ligand surfaces are minimally exposed to the aqueous environment. A “diffuse pressure” applied by the hydrophobic effect would compensate for the strain thus engendered. Extension of this strategy may permit the use of self-assembly to construct other strained structures, which tend to have unusual and technologically interesting properties.<sup>50</sup>

### 3. Substitution/Reconfiguration

Many of the complexes prepared through subcomponent self-assembly underwent substitution chemistry, which may operate both at covalent and coordinative levels. Several of these transformations were investigated with a particular focus upon reactions that are capable of cleanly transforming one structure into another. As discussed

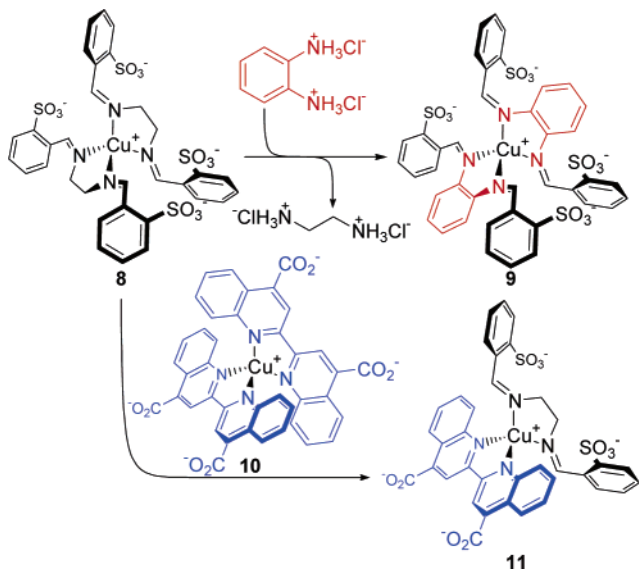


**FIGURE 3.** ORTEP diagram of tetracationic grid **7** (the  $-\text{CONHCH}_2\text{CH}_2\text{OH}$  groups of the ligands are not shown).

below, driving forces for such substitutions included relief of steric encumbrance, substitution of an electron-poor subcomponent for an electron-rich one, use of  $\text{p}K_a$  differentials, and the chelate effect.

**3.1. New Cascade Reaction.** Pseudotetrahedral complexes such as **8** (Scheme 9) were observed to possess a particularly rich substitution chemistry.<sup>51</sup> Complex **8** reacted cleanly with *o*-phenylenediammonium to give the covalent substitution product **9** shown in Scheme 9. This imine substitution was driven by the same  $\text{p}K_a$  effect employed in the 1-to-2 transformation of Scheme 2. In addition, **8** reacted cleanly with copper bis(biquinoline) complex **10** to give the coordinative substitution product

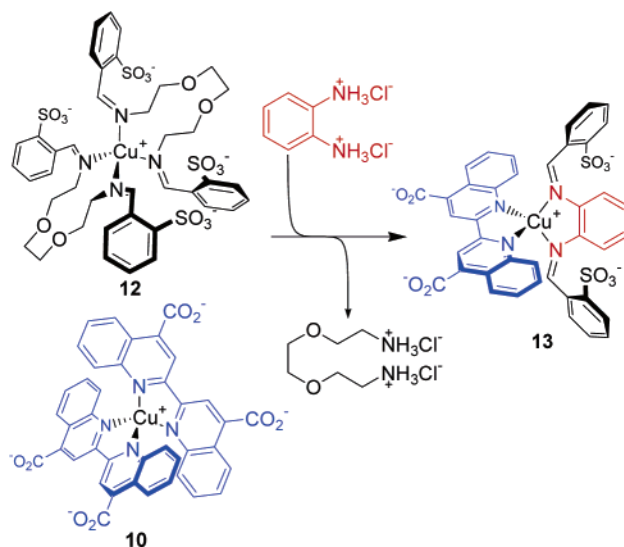
**Scheme 9. Covalent (above) and Coordinative (below) Rearrangements of Complex 8 To Give 9 and 11 Driven by  $\text{p}K_a$  Differences and Sterics, Respectively**



**11.** This ligand exchange appears to have been sterically driven: substitution of one of the encumbering di(imine) ligands for a less bulky biquinoline provided the driving force for this reaction.<sup>52</sup>

In contrast with **8**, complex **12** did not undergo ligand substitution with the copper(I) bis(biquinoline) complex, possibly as a result of the different steric properties of the two complexes. The imine exchange reaction with phenylenediammonium worked well, creating the possibility of a new kind of domino or cascade reaction (Scheme 10). The intermediate product **9** (from Scheme 9), formed following reaction between **10** and phenylenediammonium, reacted immediately with **10** to give the final product **13**.

**Scheme 10. Cascade Reaction of 10 and 12: Rearrangement on Both Covalent and Coordinative Levels To Give 13 Upon Addition of *o*-Phenylenediammonium Dichloride**



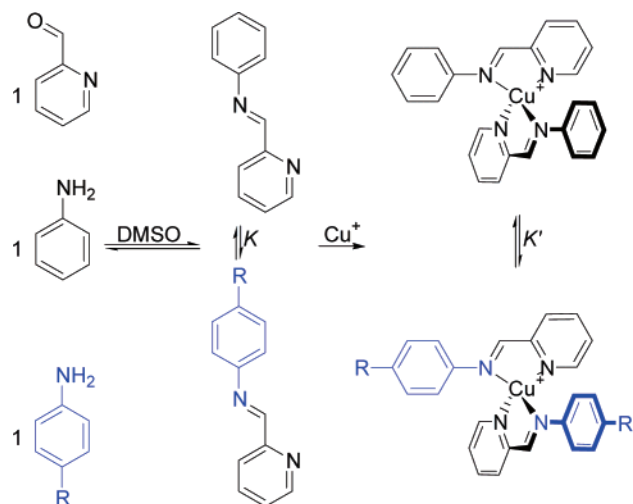
Addition of phenylenediammonium to a mixture of **10** and **12** thus caused two distinct rearrangements to occur: initial (covalent) imine exchange followed immediately by (coordinative) ligand exchange, resulting in exclusive formation of mixed-ligand complex **13**.

**3.2. Hammett Effects.** The electronic nature of the amine incorporated into these imine complexes should play an important role in determining the stability of their  $\text{Cu}^{\text{I}}$  complexes and, therefore, the composition of equilibrium mixtures when several amines compete as subcomponents. To investigate the influence of electronic effects, we ran a series of competition experiments between unsubstituted and substituted anilines<sup>53</sup> (Scheme 11).

One equivalent each of unsubstituted aniline, substituted aniline, and pyridine-2-carbaldehyde were mixed in DMSO. Following equilibration, no free aldehyde could be detected: An equilibrium mixture of imines and free anilines was observed in each case. Once the equilibrium had stabilized, one-half of an equivalent of copper(I) was added, and the equilibrium population of the two free anilines was again measured.

A high-quality correlation was found between the Hammett  $\sigma_{\text{para}}$  value<sup>54</sup> of a given aniline and the  $K_{\text{eq}}$  of

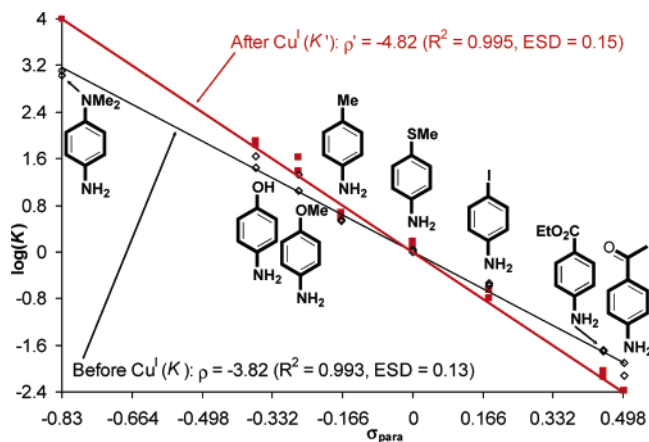
**Scheme 11. Competition between Unsubstituted Aniline and 4-Substituted Anilines ( $-R = -NMe_2, -OH, -OMe, -Me, -SMe, -I, -CO_2Et, -Ac$ ) in the Absence and Presence of  $Cu^I$**



the competition between free and substituted aniline, as shown in Figure 4. The increased magnitude of  $\rho$  following copper coordination indicated that the cationic copper complex was better stabilized by an electron-donating group than was the free neutral ligand, as expected.

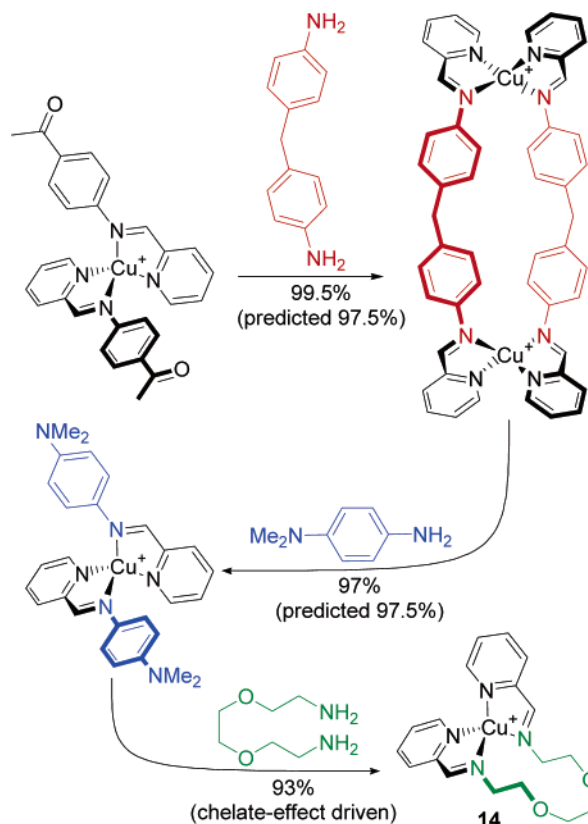
The quality of this linear free energy relationship allowed us to predict with confidence the equilibrium constant of a subcomponent substitution reaction between an arbitrary pair of anilines. The large magnitude of  $\rho$  also indicated that such substitution reactions might be expected to proceed in high yields. For example, in Scheme 12 we demonstrate a series of transformations between four distinct structures, ending with metallacycle **14**. The entire sequence could be carried out in the same reaction flask, and the yields of the individual displacement reactions were close to those predicted using the Hammett equation. The driving force for the last displacement, as well as part of the first, is entropic in nature and may be considered as a special case of the chelate effect.<sup>53</sup>

**3.3. Helicate Reconfigurations.** The dicopper double-helicate moiety<sup>46</sup> has exhibited rich and varied substitution



**FIGURE 4.** Linear free energy relationships that correlate the  $\sigma_{para}$  of 4-substituted anilines with the stability of their 2-pyridylimines and the  $Cu^I$  complexes thereof.

**Scheme 12. One-Pot Series of Transformations between Four Distinct Products, Bearing Alternately Macrocylic and Open Topologies, Ending with Metallamacrocycle 14**



chemistry, as discussed below.<sup>27,44,53</sup> It is more rigid and structurally better defined than the mononuclear complexes discussed above, which allows one to use it as a persistent, well-defined tecton.<sup>20</sup>

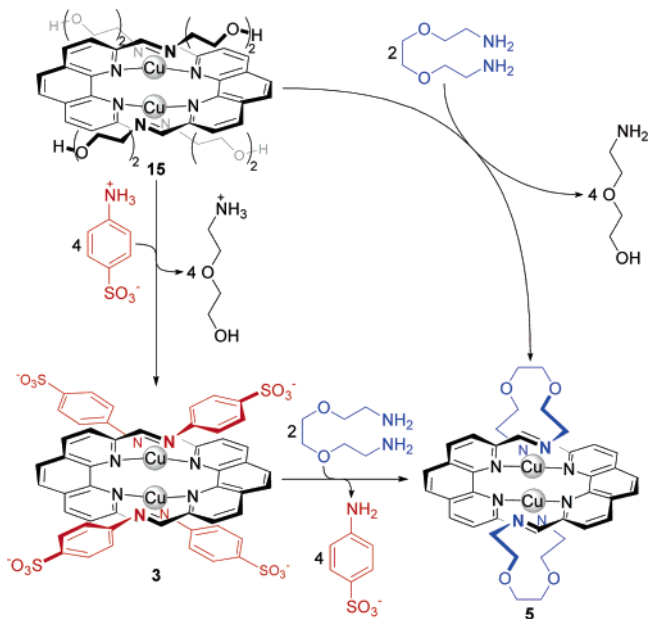
The  $pK_a$ -differential-driven chemistry that functions in mononuclear cases (Schemes 2, 9, and 10) also works well in the context of helicates. As shown in Scheme 13, helicate **15** was transformed into **3** upon addition of sulfanilic acid.

Entropy may be harnessed as a driving force in the context of helicates as well as in mononuclear complexes, as evidenced by the **15**-to-**5** and **3**-to-**5** conversions shown in Scheme 13. Two distinct hierarchical layers of control over subcomponent substitution may thus be employed in tandem based upon  $pK_a$  differences and the chelate effect.

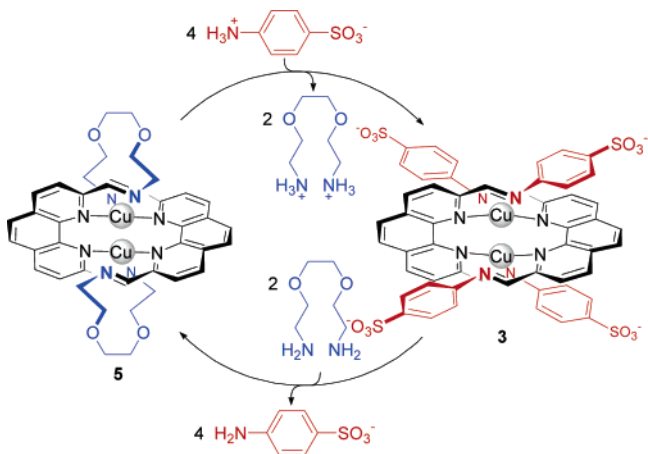
The entropy-driven conversion of **3** to **5** may be reversed upon lowering the pH (Scheme 14). Addition of sulfanilic acid to macrocycle **5** resulted in its conversion to helicate **3**. Basification of this solution through addition of  $NaHCO_3$  resulted in regeneration of **5**, closing the cycle. By changing the pH it was thus possible to switch dynamically between the open topology of helicate **3** and the closed topology of macrocycle **5**.<sup>44</sup>

Tricopper double-helicate **4** may also be synthesized through subcomponent substitution, starting with the 4-chloroaniline-containing dicopper helicate shown in Scheme 15. The electron-poor 4-chloroaniline residue ( $\sigma_{para} = 0.23$ )<sup>54</sup> thus serves as an excellent leaving group

**Scheme 13.** Subcomponent Substitution of Diamine **a** for Both Aryl (3 → 5) and Alkyl (15 → 5) Monoamines, Complementing the Substitution of Arylamines for Alkylamines (15 → 3)



**Scheme 14.** Cycling between 5 and 3 as a Function of pH

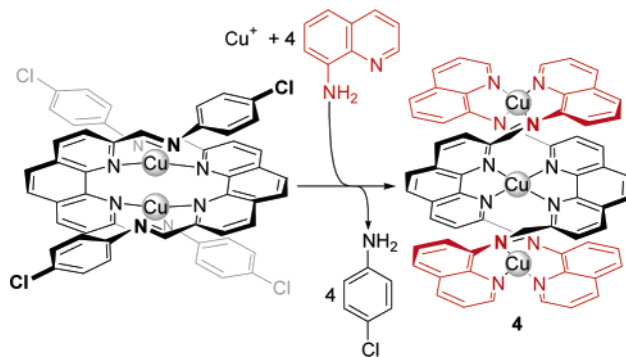


in this substitution reaction. Starting with a dicopper helicate containing more electron-rich 4-methoxyaniline residues ( $\sigma_{\text{para}} = -0.27$ )<sup>54</sup> we observed only 18% of **4** following equilibration.

## 4. Sorting

A particular challenge of subcomponent self-assembly lies in the fact that one must employ building blocks that contain proportionally more self-assembly information than is required in the case of presynthesized ligands: “assembly instructions” for both ligands and supra-molecular structure must be included. It is therefore worthwhile to investigate ways in which this information might be encoded, such that individual subcomponents might be directed to react with specific partners within mixtures. This idea allows complex dynamic libraries to be sorted into a limited number of structures or individual subcomponents to be directed to specific locations within larger structures.

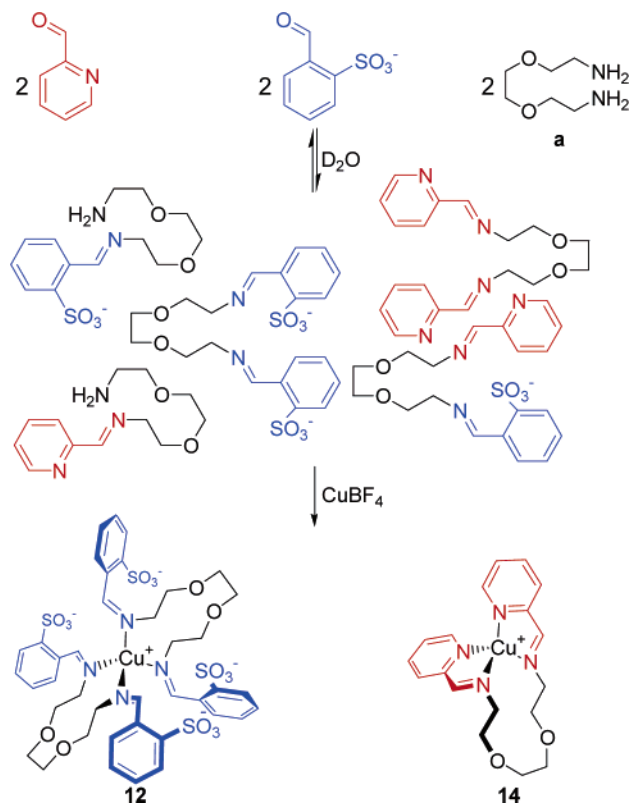
**Scheme 15.** Substitution of Aminoquinoline for Chloroaniline, Generating Trimetallic **4** from a Chloroaniline-Containing Dimetallic Double-Helicate

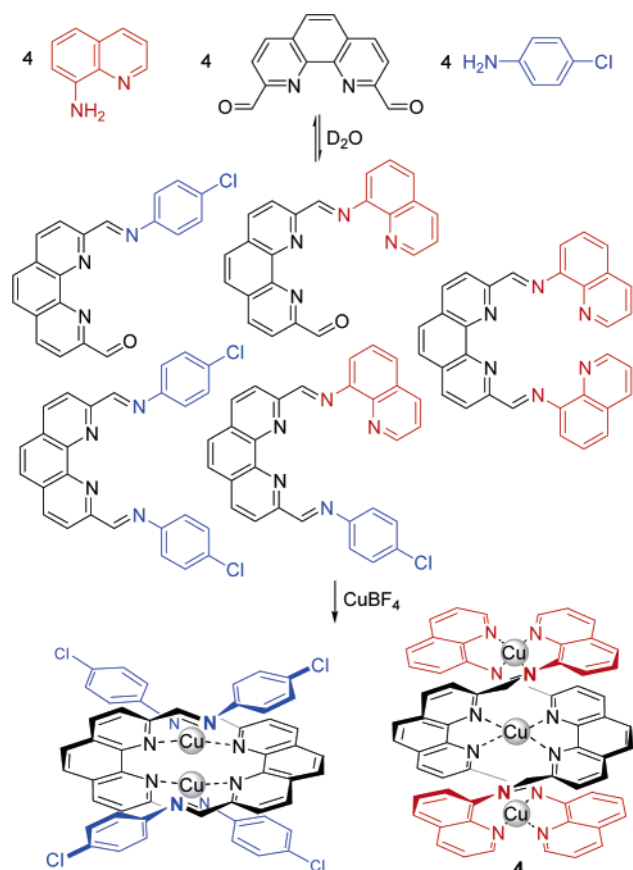


**4.1. Sorting Ligand Structures with Cu(I).** In initial work<sup>51</sup> we demonstrated that complexes containing different imine ligands could be synthesized in each other's presence. When pyridine-2-carbaldehyde and benzaldehyde-2-sulfonate were mixed with diamine **a** (Scheme 16) in aqueous solution, a library of ligands is created in dynamic equilibrium with the starting materials. Addition of copper(I) eliminated all but two of these ligands, forming complexes **12** and **14** in quantitative yield.<sup>51</sup>

The simultaneous formation of **12** and **14** results in a situation in which all copper(I) ions are tetracoordinate and all of the ligands' nitrogen atoms are bound to copper centers. Any other structures formed from this mixture of subcomponents would either contain more than one metal center (entropically disfavored) or have unsatisfied

**Scheme 16.** Dynamic Reconstitution of a Library of Imine Ligands Into a Mixture of **12** and **14** Following Addition of Copper(I)



**Scheme 17. Simultaneous Preparation of Dicopper and Tricopper Helicates from a Dynamic Library of Ligands**

valences at either metal or ligand (enthalpically disfavored).

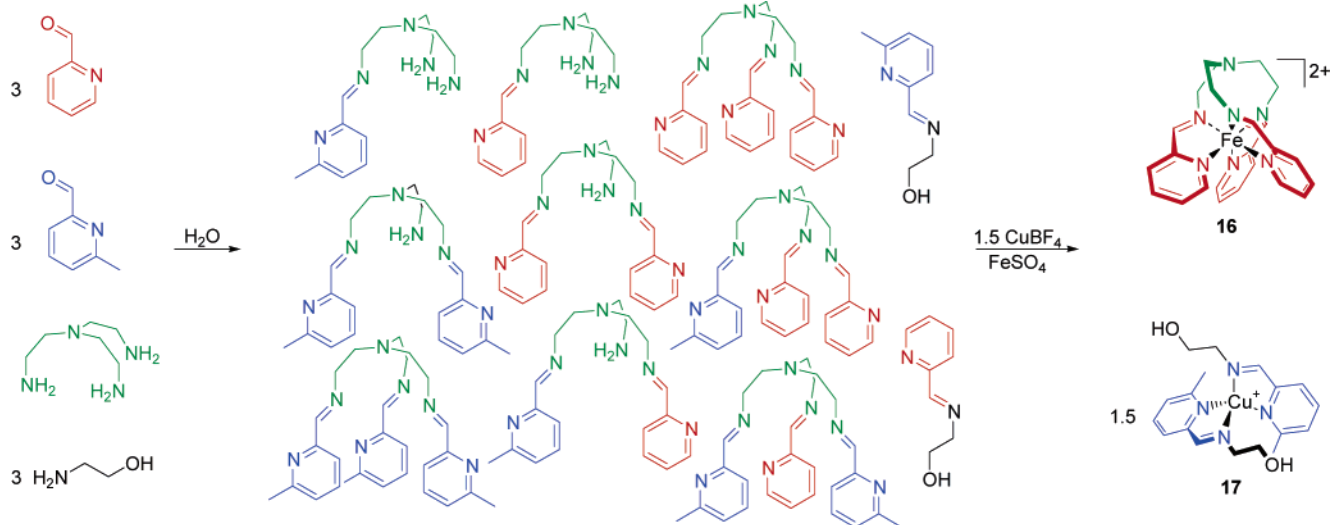
**4.2. Simultaneous Syntheses of Helicates.** This methodology may also be extended to polynuclear helicates.<sup>55</sup> When 2-aminoquinoline and 4-chloroaniline were mixed with the phenanthroline dialdehyde shown in Scheme 17, a dynamic library of potential ligands was observed to form. Addition of copper(I) causes this library to collapse,

generating only dicopper and tricopper helicates. As in the mononuclear case of Scheme 16, the driving force behind this self-selection reaction appeared to be formation of structures in which all ligand and metal valences are satisfied. Use of supramolecular (coordination) chemistry to drive the covalent reconfiguration of intraligand bonds appears to be a general phenomenon, applicable in polynuclear as well as mononuclear cases.

**4.3. Cooperative Selection by Iron and Copper.** Extending this sorting methodology further, we examined a larger self-organizing system in which  $Fe^{II}$  and  $Cu^I$  act together to sort a more complex dynamic library of ligand subcomponents (Scheme 18).<sup>51</sup> When pyridine-2-carbaldehyde, 6-methylpyridine-2-carbaldehyde, ethanolamine, and tris(2-aminoethyl)amine were mixed together in water, a dynamic library of imines formed in equilibrium with the starting materials. When copper(I) tetrafluoroborate and iron(II) sulfate were added, this dynamic library was observed to collapse, leaving compounds **16** and **17** as the sole remaining products. This thermodynamic sorting process thus directed each building block to its unique destination.

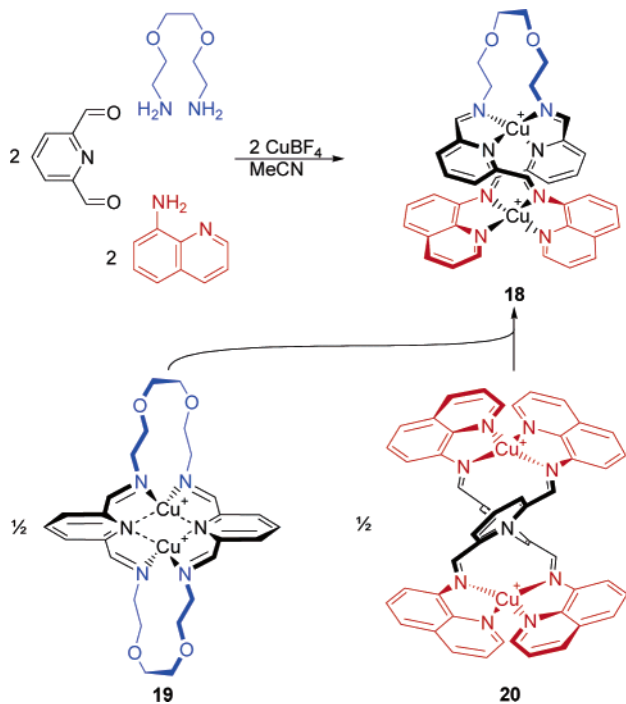
Certain factors play an obvious role in winnowing down the number of observed product structures. The template effect<sup>21</sup> should eliminate all partially formed ligands and ligand subcomponents from the mixture. The chelate effect should favor structures containing ligands that bear the highest number of bound donor atoms possible. Iron(II) and copper(I) should be bound to six and four donor atoms, respectively. Within these bounds, a variety of different product structures might nonetheless be envisaged.

During the course of our study we identified and quantified the important thermodynamic driving forces behind this selectivity. The most interesting of these was a “spin-selection” phenomenon, whereby iron complex **16** rejected incorporation of the methylated pyridine carbaldehyde. Pseudo-octahedral complex **16** contains  $Fe^{II}$  in the diamagnetic, low-spin state over a wide temperature

**Scheme 18. Formation of a Dynamic Combinatorial Library of Ligands, and the Collapse of This Library Into Complexes 16 and 17 Following Addition of  $Cu^I$  and  $Fe^{II}$** 



**Scheme 19. Preparation of Structure 19 from a Mixture of Ligand Subcomponents (top) and Through Covalent Conproportionation of Subcomponents from Preformed Structures 20 and 21 (bottom)**



range<sup>56</sup> with short strong Fe–N bonds. Analogous complexes incorporating 2-methylpyridine residues possess some high-spin character with correspondingly longer, weaker Fe–N bonds. Formation of the stronger metal–ligand bonds of **16** provided an important driving force for incorporation of non-methylated pyridine carbaldehyde residues.<sup>57</sup>

**4.4. Sorting within a Structure.** Preparation of structure **18**, shown in Scheme 19, requires a different kind of selectivity in the choice of ligand subcomponents. Whereas during the simultaneous formation of dicopper and tricopper helicates (Scheme 17) all mixed ligands were eliminated from the dynamic library initially formed, in Scheme 19 the mixed ligand forms the unique structure selected during equilibration.<sup>58</sup>

This differential selectivity results from the differing numbers of donor atoms offered by the two dialdehydes upon which these structures are based. Phenanthroline dicarbaldehyde readily lends itself to the construction of a set of *homoligands* bearing a number of donor atoms divisible by four, matching the coordination preference of copper(I), as seen in the dicopper and tricopper helicate structures discussed earlier.

In contrast, pyridine dicarbaldehyde must make *heteroligands* incorporating an odd number of donor sites. In order to generate ligand sets bearing a number of donor sites divisible by four, *heteroligands* are necessary. In following this principle, formation of heteroligand-containing structure **18** is selected from the components shown in Scheme 19.

The special stability of compound **18** was demonstrated by the fact that it could also be generated by mixing together the two homoligand-containing complexes **19**

and **20**. Although both of these complexes are thermodynamically stable, **19** contains only three donor atoms per copper whereas **20** contains five such donors. The possibility of achieving coordinative saturation thus drives an imine metathesis reaction, redistributing the subcomponents to give structure **18** as the uniquely observed product. We are not aware of another such case in which different subcomponents are sorted *within* a single product structure.

## 5. Conclusion and Outlook

Creation of structural complexity, including topological complexity,<sup>29,33</sup> is feasible using subcomponent self-assembly, and the structures thus made may be induced to reassemble in well-defined ways using a variety of driving forces. Demonstration of directing “nonorthogonal” sets of subcomponent building blocks to come together in well-defined ways also opens up the possibility of linking such subunits together covalently, such that their self-assembly instructions serve as “subroutines” to guide the generation of a more complex superstructure.

We are currently investigating the use of subcomponent self-assembly to prepare new metal-containing polymeric materials. Following the same methodology that allowed the preparation of macrocycle **5** and catenane **6** (Scheme 7), further variations in the length, rigidity, and geometry of diamine subcomponents might allow for the generation of double-helical polymers, cyclic catenanes, or perhaps even polymeric catenanes.

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