Part One
Self-Organization, Nanoscience and Nanotechnology
1

Subcomponent Self-Assembly as a Route to New Structures and Materials

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1.1 Introduction

The concept of self-organization cuts across many of the sciences [1]. Gas and dust within nebulae coalesce into stars, which in turn arrange into galaxies that adopt a remarkable foamlike large-scale structure [2]. Biomolecules likewise self-organize—and organize each other—into the complex structures that compose cells, which may undergo further self-organization to create multicellular organisms. Living creatures aggregate also into herds, populations, communities, and biomes [3].

Human intelligence has proven skilled at examining organized structures and deducing the principles of self-organization that lead to their formation from less complex matter. This kind of deductive reasoning is one of the cornerstones of science, allowing for future predictions to be made based upon the principles uncovered.

The soul of chemistry lies in the art of synthesis. Through understanding chemical self-organization, new synthetic possibilities arise in ways that are not possible in the other sciences. When chemical bonds are formed in well-defined ways under thermodynamic [4, 5], as opposed to kinetic [6], control, one may refer to the resulting self-organization process as “self-assembly.” An understanding of the rules and principles guiding a self-assembly process can allow one to utilize these rules synthetically, creating new structures that possess new functions.

As one example, the observation of hydrogen bonding [7] in natural systems such as peptide helices and DNA base pairs led to a theoretical understanding of this phenomenon. This understanding has permitted the use of hydrogen bonding in synthesis, leading to the preparation of such diverse structures as Rebek’s capsules [8], Lehn’s supramolecular polymers [9], and Whitesides’ rosettes [10].

Over the course of the past four 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 [11–13],
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 [14]. Before and after the inception of our research program, other researchers have employed this method to synthesize a wealth of structures, including macrocycles [15], helicates [16, 17], rotaxanes [18], catenanes [19], grids [20, 21], and a Borromean link [22].

The preparation of the Borromean link, in particular, represents a remarkable synthetic accomplishment. This topological tour de force was created in one pot from zinc acetate and the two simple subcomponents shown at right in Figure 1.1, one of which is commercially available!

Stoddart et al.’s preparation of a Borromean link [22] and, more recently, a Solomon link [23] together with Leigh et al.’s preparations of rotaxanes [18] and catenanes [19] demonstrates the power of subcomponent self-assembly to prepare topologically complex structures from simple building blocks. In order to construct the Borromean link of Figure 1.1, for example, one cannot start with preformed macrocycles—it is necessary that the subcomponents be linked reversibly (via imine bonds in this case). These reversible linkages allow the macrocycles to open up in order to generate the topological complexity of the final product.

In our own laboratories, initial proof-of-concept experiments established the utility of subcomponent self-assembly based upon copper(I) coordination and imine bond formation, most usefully in aqueous solution [24]. We have subsequently developed our research program along three main lines, seeking responses to a series of questions.

Figure 1.1 Borromean link [22] prepared by Stoddart et al. from zinc(II) and the dialdehyde and diamine subcomponents shown at right via the simultaneous, reversible formation of covalent (C=N) and coordinative (N→Zn) bonds. Two of the six corners of the link (at left) have been replaced with straight lines for clarity.
Our first line of research asks how simple subcomponents might be used to create complex structures via self-assembly. How may self-assembly information be encoded into the subcomponents? What other means of encoding self-assembly information into the system might be employed, such as solvent effects and pH? Are there structures that are readily accessible using subcomponent self-assembly that are difficult or impossible to create otherwise? How may this method be used to generate topological complexity?

Our second line of investigation delves into the possibility of utilizing this methodology in sorting complex mixtures, using the techniques and ideas of dynamic combinatorial [25, 26] chemistry: Is it possible to direct given subcomponents 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?

Our third line of inquiry deals with the dynamic-evolutionary aspects of the structures we create. The reversibly-formed linkages holding these structures together allow a wide range of substitution and reconfiguration chemistry, on both dynamic covalent [5] (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?

1.2 Aqueous Cu(I)

The first study we undertook [24] validated the use of subcomponent self-assembly using aqueous copper(I), as well as taking initial steps in the directions of construction, sorting, and reconfiguration.

In aqueous solution CuI is frequently observed to disproportionate to CuII and copper metal, and imines are in most cases the minority species when amines and carbonyl compounds are mixed in water [27]. When imines and copper(I) are present in the same solution, however, this pattern of stability reverses. Imines are excellent ligands for CuI, 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 left in Scheme 1.1 [24].

Conceptually, one may imagine two different spaces within the flask wherein 1 self-assembles: a dynamic covalent [5] space and a supramolecular [11] space (Figure 1.2). 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.
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Scheme 1.1 Mutual stabilization of imines and Cu\(^{I}\) in aqueous solution during the formation of 1.

Figure 1.2 Intersection of dynamic covalent and supramolecular spaces during subcomponent self-assembly.

Certain ligand structures are certain to be favored, and others not present at all ("virtual") [26]. 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 may act in concert to amplify a limited subset of structures out of the dynamic library of all possible structures. The preparation of 1 thus represents a sorting of the dynamic combinatorial library of Figure 1.2.

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 aminal or hemiaminal ligands. Copper(I)/imine systems are thus particularly fruitful for use in 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 the formation of complex structures based on simple starting materials.

Although thermodynamically stable in aqueous solution, complex 1 nonetheless readily underwent covalent imine substitution in the presence of sulfanilic acid to form 2 (Scheme 1.2).

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 the displacement of the protonated form of the weaker acid (taurine) from 1 and the incorporation of the deprotonated form of the stronger acid (sulfanilic acid) during the formation of 2 [24].

1.3 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 [28] revealed that (S)-3-aminopropane-1,2-diol may be used to synthesize a mononuclear complex similar to 1 (Scheme 1.3). 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!

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 1.3, 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 [29], 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 [28].

1.4

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. The use of a copper(I) template allowed the linking of two amine and two aldehyde subcomponents in a well-defined way, in which the two imine ligands lie at a 90° angle about the copper center, as shown in Scheme 1.4. We sought to build more complex structures by using this motif as a tecton [30], or fundamental building block, as described below.

1.4.1

Dicopper Helicates

The reaction of sulfanilic acid with 2,9-diformyl-1,10-phenanthroline, copper(I) oxide, and sodium bicarbonate gave a quantitative yield of the anionic double

![Scheme 1.4](image-url) The organization of subcomponents around a metal center.
helicate 3, as shown in Scheme 1.5 [17]. Two of the bis-pyridine(imine) building blocks shown in Scheme 1.2 were thus incorporated into a single phenanthroline-bis(imine) subcomponent. The geometry of the phenanthroline molecule prevents all four nitrogen atoms of one of the ligands of 3 from coordinating to a single copper(I) ion, but two copper centers may readily be chelated together to generate the helical structure of 3.

In the crystal, the copper(I) centers of 3 adopt a flattened tetrahedral geometry (Figure 1.3), in very similar fashion to what has been observed in related structures [31, 32]. The deep green color of such complexes has been noted [31] 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 abs 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 addi-
tional positive charge is delocalized across both copper ions, as has been seen in other dicopper(I) structures [33]. Theoretical investigations are underway.

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 1.1 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 1.1) to form complexes in competition with the solvent. More hindered amines as well as cationic amines were not incorporated in either solvent, which we attribute to steric and Coulombic repulsion, respectively.

1.4.2 Tricopper Helicates

Tricopper helicates could also be synthesized using a simple modification of the dicopper helicate preparation [28]. 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 1.6).
1.4 Construction

1.4.3 Catenanes and Macrocycles

When short, flexible diamine was used as a subcomponent in helicate formation, as shown on the left side of Scheme 1.7, 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 [28].

When a longer diamine subcomponent that contained rigid phenylene segments was used, as shown in Scheme 1.7 at right, the 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 [28].

Unlike the original Sauvage catenates [34], catenate 6 is helically chiral in addition to possessing the possibility of becoming topologically chiral through the incorporation of an asymmetrical dianiline. The investigation of both kinds of chirality in catenates similar to 4 is currently under investigation.

Scheme 1.6 The preparation of tricopper helicate 4.

Scheme 1.7 The selection of a macrocyclic (5) or catenated (6) topology based on the rigidity and length of the subcomponents employed.
1.4.4

[2 × 2] Tetracopper(I) Grid

The aqueous reaction of Cu\(^{+}\), pyridine-2-carbaldehyde and a water-soluble \textit{m}-phenylenediamine resulted in the quantitative formation of the tetracopper(I) grid complex 7 shown in Scheme 1.8 [21].

The crystal structure of the grid (Figure 1.4) 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.

Scheme 1.8  Self-assembly of [2 × 2] grid complex 7 that forms only in water among all solvents tried (R = — CONHCH\(_2\)CH\(_2\)OH).

Figure 1.4  Orthogonal views of the crystal structure of the tetracationic grid 7 (the —CONHCH\(_2\)CH\(_2\)OH groups of the ligands are replaced by purple spheres at left).
A “diffuse pressure” applied by the hydrophobic effect would compensate 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 [35].

1.5 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 supramolecular 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 [36] to be sorted into a limited number of structures, or individual subcomponents to be directed to specific locations within larger structures.

1.5.1 Sorting Ligand Structures with Cu(I)

In initial work [37], we demonstrated that complexes containing different imine ligands could be synthesized in each others’ presence. When pyridine-2-carbaldehyde and benzaldehyde-2-sulfonate were mixed in aqueous solution with the diamine shown in Scheme 1.9, a library of ligands is created in dynamic equilibrium with the starting materials. The addition of copper(I) eliminated all but two of these ligands, forming complexes 8 and 9 in quantitative yield [37].

The simultaneous formation of 8 and 9 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 valences at either metal or ligand (enthalpically disfavored).

1.5.2 Simultaneous Syntheses of Helicates

This concept may also be extended to polynuclear helicates [38]. When 2-aminoquinoline and 4-chloroaniline were mixed with the phenanthroline dialdehyde shown in Scheme 1.10, a dynamic library of potential ligands was observed to form. The addition of copper(I) causes this library to collapse, generating only dicopper and tricopper helicates. As in the mononuclear case of Scheme 1.9, the driving force behind this selectivity appeared to be the formation of structures in which all ligand and metal valences are satisfied. The use of supramolecular (coordination) chemistry to drive the covalent reconfiguration of intraligand bonds thus
appears to be a general phenomenon, applicable in polynuclear as well as mononuclear cases.

1.5.3 Sorting within a Structure

The preparation of structure 10, shown in Scheme 1.11, requires a different kind of selectivity in the choice of ligand subcomponents. Whereas during the simultaneous formation of dicopper and tricopper helicates (Scheme 1.10) all mixed ligands were eliminated from the dynamic library initially formed, in Scheme 1.11 the mixed ligand forms the unique structure selected during equilibration [39].

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 homo-ligands bearing a number of donor atoms divisible by 4, matching the coordination preference of copper(I), as seen in the dicopper and tricopper helicate structures discussed earlier.
In contrast, pyridine dicarbaldehyde must make homo-ligands incorporating an odd number of donor sites. In order to generate ligand sets bearing a number of donor sites divisible by 4, hetero-ligands are necessary. In following this principle, the formation of hetero-ligand-containing structure 10 is selected from the components shown in Scheme 1.11.

The special stability of compound 10 was demonstrated by the fact that it could also be generated by mixing together the two homo-ligand-containing complexes 11 and 12 (Scheme 1.11, bottom). Although both of these complexes are thermodynamically stable, 11 contains only three donor atoms per copper, whereas 12 contains five such donors. The possibility of achieving coordinative saturation thus drives an imine metathesis reaction, redistributing the subcomponents to give structure 10 as the uniquely observed product. We are not aware of another such case in which different subcomponents are sorted within a single product structure.

In addition to structure 10, in which the ligand adopts a head-to-head orientation, we were able to prepare structure 13 (Scheme 1.12), in which the ligands...
Scheme 1.11 The preparation of structure 10 from a mixture of ligand subcomponents (top) and through the covalent conproportionation of subcomponents from preformed structures 11 and 12 (bottom).

Scheme 1.12 The preparation of 13, in which the ligands adopt a head-to-tail configuration.

adopt a head-to-tail orientation [39]. This orientation is favored by the antiparallel orientation of the ligands’ dipoles, which is not possible in the case of 10 due to the insufficient length of the diamine subcomponent. In addition to the constitutional selectivity engendered through the avoidance of valence frustration, we were
able thus to observe an orientational selectivity by employing either two equivalents of aniline or one equivalent of diamine subcomponent.

1.5.4 Cooperative Selection by Iron and Copper

Extending this sorting methodology further, we have 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 1.13) [37]. 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 14 and 15 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 \[14\] should eliminate all partially formed ligands and ligand subcomponents from the mixture, the chelate effect \[40\] should favor structures containing ligands that bear the highest number of bound donor atoms possible, and 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. We discuss below our investigations of three distinct preferences exhibited by copper(I) and iron(II). These preferences act in concert to select 14 and 15 alone as products of the reaction of Scheme 1.13.

Firstly, copper(I) preferentially formed complexes that incorporated the methylated aldehyde. All three possible products shown in Scheme 1.2 were observed in the reaction of Scheme 1.14. The two aldehydes were incorporated into the product mixture in a molar ratio of 30:70, which indicates a slight thermodynamic preference for the incorporation of the methylated aldehyde, whose more electron-rich character would allow ligands that incorporate this residue to better stabilize the cationic copper(I) center.

Secondly, iron(II) was observed to form octahedral complexes that incorporate the triamine in preference to the monoamine. When complex 16 was mixed with an equimolar amount of triamine in aqueous solution, complex 14 and monoamine were the only products observed (Scheme 1.15). The chelate effect \[40\] may be understood to drive this substitution: The incorporation of one equivalent of triamine results in the liberation of three equivalents of monoamine, which provided the entropic driving force for this reaction.

![Scheme 1.14](image_url)

**Scheme 1.14** The choice of copper: methylated aldehyde was preferentially incorporated into copper(I) complexes in aqueous solution.
A third driving force for the observed selectivity, complementing and amplifying copper’s choice of the methylated aldehyde, is the preference of iron(II) to incorporate the nonmethylated aldehyde into complexes of type 14. As shown in Scheme 1.16, the addition of iron(II) to a mixture of triamine and both aldehydes gave a product mixture in which nonmethylated and methylated aldehydes are present in a 3:97 ratio following equilibration. Only the two products shown in Scheme 1.16 were observed in the product mixture. The reaction of Scheme 1.16 thus deviates substantially from a statistical mixture of products; indeed, only two of the expected four products are observed to form. No evidence was found of complexes incorporating two or three equivalents of methylated aldehyde.

When either cobalt(II) or zinc(II) sulfate was used in place of the iron(II) salt in the reaction of Scheme 1.13, mixtures of products were obtained. In the crystal, iron(II) is bound more tightly in 1 (mean $r_{Fe-N} = 1.95\,\text{Å}$) [41] than are cobalt(II) (mean $r_{Co-N} = 2.15\,\text{Å}$) [41] or zinc(II) (mean $r_{Zn-N} = 2.18\,\text{Å}$) [41] in complexes with the same ligand; this observation was correlated with the finding that iron(II) is the only divalent first-row transition metal having a low-spin ground state with this ligand [41]. The groups of Drago [42], Hendrickson [43], and Hauser [44] have investigated the magnetic behavior of the two iron complexes shown in Scheme 1.15.
1.16, in addition to the other two congeners incorporating 2 and 3 equivalents of methylated aldehyde, respectively. They determined that although 14 remains in the low-spin $^1A_1$ state from 30 to 450 K [43, 44], the complexes containing methylated aldehyde residues undergo spin crossover to the high-spin $^3T_2$ state as the temperature increases. The more such residues a complex contains, the lower the temperature at which it undergoes spin crossover. A steric clash between the methyl groups and facing pyridyl rings, as shown in Scheme 1.16, appears to destabilize the low-spin state with respect to the high-spin state by elongating the Fe–N bonds.

The strong thermodynamic preference of iron(II) to incorporate nonmethylated aldehyde might thus be attributed to the high energetic penalty paid for a steric clash in iron(II) complexes of this type. Since the presence of high-spin iron(II) may be inferred in complexes bearing one or more methylated aldehyde residues, one might also invoke the possibility of a “spin-selection” phenomenon, whereby the formation of short, strong bonds between low-spin iron(II) and sp$^2$ nitrogen atoms serves as a thermodynamic driving force for the preferential incorporation of sterically unhindered aldehyde.

1.6 Substitution/Reconfiguration

Many of the complexes prepared through subcomponent self-assembly underwent clean substitution chemistry, which may operate both at covalent and coordinative levels. As discussed below, driving forces for such substitutions included the relief of steric encumbrance, the substitution of an electron-poor subcomponent for an electron-rich one, the use of pK$\alpha$ differentials, and the chelate effect.

1.6.1 New Cascade Reaction

Pseudotetrahedral complexes such as 17 (Scheme 1.17) were observed to possess a particularly rich substitution chemistry [37]. Complex 17 reacted cleanly with o-phenylenediammonium to give the covalent substitution product 18 shown in Scheme 1.17. This imine substitution was driven by the same pK$\alpha$ effect employed in the 1-to-2 transformation of Scheme 1.2. In addition, 17 reacted cleanly with copper bis(biquinoline) complex 10 to give the coordinative substitution product 20. This ligand exchange appears to have been sterically driven: the substitution of one of the encumbering di(imine) ligands for a less bulky biquinoline provided the driving force for this reaction [45].

In contrast with 17, complex 21 (Scheme 1.18) 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 1.18). The intermediate product 18 (from
Scheme 1.17 Covalent (above) and coordinative (below) rearrangements of complex 17 to give 18 and 20, driven by $pK_a$ differences and sterics, respectively.

Scheme 1.18 The cascade reaction of 19 and 21, rearranging on both covalent and coordinative levels to give 22 upon the addition of o-phenylenediammonium dichloride.
Scheme 1.17) formed following the reaction between 21 and phenylenediammonium, reacted immediately with 19 to give the final product 22.

The addition of phenylenediammonium to a mixture of 19 and 21 thus caused two distinct rearrangements to occur: initial (covalent) imine exchange followed immediately by (coordinative) ligand exchange, resulting in the exclusive formation of mixed-ligand complex 22.

### 1.6.2 Hammett Effects

The electronic nature of the amine incorporated into these imine complexes should play an important role in determining the stability of CuI 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 [46] (Scheme 1.19).

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, 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 $\sigma_{para}$ value [47] of a given aniline and the $K_{eq}$ of the competition between free and substituted aniline, as shown in Figure 1.5. 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 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 differently substituted anilines might be used to effect clean transformations between assemblies. For example, in Scheme 1.20 we demonstrate a series of transformations between four distinct structures, ending with metallocycle 23. 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 [46].

1.6.3 Helicate Reconfigurations

The dicopper double-helicate moiety [31] has exhibited rich and varied substitution chemistry, as discussed below [17, 28, 46]. 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 [13].

The \( \text{pK}_a \)-differential-driven chemistry that functions in mononuclear cases (Schemes 1.2, 1.17, and 1.18) also works well in the context of helicates. As shown in Scheme 1.21, helicate 24 was transformed into 3 upon the 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 24-to-5 and 3-to-5 conversions shown in Scheme 1.21. Two distinct hierarchical layers of control over subcomponent substitution may thus be employed in tandem, based upon \( \text{pK}_a \) differences and the chelate effect.

The entropy-driven conversion of 3 to 5 may be reversed upon lowering the pH (Scheme 1.22). The addition of sulfanilic acid to macrocycle 5 resulted in its con-
version to helicate 3. Basification of this solution through the addition of NaHCO₃ resulted in the 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 [28].

Tricopper double-helicate 4 may also be synthesized through subcomponent substitution, starting with the 4-chloroaniline-containing dicopper helicate shown in Scheme 1.23. The electron-poor 4-chloroaniline residue (σ<sub>para</sub> = 0.23) [47] thus serves as an excellent leaving group in this substitution reaction. Starting with a dicopper helicate containing more electron-rich 4-methoxyaniline residues (σ<sub>para</sub> = −0.27) [47] we observed only 18% of 4 following equilibration.

1.6.4
Substitution as a Route to Polymeric Helicates

The reaction of dicopper helicate 25 (Scheme 1.24) with o-phenylenediamine produced the dimeric tetracopper helicate 26 in 51% yield. This reaction is the first step of a step polymerization reaction [48]; during the course of the reaction, a substantial amount of insoluble brown material is also produced. The elemental analysis of this insoluble co-product is consistent with that of a higher oligomer
Scheme 1.21 The subcomponent substitution of diamine for both aryl (3→5) and alkyl (24→5) monoamines, complementing the substitution of arylamines for alkylamines (24→3).

Scheme 1.22 Cycling between 5 and 3 as a function of pH.
or polymer; the mass of this material, formulated as a polymer, corresponds well to the lost mass of subcomponents that are not incorporated into 26.

Tetracopper helicate 26 thus appears only to be isolable as a result of its greater solubility, with respect to higher oligomers. The use of more-soluble subcomponents might thus allow for the preparation of soluble polymers based upon the stacked-helicate motif of 26.

Such polymers might be of substantial technological interest as electrically conductive “molecular wires.” Density functional (DFT) calculations indicated that the metal-based HOMO of 26 is delocalized across all four of the central copper(I) ions, as shown in Figure 1.6. Calculations also indicate that removal of one electron from this HOMO likewise results in a fully delocalized singly occupied orbital. This delocalization could provide a path for conductivity, allowing an electric current to flow from one end of a helicate polymer strand to the other.
1.7 Conclusion and Outlook

The creation of structural complexity, including topological complexity [19, 22], 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. The 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 1.7), 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.

1.8 Acknowledgments

This work was carried out by Marie Hutin, David Schultz, David Gérard, and Sonya Torche, in addition to our collaborators Christopher Cramer, Laura Gagliardi,
Gérald Bernardinelli, Christoph Schalley, Jérôme Lacour, Richard Frantz, Damien Jeannerat, André Pinto and Philippe Perrotet. Financial support has been provided by the Walters-Kundert Chairitable trust, the University of Geneva, the Swiss National Science Foundation, the ERA-Chemistry Network, and the Swiss State Secretariat for Education and Research.

References

References
