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Selection Rules for Helicate Ligand Component Self-Assembly: Steric, pH, Charge, and Solvent Effects

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Abstract: The reaction between 1,10-phenanthroline-2,9-dicarboxaldehyde, copper(I), and certain primary amines was found to give quantitatively a dicopper double-helicate product (two of which were crystallographically characterized) by imine self-assembly around Cu^{I} templates. The parameters of this reaction were investigated, and important roles were found to be played by (i) the steric bulk of the amine, (ii) the charge of the amine, (iii) the solvent used, and (iv) the pH of the solution. Water was found to allow the broadest range of structures to form, and ligand-component exchange reactions (involving the substitution of an aromatic for an aliphatic amine) were demonstrated to proceed readily in this solvent.

Introduction

Metalloorganic self-assembly has proven a versatile and powerful means to construct nanoscale architectures, which are beginning to approach the necessary degree of complexity to serve as useful molecular machines.[1−7] Building upon the successes of the programmed self-assembly of preformed ligands with metals[8−13] and Busch's concept of template synthesis,[14] ligand-component self-assembly is emerging as a powerful means to create such structures. Starting from the fundamental building blocks of *ligand subcomponents* and metal ions, such diverse structures as catenanes[15] (including Borromean rings[16]), rotaxanes,[17] grids,[18,19] and helicates[20−22] have been generated by the metal-templated[14] formation of imine bonds, bringing both ligands and supramolecular complexes into being at the same time.

The use of ligand-component assembly reactions not only reduces the effort required for ligand synthesis[23] but also furnishes a means to create structures capable of dynamic rearrangement[24] in solution through Schiff-base metathesis.[25,26] Dynamic reassembly reactions of metalloorganic complexes, such as have been induced by transmetalation,[18,27] redox processes,[28] the presence of guest species,[29−34] or interactions with a different complex,[35] constitute means for these complexes to interact with the environment in well-defined ways, possibly

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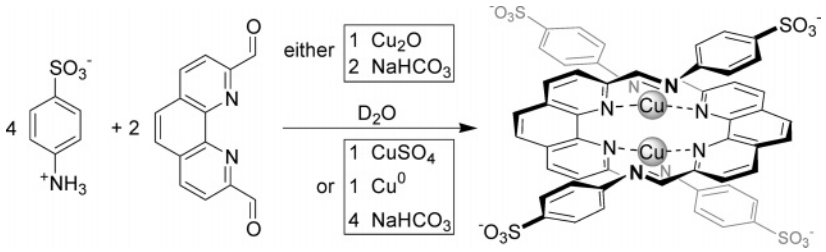
(1) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348−3381.
(2) Jimenez-Molero, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Chem. Commun.* **2003**, 1613−1616.
(3) Thordarson, P.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Nature* **2003**, *424*, 915−918.
(4) Barboiu, M.; Vaughan, G.; Kyritsakas, N.; Lehn, J.-M. *Chem. Eur. J.* **2003**, *9*, 763−769.
(5) Stoddart, J. F. *Acc. Chem. Res.* **2001**, *34*, 410−411. C. Bustamante, I. Willner, V. Balzani, A. Harada, F. Vögtle, J.-P. Sauvage, L. Fabbrizzi, S. Shinkai, B. L. Feringa, and T. R. Kelly also contributed relevant articles to this special issue.
(6) Collin, J.-P.; Dietrich-Buchecker, C.; Gaviña, P.; Jimenez-Molero, M. C.; Sauvage, J.-P. *Acc. Chem. Res.* **2001**, *34*, 477−487.
(7) Schalley, C. A.; Lutzen, A.; Albrecht, M. *Chem. Eur. J.* **2004**, *10*, 1072−1080.
(8) Lehn, J. M. *Supramolecular Chemistry: Concepts and Perspectives*; Wiley-VCH: Weinheim, Germany, 1995.
(9) Albrecht, M. *J. Inclusion Phenom. Macrocycl. Chem.* **2000**, *36*, 127−151.
(10) Swiegers, G. F.; Malefetse, T. J. *Chem. Rev.* **2000**, *100*, 3483−3537.
(11) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972−983.
(12) Sun, W.-Y.; Yoshizawa, M.; Kusukawa, T.; Fujita, M. *Curr. Opin. Chem. Biol.* **2002**, *6*, 757−764.
(13) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975−982.
(14) Hubin, T. J.; Busch, D. H. *Coord. Chem. Rev.* **2000**, *200*, 5−52.
(15) Leigh, D. A.; Lusby, P. J.; Teat, S. J.; Wilson, A. J.; Wong, J. K. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1538−1543.
(16) Chichak, K. S.; Cantrill, S. J.; Pease, A. R.; Chiu, S.-H.; Cave, G. W. V.; Atwood, J. L.; Stoddart, J. F. *Science* **2004**, *304*, 1308−1312.
(17) Hogg, L.; Leigh, D. A.; Lusby, P. J.; Morelli, A.; Parsons, S.; Wong, J. K. Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 1218−1221.
(18) Brooker, S.; Hay, S. J.; Plieger, P. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1968−1970.
(19) Nitschke, J. R.; Lehn, J. M. *Proc. Natl. Acad. Sci. U. S. A.* **2003**, *100*, 11970−11974.
(20) Childs, L. J.; Alcock, N. W.; Hannon, M. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4244−4247.
(21) Houjou, H.; Iwasaki, A.; Ogihara, T.; Kanesato, M.; Akabori, S.; Hiratani, K. *New J. Chem.* **2003**, *27*, 886−889.
(22) Hamblin, J.; Childs, L. J.; Alcock, N. W.; Hannon, M. J. *J. Chem. Soc., Dalton Trans.* **2002**, 164−169.
(23) Hannon, M. J.; Painting, C. L.; Jackson, A.; Hamblin, J.; Errington, W. *Chem. Commun.* **1997**, 1807−1808.
(24) Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 898−952.
(25) Oh, K.; Jeong, K. S.; Moore, J. S. *Nature* **2001**, *414*, 889−893.
(26) Ro, S.; Rowan, S. J.; Pease, A. R.; Cram, D. J.; Stoddart, J. F. *Org. Lett.* **2000**, *2*, 2411−2414.
(27) Brooker, S.; Kelly, R. J. *Dalton Trans.* **1996**, 2117−2122.
(28) Funeriu, D. P.; Lehn, J.-M.; Baum, G.; Fenske, D. *Chem. Eur. J.* **1997**, *3*, 99−104.
(29) Hasenknopf, B.; Lehn, J.-M.; Boumediene, N.; Dupont-Gervais, A.; Van Dorsselaer, A.; Kneisel, B.; Fenske, D. *J. Am. Chem. Soc.* **1997**, *119*, 10956−10962.
(30) Houghton, M. A.; Bilyk, A.; Harding, M. M.; Turner, P.; Hambley, T. W. *Dalton Trans.* **1997**, 2725−2734.
(31) Scherer, M.; Caulder, D. L.; Johnson, D. W.; Raymond, K. N. *Angew. Chem., Int. Ed.* **1999**, *38*, 1588−1592.
(32) Saalfrank, R. W.; Bernt, I.; Uller, E.; Hampel, F. *Angew. Chem., Int. Ed.* **1997**, *36*, 2482−2485.
(33) Severin, K. *Coord. Chem. Rev.* **2003**, *245*, 3−10.
(34) Stulz, E.; Ng, Y.-F.; Scott, S. M.; Sanders, J. K. M. *Chem. Commun.* **2002**, 524−525.
(35) Fujita, M.; Fujita, N.; Ogura, K.; Yamaguchi, K. *Nature* **1999**, *400*, 52−55.

10.1021/ja046001z CCC: $27.50

Scheme 1. Aqueous Template Synthesis of Dicopper(I) Double Helicate $\mathbf{1}^{2-}$, from Copper(I) Oxide or from Conproportionation of Copper(II) Sulfate and Copper Metal



doing useful work. We have recently explored dynamic ligand-component assembly and exchange using mononuclear Cu^{I} bis-imine complexes[36] and tetranuclear strained grids[37] that self-assemble in aqueous solution.

To extend the chemistry of ligand-component self-assembly, knowledge must be gained as to which building blocks will be incorporated into a given structure under a given set of conditions. The development of such "selection rules" is necessary for the construction of complex, functional architectures: specific components must be guided to specific sites of incorporation based upon steric and electronic factors. Complementing such guidelines would be reassembly guidelines detailing under what conditions a structure reconfigures itself, and into what products. Herein we describe the results of investigations into the rules governing the synthesis and reassembly of a class of dicopper(I) double-helicate complexes, which were generated by ligand-component self-assembly in aqueous and acetonitrile solutions.

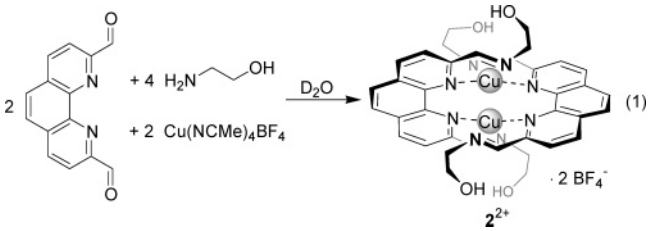
Results and Discussion

A mixture of 1,10-phenanthroline-2,9-dicarboxaldehyde[38] (2 equiv), sulfanilic acid (4-aminobenzenesulfonic acid, 4 equiv), copper(I) oxide (1 equiv), and sodium bicarbonate (2 equiv) dissolved over several hours in deuterium oxide under an argon atmosphere to give a dark green solution. Despite this color, which is often associated with copper(II), NMR spectra showed that the unique product was diamagnetic and were consistent with the double-helical structure $\mathbf{1}^{2-}$ shown in Scheme 1. The complex is inert to both imine hydrolysis and Cu^{I} disproportionation in solution, with the ligands and metals being mutually stabilized in aqueous solution by complex formation.[36] The thermodynamic stability of this complex is demonstrated by the fact that it may also be prepared by the conproportionation of copper(II) sulfate and copper(0) metal in place of copper(I) oxide (Scheme 1).

The identity of this complex was confirmed by X-ray crystallography; an ORTEP diagram of $\mathbf{1}^{2-}$ is shown in Figure 1. The helicate consists of two ligand strands wrapped around two Cu^{I} ions of flattened tetrahedral coordination geometry (Figure 1).

The crystal, obtained through the diffusion of an aqueous solution of $Na_2\mathbf{1}$ into an aqueous solution of $Ba(ClO_4)_2$, is composed of layers of helicate dianions separated and bridged by layers of barium cations and water molecules. A network of hydrogen bonds serves to order and orient the water molecules within the layers (Figure 2).

The generality of this double-helicate-forming reaction was demonstrated by the synthesis of $\mathbf{2}^{2+}$ (eq 1), employing 2-aminoethanol and copper(I) tetrakis(acetonitrile) tetrafluoroborate in place of sulfanilic acid and copper(I) oxide.



(1)

The crystal structure of $\mathbf{2}^{2+}$ is shown in Figure 3. The helical core of this molecule is nearly isostructural with that of $\mathbf{1}^{2-}$, showing no statistically significant deviations in bond lengths and angles despite the substitution of alkyl chains for aryl rings.

Copper(I) helicate complexes have been used as a platform to develop much fundamental supramolecular chemistry,[20,22,39−57] and dicopper double helicates structurally similar to these have been reported by Ziessel[58] and Henkel.[59] This led us to develop our aqueous Cu(I)-templated ligand-component assembly[36,37] in this direction, using these helicate complexes to explore the

(36) Nitschke, J. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 3073−3075.
(37) Nitschke, J. R.; Hutin, M.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2004**, in press.
(38) Angeloff, A.; Daran, J.-C.; Bernadou, J.; Meunier, B. *Eur. J. Inorg. Chem.* **2000**, 1985−1996.
(39) Lehn, J. M.; Rigault, A.; Siegel, J.; Harrowfield, J.; Chevrier, B.; Moras, D. *Proc. Natl. Acad. Sci. U. S. A.* **1987**, *84*, 2565−2569.
(40) Kramer, R.; Lehn, J. M.; Marquis-Rigault, A. *Proc. Natl. Acad. Sci. U. S. A.* **1993**, *90*, 5394−5398.
(41) Constable, E. C.; Edwards, A. J.; Hannon, M. J.; Raithby, P. R. *Chem. Commun.* **1994**, 1991−1992.
(42) Constable, E. C.; Heirtzler, F. R.; Neuburger, M.; Zehnder, M. *Supramol. Chem.* **1995**, *5*, 197−200.
(43) Woods, C. R.; Benaglia, M.; Cozzi, F.; Siegel, J. S. *Angew. Chem., Int. Ed.* **1996**, *35*, 1830−1833.
(44) Smith, V. C. M.; Lehn, J.-M. *Chem. Commun.* **1996**, 2733−2734.
(45) Constable, E. C.; Heirtzler, F.; Neuburger, M.; Zehnder, M. *J. Am. Chem. Soc.* **1997**, *119*, 5606−5617.
(46) Baxter, P. N. W.; Lehn, J. M.; Rissanen, K. *Chem. Commun.* **1997**, 1323−1324.
(47) El-ghayouy, A.; Harriman, A.; De Cian, A.; Fischer, J.; Ziessel, R. *J. Am. Chem. Soc.* **1998**, *120*, 9973−9974.
(48) El-ghayoury, A.; Douce, L.; Skoulios, A.; Ziessel, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 2205−2208.
(49) Greenwald, M.; Wessely, D.; Goldberg, I.; Cohen, Y. *New J. Chem.* **1999**, *23*, 337−344.
(50) Constable, E. C.; Housecroft, C. E.; Kulke, T.; Baum, G.; Fenske, D. *Chem. Commun.* **1999**, 195−196.
(51) Baum, G.; Constable, E. C.; Fenske, D.; Housecroft, C. E.; Kulke, T. *Chem. Eur. J.* **1999**, *5*, 1862−1873.
(52) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Woods, C. R.; Siegel, J. S. *Eur. J. Org. Chem.* **2001**, 173−180.
(53) Kawano, T.; Kato, T.; Du, C.-X.; Ueda, I. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 709−719.
(54) Tuna, F.; Hamblin, J.; Jackson, A.; Clarkson, G.; Alcock, N. W.; Hannon, M. J. *Dalton Trans.* **2003**, 2141−2148.
(55) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457−3497.
(56) Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev.* **1997**, *97*, 2005−2062.
(57) Dietrich-Buchecker, C. O.; Sauvage, J. P. *Angew. Chem., Int. Ed.* **1989**, *101*, 192−194.
(58) Ziessel, R.; Harriman, A.; Suffert, J.; Youinou, M.-T.; De Cian, A.; Fischer, J. *Angew. Chem., Int. Ed.* **1997**, *36*, 2509−2511.
(59) Ameerunisha, S.; Schneider, J.; Meyer, T.; Zacharias, P. S.; Bill, E.; Henkel, G. *Chem. Commun.* **2000**, 2155−2156.

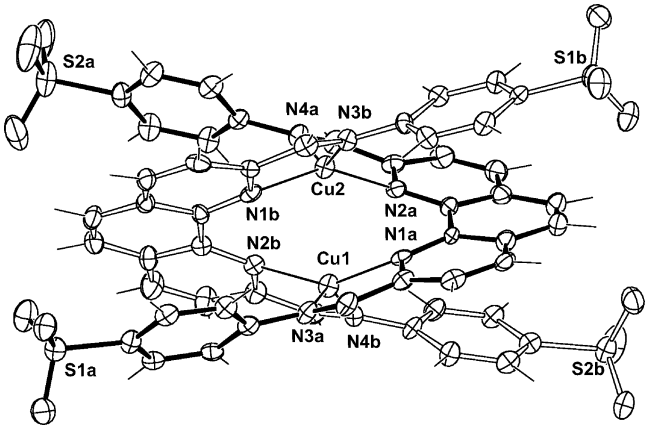


Figure 1. ORTEP view of $\mathbf{1}^{2-}$. Ellipsoids are represented at the 50% probability level. Selected mean bond distances [Å] and angles [°]: Cu1···Cu2 2.730(1), $Cu-N_{imine(N3,N4)}$ 2.026(9), $Cu-N_{phen(N1,N2)}$ 2.089(8); $N_{imine}-Cu-N_{imine}$ 142(1), $N_{phen}-Cu-N_{phen}$ 148.8(2), $N_{imine}-Cu-N_{phen}$(intra) 79.9(4), $N_{imine}-Cu-N_{phen}$(inter) 111(2).

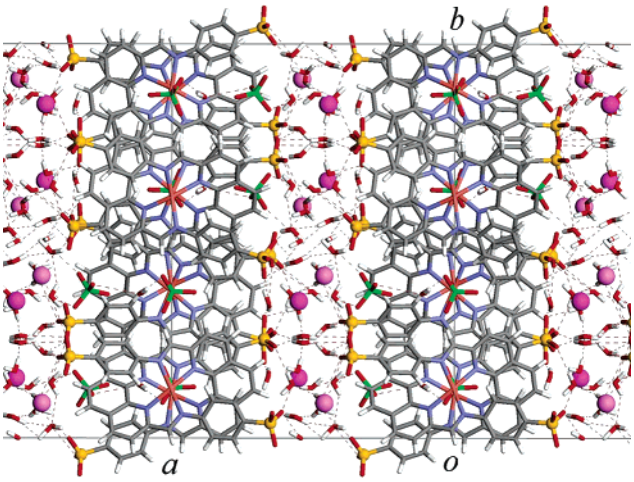


Figure 2. View parallel to the *c*-axis of $Ba^{2+}\mathbf{1}^{2-}\cdot Ba^{2+}(ClO_4^-)_2$ in the crystal, showing the layered structure. The purple spheres represent Ba^{2+} ions; hydrogen bonds are indicated by dashed lines.

parameters and limits of our methodology. Noting the aqueous stability and quantitative formation of the double-helical motif of $\mathbf{1}^{2-}$ and $\mathbf{2}^{2+}$, we sought to investigate what other amines might be similarly incorporated, as shown in Chart 1. The general procedure consisted of mixing amines **a**−**h** (4 equiv), 1,10-phenanthroline-2,9-dicarboxaldehyde (2 equiv), and copper(I) tetrakis(acetonitrile) tetrafluoroborate (2 equiv) in deuterium oxide or acetonitrile-d_3. In all cases where helicate formation was noted to have occurred, all solids dissolved within 2 h of ultrasonication to give a dark solution, the ^{1}H and ^{13}C NMR spectra of which were consistent with quantitative double-helicate formation. In cases where helicate formation is listed as not having occurred, ultrasonication for 12 h failed to give a green solution, and NMR spectra indicated mixtures of products.

Certain patterns were noted through this series of experiments (Chart 1). In aqueous solution, amines bearing a methoxy-(ethanol) group or one or two hydroxymethyl groups on the α-carbon were thus "allowed" as shown by entries **a**−**c**. Sulfonated aryl and primary amines **d** and **e** were likewise readily incorporated into these helicates. Amines such as **f** bearing three alkyl groups on the α-carbon, however, as well

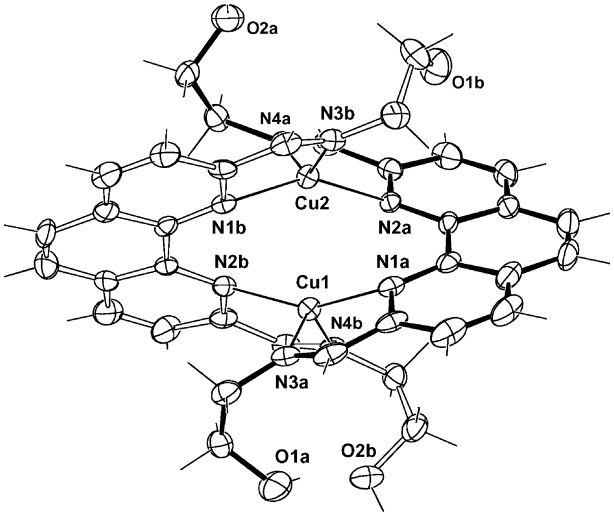
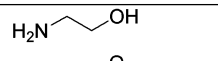
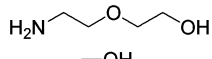
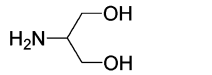
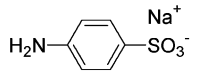
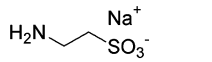
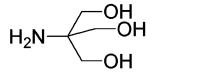
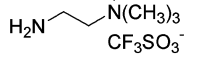
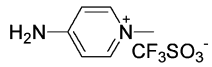


Figure 3. ORTEP diagram of $\mathbf{2}^{2+}$. Ellipsoids are represented at the 50% probability level. Selected mean bond distances [Å] and angles [°]: Cu1···Cu2 2.7321(6), $Cu-N_{imine(N3,N4)}$ 2.011(12), $Cu-N_{phen(N1,N2)}$ 2.087(17); $N_{imine}-Cu-N_{imine}$ 133(7), $N_{phen}-Cu-N_{phen}$ 152(3), $N_{imine}-Cu-N_{phen}$(intra) 81.1(5), $N_{imine}-Cu-N_{phen}$(inter) 110(2).

Chart 1. Helicate Formation Selection Rules in Water and Acetonitrile

	Amine	Helicate in H_2O	Helicate in MeCN
a		Yes	Yes
b		Yes	Yes
c		Yes	No
d		Yes	No
e		Yes	No
f		No	No
g		No	No
h		No	No

as the cationic amines **g** and **h**, appeared to be excluded by the self-assembly process. Models suggest that steric encumbrance would prevent the incorporation of **f** and might hinder the incorporation of **g**. Mutual repulsion between the positive charges of **g** and **h** and the cationic helicate backbone appear to disfavor helicate formation. The low nucleophilicity of **h**, a result of the partial positive charge on its NH_2 group, also could help to explain its nonincorporation.

The use of acetonitrile as a reaction solvent brought to bear a more restricted set of selection rules upon the helicate self-assembly process. In addition to the cationic amines, the anionic amines **d** and **e** did not give helicates. This could be a result of the negligible solubility of sodium sulfonates in acetonitrile, which is a poor hydrogen bond donor.

Serinol (2-aminopropane-1,3-diol) (**c**) likewise did not give a helicate in acetonitrile, although it is soluble in this solvent.

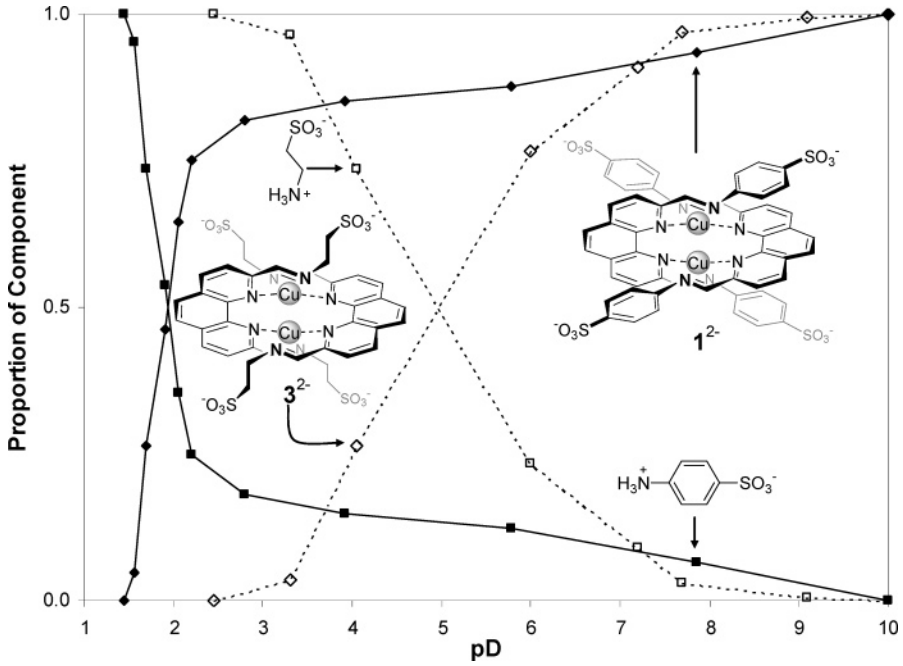


Figure 4. Disassembly of helicates $\mathbf{1}^{2-}$ and $\mathbf{3}^{2-}$ as a function of acidity.

The serinol-derived helicate formed in D_2O is sterically hindered, as was revealed by its ^1H spectrum at 298 K. Although the phenanthroline and imine resonances were sharp, the peaks resulting from the serinol-derived diastereotopic protons were broad. This is ascribed to rapid racemization between (*P*) and (*M*) helicates on the NMR time scale, which suggests a ground-state steric destabilization of the helical structure. Although NMR and mass spectra are consistent with helicate formation, the color of the serinol-containing helicate is dark brown, contrasting with the dark green color of all of the other helicates observed. This might indicate a structural perturbation to the di-copper(I) chromophore.

In contrast to the serinol-derived helicate, the helicates formed from the less sterically demanding amines **a** and **b** have diastereotopic protons that gave sharp and distinct ^1H signals at 298 K in D_2O. The diastereotopic protons of the helicate derived from amine **b** were broadened nearly to coalescence at 363 K in D_2O, which indicates a barrier to racemization above 67.5 kJ mol^{-1}.[60] In acetonitrile, however, these protons gave broad resonances at room temperature, and decoalesce only below 273 K, which indicates a barrier to racemization of 50 kJ mol^{-1}.[60] This solvent effect thus gives a $\Delta\Delta G^{\ddagger}$ greater than 17.5 kJ mol^{-1} between water and acetonitrile, presumably because acetonitrile stabilizes the racemization transition state by coordinating to Cu^I. In the case of serinol in acetonitrile, the ground-state destabilizing steric effects and the transition-state stabilizing solvent effects, acting in concert, appear to lower the energy of the "transition state" below that of the "ground state," which made helicate formation energetically disfavorable.

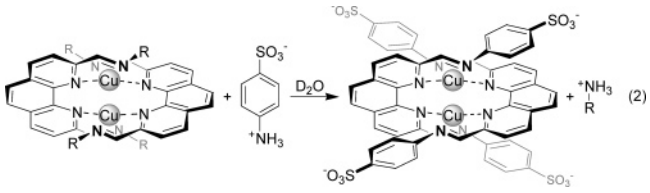
Although capable of dynamic exchange, these systems are not readily treated using the techniques of dynamic combinatorial chemistry[19,61−65] due to the low solubility of the 1,10-phenanthroline-2,9-dicarboxaldehyde. One may nonetheless consider the amplification effect of the copper(I) template[14] upon its chosen ligand, taking into account the fact that not only the equilibria between solution species, but also the partitioning of species between solution and the solid state, are perturbed. In acetonitrile, ^1H NMR showed that the hydroxyamines **a** and **b** reacted to form bis-imines quantitatively with 1,10-phenanthroline-2,9-dicarboxaldehyde, thus allowing for no amplification effect. In D_2O amines **a**, **b**, and **c** gave respectively 57%, 44%, and 63% imine (by ^1H integration), corresponding to modest amplification factors of 1.7, 2.3, and 1.6 upon quantitative templating of the imines by copper. More remarkably, no imine at all was observed by NMR with sulfonated amines **d** and **e** in the absence of copper. The quantitative formation of helicates (having a ligand concentration of 50 mM) from these components thus implies an amplification of the bis-imine ligands by a factor of more than 500, conservatively assuming an ^1H NMR detection limit of 0.1 mM.

We were also able to utilize pH as a means to control the self-assembly reaction. Figure 4 shows the disassembly of helicates $\mathbf{1}^{2-}$ and $\mathbf{3}^{2-}$ (formed from amines **d** and **e**) during titration with D_2SO_4 in D_2O, as followed by ^1H NMR integration of peaks corresponding to free and incorporated amine. The liberated dialdehyde precipitated during the course of titration, but the process was nonetheless reversible. Upon the addition of excess hydroxide, helicates reassembled from the ligand components as the dialdehyde redissolved.

The difference in pH stability between the two helicates reflects the difference between the pK_a's of the corresponding protonated amines. Taurine (**e**) is less acidic (pK_a = 9.1)[66] than sulfanilic acid (**d**) (pK_a = 3.2),[67] indicating that taurine should be more readily displaced from a helicate than sulfanilic acid by proteolysis, as observed.

(60) Braun, S.; Kalinowski, H.-O.; Berger, S. *150 and More Basic NMR Experiments*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 1998; p 596.
(61) Severin, K. *Chem. Eur. J.* **2004**, *10*, 2565−2580.
(62) Telfer, S. G.; Yang, X. J.; Williams, A. F. *Dalton Trans.* **2004**, 699−705.
(63) Nguyen, R.; Huc, I. *Chem. Commun.* **2003**, 942−943.
(64) Lehn, J. M.; Eliseev, A. V. *Science* **2001**, *291*, 2331−2332.
(65) Otto, S.; Furlan, R. L. E.; Sanders, J. K. M. *Science* **2002**, *297*, 590−593.
(66) Madura, J. D.; Lombardini, J. B.; Briggs, J. M.; Minor, D. L.; Wierzbicki, A. *Amino Acids* **1997**, *13*, 131−139.
(67) Wronski, M. *J. Chromatogr., A* **1997**, *772*, 19−25.

In addition to controlling the extent of self-assembly, this difference in pK_a's may also be used to drive ligand-component substitution reactions, in fashion similar to what we have shown in mononuclear systems.[36] When sulfanilic acid (1.2 equiv per incorporated amine) was added to a solution of helicate incorporating amine **a**, **b**, **c**, or **e**, the aliphatic amine was quantitatively displaced within 2 h, as shown in eq 2. The



difference in pK_a values thus favored the displacement of the protonated form of the weaker acid (aliphatic ammonium ion) and the incorporation of the deprotonated form of the stronger acid (sulfanilic acid) to form $\mathbf{1}^{2-}$.

Conclusion

In summary, we have developed a set of "selection rules" granting a degree of control over the self-assembly and ligand-component exchange of a set of bis-Cu^I double-helicate complexes. These rules are based upon steric, charge, and solvent effects, as well as upon pH. The use of water as a reaction solvent has also been shown to be particularly advantageous, which could be seen as counterintuitive for copper(I)/imine based structures. In the present study water has allowed for the synthesis of a wider range of structures, and elsewhere it has been shown that more highly charged assemblies[13,68] may be generated in water than in other solvents. Water is also the necessary solvent for interfacing metalloorganic species with biological systems.[69,70] The exploration and development of the assembly and reassembly rules detailed herein are currently allowing us to build up larger and more complex structures, as well as to transform these structures using ligand-component exchange.

Experimental Section

All manipulations were carried out under argon or dinitrogen using degassed solvents. Starting materials of the highest commercially available purity were used as received; 1,10-phenanthroline-2,9-dicarboxaldehyde[38] and 1-methyl-4-aminopyridinium triflate (amine **h** in Chart 1)[71] were prepared according to literature procedures.

NMR Studies of Helicate and Ligand Formation. For each of the amines listed in Chart 1, amine **a**−**h** (0.050 mmol), 1,10-phenanthroline-2,9-dicarboxaldehyde (0.025 mmol, 0.0066 g), and $Cu(NCMe)_4BF_4$ (0.025 mmol, 0.0079 g,) were loaded into an NMR tube with a Teflon screw cap. Deuterium oxide or acetonitrile-d_3 (0.5 mL) was then added, and the tube's atmosphere was purged of dioxygen with three evacuation/argon purge cycles. The mixture was then sonicated until all reagents dissolved, or for 12 h if dissolution was incomplete. Experiments in which helicate formation was observed were repeated without copper to determine the extent of ligand formation in its absence.

Preparative Synthesis of $Na^+_2\mathbf{1}^{2-}$. To a 100 mL Schlenk flask was added 1,10-phenanthroline-2,9-dicarboxaldehyde (0.0197 g, 0.0834 mmol), sulfanilic acid (0.0288 g, 0.166 mmol), copper(I) oxide (0.0059 g, 0.041 mmol), and sodium bicarbonate (0.0069 g, 0.082 mmol). A magnetic stir bar was added and the flask was sealed. The atmosphere was purified of dioxygen by three evacuation/argon fill cycles. Water (16 mL) was then added, causing gas evolution and development of a green color. Once gas evolution had ceased, the flask was sealed and the reaction was allowed to stir overnight at room temperature. Volatiles were then removed under dynamic vacuum, giving an isolated yield of 0.051 g (98%) of green microcrystalline product, which was pure by NMR. ^{1}H NMR (500 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 1.24 ppm as internal standard): $\delta = 8.98$ (s, 4 H, imine), 8.46 (d, $J = 8.2$ Hz, 4 H, 4,7-phenanthroline), 8.20 (d, $J = 8.2$ Hz, 4 H, 3,8-phenanthroline), 7.69 (s, 4 H, 5,6-phenanthroline), 6.92 (d, $J = 8.3$ Hz, 8 H, phenylene), 6.13 (d, $J = 8.3$ Hz, 8 H, phenylene). ^{13}C NMR (125.77 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 30.29 ppm as internal standard): $\delta = 159.5$, 148.6, 146.7, 142.8, 140.8, 138.4, 133.1, 129.2, 127.5, 126.6, 121.8. ESI-MS: $m/z = -608.1$ ($\mathbf{1}^{2-}$), −384.7 ($\mathbf{1}^{2-}$ lacking one Cu^+), −272.4 (metal-free imine ligand of $\mathbf{1}^{2-}$).

Synthesis of $\mathbf{2}^{2+}(BF_4^-)_2$. Into an NMR tube with a Teflon screw cap was added 1,10-phenanthroline-2,9-dicarboxaldehyde (0.0105 g, 0.0444 mmol), 2-aminoethanol (0.0054 g, 0.0884 mmol), copper(I) tetrakis(acetonitrile) tetrafluoroborate (0.0139 g, 0.0442 mmol), and deuterium oxide (0.5 mL). The tube's atmosphere was purged of dioxygen with three evacuation/argon purge cycles. Crystals began to form spontaneously from the dark green solution after 1 h. No side products were observed in the NMR spectra of this compound. ^{1}H NMR (400 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 1.24 ppm as internal standard; peak assignments are consistent with COSY and NOESY spectra): $\delta = 8.81$ (d, $J = 8.2$ Hz, 4 H, 4,7-phenanthroline), 8.66 (s, 4 H, imine), 8.24 (s, 4 H, 5,6-phenanthroline), 8.19 (d, $J = 8.2$ Hz, 4 H, 3,8-phenanthroline), 3.19 (m, 4 H, NCH_2CH_2OH), 2.85 (m, 4 H, NCH_2CH_2OH), 2.52 (m, 4 H, NCH_2CH_2OH), 2.03 (m, 4 H, NCH_2CH_2OH). ^{13}C NMR (100.62 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 30.29 ppm as internal standard): $\delta = 163.4$, 149.9, 141.8, 138.8, 133.2, 129.2, 126.7, 60.6, 60.5. ESI-MS: $m/z = 385.3$ ($\mathbf{2}^{2+}$), 707.2 ($\mathbf{2}^{2+}$ lacking one Cu^+).

Preparative Synthesis of $Na^+_2\mathbf{3}^{2-}$. The helicate complex $Na^+_2\mathbf{3}^{2-}$ was obtained in 97% yield by the same procedure as used in the case of $\mathbf{1}^{2-}$, using taurine in place of sulfanilic acid. ^{1}H NMR (500 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 1.24 ppm as internal standard; peak assignments are consistent with COSY and NOESY spectra): $\delta = 8.84$ (d, $J = 8.2$ Hz, 4 H, 4,7-phenanthroline), 8.74 (s, 4 H, imine), 8.24 (s, 4 H, 5,6-phenanthroline), 8.22 (d, $J = 8.2$ Hz, 4 H, 3,8-phenanthroline), 3.45 (m, 4 H, NCH_2CH_2S), 2.29 (m, 4 H, NCH_2CH_2S), 2.18 (m, 4 H, NCH_2CH_2S), 1.67 (m, 4 H, NCH_2CH_2S). ^{13}C NMR (125.77 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 30.29 ppm as internal standard): $\delta = 163.5$, 149.7, 141.6, 139.2, 133.8, 129.7, 127.1, 54.2, 50.6. ESI-MS: $m/z = -511.2$ ($\mathbf{3}^{2-}$), −224.4 (imine ligand of $\mathbf{3}^{2-}$).

X-ray Crystal Structure of $\mathbf{1}^{2-}$. Single crystals suitable for X-ray diffraction were obtained through diffusion of an aqueous solution of $Na^+_2\mathbf{1}^{2-}$ into an aqueous solution of $Ba(ClO_4)_2$. $[Cu_2(C_{26}H_{12}N_4O_6S_2)_2]^{2-}\cdot(ClO_4^-)_2\cdot Ba^{2+}_2\cdot(H_2O)_{13}$; $M_r = 1924.1$; $\mu = 2.062$ mm^{-1}, $d_x = 1.882$ g·cm^{-3}, monoclinic, $P2_1/c$, $Z = 4$, $a = 18.6339(16)$, $b = 25.6027(14)$, $c = 14.4414(11)$ Å, $\beta = 99.762(10)°$, $U = 6798.9(9)$ Å^3. Cell dimensions and intensities were measured at 200 K on a Stoe IPDS diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.710\,73$ Å), 48 564 measured reflections, 13 136 unique reflections of which 8088 were observable ($|F_o| > 4\,\sigma\,(F_o)$); R_{int} for 34 786 equivalent reflections 0.060. Data were corrected for Lorentz and polarization effects and for absorption (T_{min}, $T_{max} = 0.5868$, 0.8933).

(68) Bennett, M. V.; Beauvais, L. G.; Shores, M. P.; Long, J. R. *J. Am. Chem. Soc.* **2001**, *123*, 8022−8032.
(69) Meistermann, I.; Moreno, V.; Prieto, M. J.; Moldrheim, E.; Sletten, E.; Khalid, S.; Rodger, P. M.; Peberdy, J. C.; Isaac, C. J.; Rodger, A.; Hannon, M. J. *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 5069−5074.
(70) Junicke, H.; Hart, J. R.; Kisko, J.; Glebov, O.; Kirsch, I. R.; Barton, J. K. *Proc. Natl. Acad. Sci. U. S. A.* **2003**, *100*, 3737−3742.
(71) Abbotto, A.; Bradamante, S.; Pagani, G. A. *J. Org. Chem.* **2001**, *66*, 8883−8892.

The structure was solved by direct methods (SIR97);[72] all other calculations were performed with the XTAL system[73] and ORTEP[74] programs. Full-matrix least-squares refinement based on F using weight of $1/(\sigma^2(F_o) + 0.0002(F_o^2))$ gave final values $R = 0.040$, $\omega R = 0.038$, and $S = 1.12(1)$ for 928 variables and 8336 contributing reflections. The maximum Δ/σ on the last cycle was 0.11×10^{-2}. Hydrogen atoms of the complex were placed in calculated positions. Hydrogen atoms of the water molecules were refined with restraints on bond lengths and angles and blocked during the last cycles.

X-ray Crystal Structure of $\mathbf{2}^{2+}$. Single crystals suitable for X-ray diffraction crystallized spontaneously from the reaction solution. $[Cu_2(C_{18}H_{18}N_4O_2)_2]^{2+}\cdot(BF_4^-)_2\cdot(H_2O)_4$; $M_r = 1017.6$; $\mu = 1.104$ mm^{-1}, $d_x = 1.602$ g·cm^{-3}, monoclinic, $P2_1/n$, $Z = 4$, $a = 12.5079(7)$, $b = 18.8569(12)$, $c = 17.9012(9)$ Å, $\beta = 92.200(6)°$, $U = 4219.1(4)$ Å^3. Cell dimensions and intensities were measured at 200 K on a Stoe IPDS diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.710\,73$ Å), 43 005 measured reflections, 8608 unique reflections of which 3967 were observable ($|F_o| > 4\sigma(F_o)$); R_{int} for 33 718 equivalent reflections 0.083. Data were corrected for Lorentz and polarization effects and for absorption (T_{min}, $T_{max} = 0.8161$, 0.8819). The structure was solved by direct methods (SIR97); [72] all other calculations were performed with the XTAL system[73] and ORTEP[74] programs. Full-matrix least-squares refinement based on F using weight of $1/(\sigma^2(F_o) + 0.00015(F_o^2))$ gave final values $R = 0.033$, $\omega R = 0.032$, and $S = 1.22(1)$ for 593 variables and 4351 contributing reflections. The maximum Δ/σ on the last cycle was 0.56×10^{-2}. One of the BF_4 anions showed disorder, which was modeled as two sets of four fluorine atoms (with occupancies of 0.60 and 0.40, respectively) around a single boron, refined with restrictions on the bond lengths and angles. The hydrogen atoms present on the hydroxyl groups and water molecules were observed and refined with restraints on bond lengths and angles and blocked during the last cycles; other hydrogen atoms were placed in calculated positions.

Full structural details for $\mathbf{1}^{2-}$ and $\mathbf{2}^{2+}$ are included in the Supporting Information as CIF files, which have also been deposited as CCDC-238838 and CCDC-242824. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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Supporting Information Available: CIF files for the structures of $\mathbf{1}^{2-}$ and $\mathbf{2}^{2+}$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(72) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115−119.
(73) Hall, S. R.; Flack, H. D.; Stewart, J. M. *Xtal 3.2 User's Manual*; Universities of Western Australia at Crawley, and Maryland at College Park: 1992.
(74) Johnson, C. K. *ORTEP II*; Report ORNL-5138; ORNL: Oak Ridge, TN, 1976.