

Adaptive Self-Assembly: Environment-Induced Formation and Reversible Switching of Polynuclear Metallocyclophanes

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Abstract: Ligand **3** has been shown to self-assemble under coordination of copper(II) cations in a 1:1 ratio in acetonitrile to give equilibrating mixtures of a [2 × 2] grid-type tetranuclear structure **1** and a hexanuclear architecture of hexagonal shape **2**. The latter was confirmed by determination of the crystal structure which further indicated that **2** contained acetonitrile molecules and hydroxo groups bound to the copper(II) centers, which are therefore five-coordinate. The structures assigned to **1** and **2** were further supported by the spectral (mass, UV/Vis) data. The self-assembly

process is strongly dependent on the conditions of the medium. An increase in concentration in acetonitrile increases the relative amount of hexamer **2**, which appears to be the favored entity at the highest concentrations that can be reached before precipitation occurs. On the other hand, in nitromethane only the tetranuclear complex **1** was detected by

mass spectrometry. Replacement of nitromethane by acetonitrile and vice versa indicated the reversible switching between a solution containing either **1** alone or an equilibrium mixture of **1** and **2**, respectively. In conclusion, the system described presents several remarkable features: 1) self-assembly with substrate binding, 2) dynamic combinatorial structure generation, and 3) environment-induced structural switching amounting in effect to a process of adaptive self-assembly.

Keywords: adaptive chemistry · copper · metallacycles · N ligands · self-assembly · structural switching · supramolecular chemistry

Introduction

Within the field of supramolecular chemistry, metal-ion-directed self-assembly provides one of the most direct methods of access to functionally complex molecular and nanomolecular architectures.^[1] This approach has enabled the successful generation of a wide range of inorganic supramolecular structures^[2] such as helicates,^[3] grids,^[4] ladders,^[5] cages,^[6] circular helicates and rings,^[7] rotaxanes,^[8a] pseudo-rotaxane racks,^[8b-d] and catenanes,^[9] in which the metal ions are positioned with a high degree of compositional and spatial organisation.

Supramolecular architectures incorporating arrays of metal ions of precisely defined position and nuclearity are expected to exhibit a wide variety of physicochemical properties such as, for example, redox, magnetic, catalytic, photochemical, optical, and mechanical functions.^[8a, 10] They therefore repre-

sent especially attractive synthetic targets with respect to future potential applications in materials science and nanotechnology.

In many metal-ion-mediated self-assembling systems, the resulting closed superstructure is formed in a high to quantitative yield and can be isolated and studied as a stable entity under a variety of conditions. However, in some cases, the reaction mixture at thermodynamic equilibrium may consist of a distribution of slowly exchanging products, which may also be accompanied by partially formed or dissociated species. Systems of this type are particularly interesting in that they may be regarded as examples of dynamic/virtual combinatorial libraries (DCL/VCL)^[11] of interconverting self-assembled inorganic structures. All the species present in such a mixture may entirely convert into a single entity upon addition of a suitably shaped and functionalized additive functioning as a template around which the components can self-assemble. This concept emerged from the study of the formation of toroidal helicates,^[11] in which a single tetra-, penta-, or hexanuclear species is expressed from the underlying VCL of equilibrating constituents according to the type of anion present.^[7a,b] Alternatively, expression of a single species from the VCL may be achieved in the solid state through crystallisation.^[12]

Another intriguing possibility concerns self-assembling systems that exist as mixtures of discrete supramolecular

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entities, or as just one of a range of potential species, and allows the reversible and selective alteration of the product distribution by external stimuli. In particular, supramolecular structures designed to reversibly assemble from and disassemble into their components through manipulation of the external environment may possess particularly interesting properties, such as the reversible inclusion of guest species and the capability to adapt to changes in the medium.^[13]

Towards this goal, we herein describe the metal-ion-mediated self-assembly of a mixture of two metallocyclophanes, tetrameric $[2 \times 2]$ grid **1** and hexameric hexagonal box **2**, that are made up of copper (II) ions and the rigid ditopic ligand **3** (Scheme 1), as well as their controlled and reversible generation/destruction through alteration of external parameters, that is, by variation in concentration and solvent.

Results and Discussion

Ligand synthesis: Ligand **3** was designed with a rigid 4,7-phenanthroline bridging unit between the metal-ion-binding sites in order to a) maximise structural preorganisation for self-assembly and b) provide cyclic architectures with walled internal cavities for the purpose of binding guest molecules. The synthesis of **3** was achieved by the route described in Scheme 2. Reaction of 4,7-phenanthroline (**4**) with methyl iodide gave 4,7-dimethyl-4,7-phenanthroline diiodide (**5**; 98%),^[14] which through oxidative hydrolysis with $K_3Fe(CN)_6$ and NaOH yielded the di-*N*-methylphenanthroline dione **6** (68%).^[14] Treatment of **6** with $POBr_3$ gave **3**, 8-dibromo-4,

7-phenanthroline (**7**; 94%), which by Stille cross-coupling with two equivalents of 2-trimethylstannylpyridine (**8**)^[15] and $[Pd(PPh_3)_4]$ catalyst afforded **3** in 80% yield.

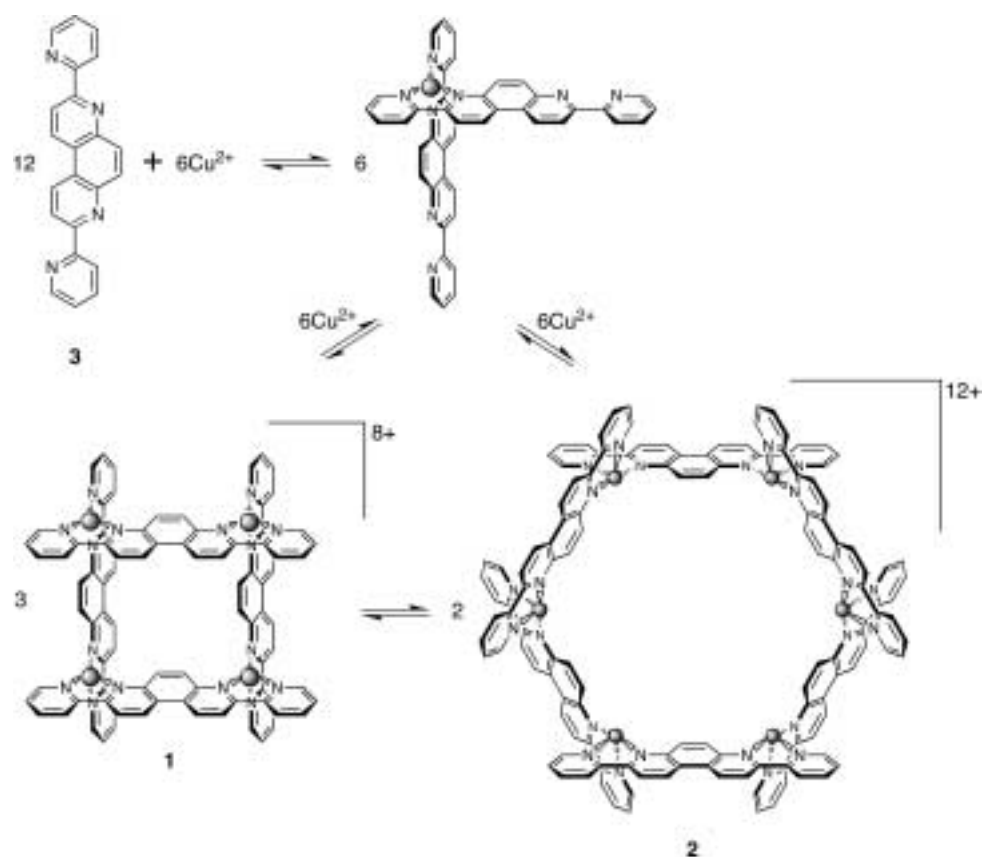
Formation and characterization of Cu^{II} complexes of ligand **3**:

When varying concentrations of a 1:1 stoichiometric mixture of **3** and $Cu(CF_3SO_3)_2$ in acetonitrile were heated, all the suspended ligand dissolved to give green solutions. The ¹H NMR spectra of the reaction mixtures containing paramagnetic Cu^{II} complexes could not be used for structure assignment. However, a progressive dilution study by electrospray mass spectrometry (ES-MS) provided direct evidence about the composition of the species present in solution; the results are illustrated in Figures 1 and 2, and summarised in Table 1. In the Cu^{2+} concentration range of 3.2×10^{-2} – 3.2×10^{-4} mol dm⁻³ in acetonitrile solution, the major cations detected were composed of species that resulted from the sequential loss of triflate anions from a tetrameric complex **1**- $(CF_3SO_3)_8$, with **1** = $[3_4Cu_4]$ and a hexameric species **2**- $(CF_3SO_3)_{12}$, with **2** = $[3_6Cu_6]$. For example, the ES mass spectral bands at m/z 1243, 779, 547, and 407 originated from the respective ions $\{1-(CF_3SO_3)_6\}^{2+}$, $\{1-(CF_3SO_3)_5\}^{3+}$, $\{1-(CF_3SO_3)_4\}^{4+}$, and $\{1-(CF_3SO_3)_3\}^{5+}$, and those at m/z 1939, 1243, 895, 686, and 547 from the ions $\{2-(CF_3SO_3)_{10}\}^{2+}$, $\{2-(CF_3SO_3)_9\}^{3+}$, $\{2-(CF_3SO_3)_8\}^{4+}$, $\{2-(CF_3SO_3)_7\}^{5+}$, and $\{2-(CF_3SO_3)_6\}^{6+}$. Smaller amounts of the ions $\{[Cu_3](CF_3SO_3)\}^+$ (m/z 881) and $\{Cu_3\}^{2+}$ (m/z 366) were also present over the 3.2×10^{-2} – 3.2×10^{-4} mol dm⁻³ $[Cu^{2+}]$ range, indicating that **1**- $(CF_3SO_3)_8$ and **2**- $(CF_3SO_3)_{12}$ coexist in equilibrium with the mononuclear dissociated species $[Cu_3](CF_3SO_3)_2$.^[16] This result suggests that $[Cu_3](CF_3SO_3)_2$ may exist as the most stable and dominant lower molecular mass entity involved in the formation and dissociation of **1**- $(CF_3SO_3)_8$ and **2**- $(CF_3SO_3)_{12}$. This conclusion was further supported by the fact that peaks assignable to ions arising through counterion loss from di-, tri-, and pentanuclear intermediates are absent on all spectra recorded.

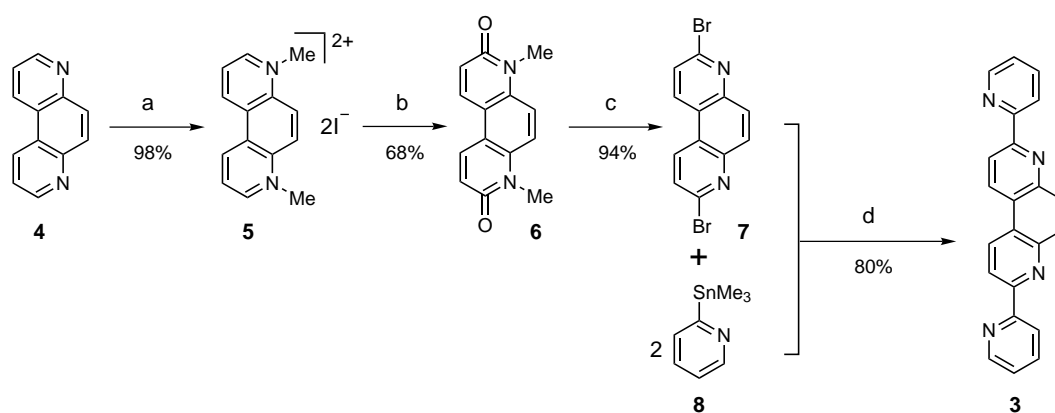
Significantly, dilution of the solution from $[Cu^{2+}] = 3.2 \times 10^{-4}$ to 3.2×10^{-5} mol dm⁻³, resulted in a dramatic change in the distribution of observed cations. All ES-MS peaks corresponding to ions generated by successive loss of triflate from **1**- $(CF_3SO_3)_8$ and **2**- $(CF_3SO_3)_{12}$ completely disappeared from the spectrum; instead it contained ions produced from the mononuclear $[Cu_3](CF_3SO_3)_2$ as the major species. The self-assembly of the complex cations **1** and **2** in acetonitrile solution is, therefore, concentration dependent, with the onset of formation occurring over a rather narrow $[Cu^{2+}]$ range of 3.2×10^{-4} – 3.2×10^{-5} mol dm⁻³.

Comparison of the ES-MS relative peak intensities (Table 1) revealed further overall trends. For example, ions derived from the tetranuclear species **1**- $(CF_3SO_3)_8$ which first appear at $[Cu^{2+}] = 3.2 \times 10^{-4}$ mol dm⁻³ increase in relative intensity upon increasing the $[Cu^{2+}]$ to 3.2×10^{-3} mol dm⁻³, then decrease in intensity upon further increase in $[Cu^{2+}]$ to 3.2×10^{-2} mol dm⁻³. However, ions originating from the hexanuclear **2**- $(CF_3SO_3)_{12}$ steadily increase in relative intensity upon increasing the $[Cu^{2+}]$ from 3.2×10^{-4} – 3.2×10^{-2} mol dm⁻³. These results suggest that the self-assembled tetramer **1** is formed in preference to the hexamer **2** at lower

Abstract in French: Le ligand **3** donne lieu à l'autoassemblage par coordination d'ions cuivre(II) en solution 1:1 dans l'acétonitrile, à des mélanges en équilibre d'une espèce tétranucléaire de type grille $[2 \times 2]$, **1** et d'une architecture hexanucléaire **2** de forme hexagonale. Cette dernière a été confirmée par détermination de la structure cristalline, qui a de plus montré qu'elle contient des molécules d'acétonitrile et des groupes hydroxo liés aux cations cuivre(II) qui de ce fait présentent une pentacoordination. Les structures attribuées à **1** et **2** sont en accord avec les propriétés spectrales (masse, UV/Vis) qu'elles présentent. Le processus d'autoassemblage dépend fortement du milieu. Une augmentation de concentration en solution dans l'acétonitrile donne lieu à une augmentation de la proportion d'hexamère **2**, qui est apparemment l'espèce favorisée aux concentrations les plus élevées que l'on peut atteindre avant précipitation. D'un autre côté, en solution dans le nitrométhane seul le complexe **1** a été détecté par spectrométrie de masse. Le remplacement du nitrométhane par l'acétonitrile et l'opération inverse donnent lieu à une interconversion réversible entre, respectivement, une solution contenant uniquement **1** et un mélange équilibré de **1** et **2**. En conclusion, le système décrit ici présente plusieurs caractéristiques remarquables qui résident dans: 1) l'autoassemblage avec fixation de substrats; 2) la génération de structures de façon dynamique et combinatoire; 3) une commutation de différentes structures induite par l'environnement, qui représente de fait un processus d'autoassemblage adaptatif.



Scheme 1. Switchable self-assembly of the $[2 \times 2]$ grid **1** and the hexameric circular complex **2** from ditopic ligand **3** and Cu^{2+} ions in acetonitrile solution (see text).



Scheme 2. Synthetic route to the ditopic ligand 3,8-bis-(2-pyridyl)-4,7-phenanthroline **3**. a) excess MeI, 120°C ; b) aq. $\text{K}_3\text{Fe}(\text{CN})_6 + \text{aq. OH}^-$; c) POBr_3 , 180°C ; d) $[\text{Pd}(\text{PPh}_3)_4]$, toluene, 140°C .

$[\text{Cu}^{2+}]$, but is increasingly converted into the hexamer **2** at higher $[\text{Cu}^{2+}]$. The hexamer **2** therefore appears to be the most stable self-assembled entity present at high $[\text{Cu}^{2+}]$. The $[\text{Cu}^{2+}]$ of $3.2 \times 10^{-2} \text{ mol dm}^{-3}$ marks the upper concentration limit of the 1:1 $\text{Cu}^{2+}/\mathbf{3}$ system in acetonitrile, above which precipitation of a microcrystalline green solid from the solution occurs. This solid is unlikely to be of a polymeric nature, as peaks assignable to cyclic and linear oligomers of greater molecular mass than $\mathbf{2} \cdot (\text{CF}_3\text{SO}_3)_{12}$ are completely absent on all recorded spectra. Rather, it may consist of $\mathbf{1} \cdot (\text{CF}_3\text{SO}_3)_8$, $\mathbf{2} \cdot (\text{CF}_3\text{SO}_3)_{12}$, or a mixture of varying proportions of both species.

Additional support for the formulation of cations **1** and **2** as the tetranuclear grid-type and hexanuclear-ring architectures, respectively, was afforded by comparative UV-visible studies with mononuclear Cu^{2+} complexes of differing pyridine donor set coordination geometries (Table 2).^[17–20] Solutions of a 1:1 mixture of $\mathbf{3}/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ gave characteristic spectra, which showed two absorption envelopes at 680 and 804 nm in acetonitrile and at 700 and 789 nm in nitromethane. UV-visible spectroscopic measurements and theoretical studies on tetrahedrally coordinated Cu^{2+} complexes with substituted bipyridine-type ligands have shown that they are characterized by low-energy absorptions in the 700–1000 nm domain.^[17]

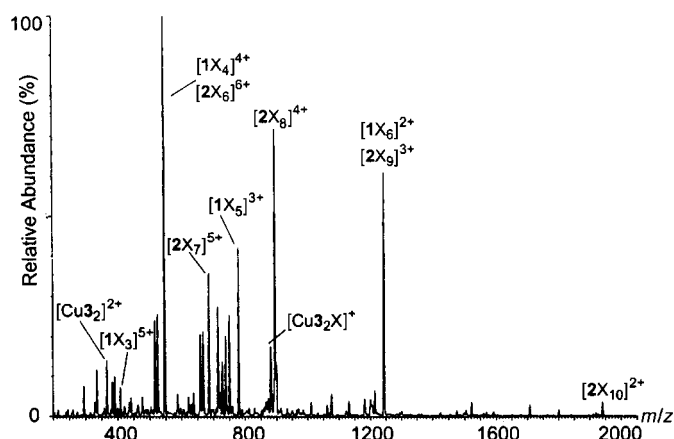


Figure 1. Electrospray mass spectrum of the $\text{CuX}_2/3$ system in acetonitrile; $[\text{Cu}^{2+}] = 3.2 \times 10^{-2} \text{ mol dm}^{-3}$, $\text{X} = \text{CF}_3\text{SO}_3^-$.

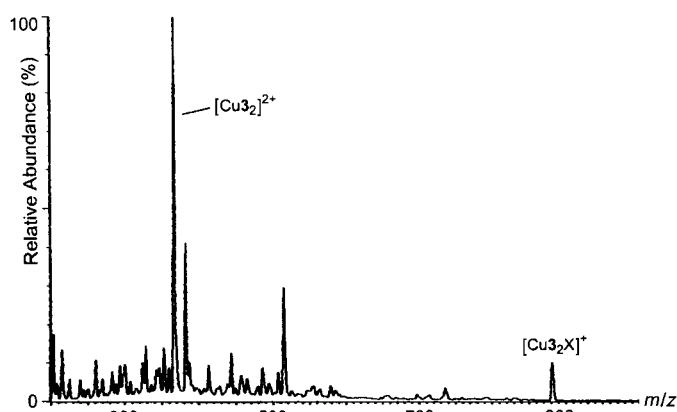


Figure 2. Electrospray mass spectrum of the $\text{CuX}_2/3$ system in acetonitrile; $[\text{Cu}^{2+}] = 3.2 \times 10^{-5} \text{ mol dm}^{-3}$, $\text{X} = \text{CF}_3\text{SO}_3^-$.

The spectra of the five-coordinate $[\text{Cu}(\text{bipy})(\text{terpy})]^{2+}$,^[18] as well as the octahedral $[\text{Cu}(\text{terpy})_2]^{2+}$ ^[19,20] and $[\text{Cu}(\text{bipy})_3]^{2+}$ ^[20] complexes (bipy: 2,2'-bipyridine; terpy: 2,2':6',2''-terpyridine) each show spectra with absorptions below 690 nm. On the other hand, the complex $[\text{Cu}(\text{dmb})_2]^{2+}$ (dmb: 6,6'-dimethyl-2,2'-bipyridine), which has an enforced four coordination by the pyridine nitrogens, gives a spectrum with a single absorption envelope at about 730 nm.^[20] The spectra of the 1:1 mixtures of $3/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ are therefore more comparable to that of the tetrahedral $[\text{Cu}(\text{dmb})_2]^{2+}$ complex in terms of the energies of the absorption maxima, and suggests that the Cu^{2+} ions are coordinated by four rather than five or six pyridine nitrogens, which is consistent with structures **1** and **2**.

Redissolution of the green solid in hot acetonitrile and successive dilution to the concentrations shown in Table 1

yielded solutions whose ES mass spectra displayed cation distributions and relative intensities identical to those of the parent solutions prior to solid formation. Conversely, reconcentration of the $3.2 \times 10^{-5} \text{ mol dm}^{-3}$ solution to the concentrations indicated in Table 1 resulted in regeneration of identical mass spectra to those obtained upon dilution of the parent $3.2 \times 10^{-2} \text{ mol dm}^{-3}$ solution generated upon dissolution of the green solid.

The formation of the tetramer **1** and hexamer **2** is, therefore, reversible in acetonitrile solution and represents an example of environment-switchable self-assembly in which the supramolecular products can be generated or destroyed simply by changing the reaction concentration from 3.2×10^{-4} to $3.2 \times 10^{-5} \text{ mol dm}^{-3}$ and vice versa.

Structure of the complexes of 3 with Cu^{II} : The ES-MS data indicate that the two main species present in 1:1 solutions of **3** and Cu^{II} in acetonitrile are oligomers $[\text{3}_n\text{Cu}^{\text{II}}_n]$ with $n = 4$ and 6 for **1** and **2**, respectively. Since these are discrete entities, they may be expected to be closed cyclic structures in which all ligand binding sites are occupied, according to the principle of maximal site occupation,^[21] and which present no “dangling ends”.

Consequently one may attribute to these self-assembled species the architectures of a tetranuclear $[2 \times 2]$ Cu^{II}_4 grid (**1**) and of a hexanuclear Cu^{II}_6 metallomacrocyclic (**2**) (Scheme 1). The latter was confirmed by crystal structure determination (see below).

Medium effect on the self-assembly of 1 and 2: In order to further explore the effects of environmental changes upon the $\text{Cu}^{2+}/3$ system, the reaction between the 1:1 mixture of $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ and **3** was conducted in propionitrile, butyronitrile, and nitromethane. In the first two solvents, the solution immediately assumed a brown coloration with the concomitant precipitation of a brown solid. An ES-MS analysis of these mixtures failed to provide any evidence for the formation of either **1** or **2**. Instead, the spectra consisted only of a complex series of unassignable peaks. The brown coloration of the reaction mixtures suggests that a redox process occurred in which the Cu^{2+} was reduced to Cu^+ , and that the latter ion reacted with **3** to give insoluble coordination polymers. A mixture of $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ and **3** at 1:1 ratio in nitromethane yielded a green solution, as when the same reaction was conducted in acetonitrile, from which a green microcrystalline solid precipitated upon concentration. ES-MS of this solution at a $[\text{Cu}^{2+}]$ of $3.2 \times 10^{-3} \text{ mol dm}^{-3}$ showed a particularly clean spectrum comprising peaks derived only from **1**- $(\text{CF}_3\text{SO}_3)_8$ through counterion loss (Figure 3). Remov-

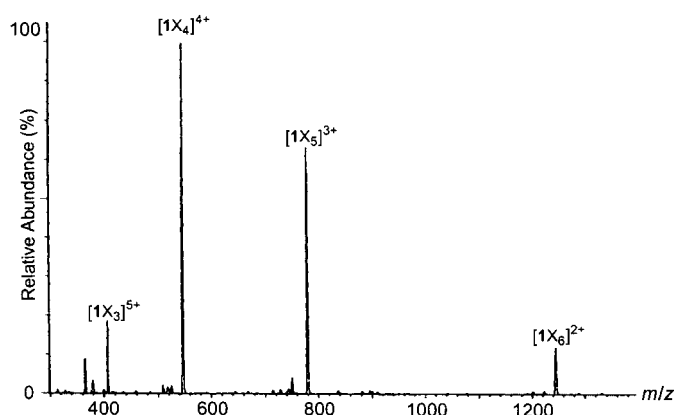
Table 1. ES mass spectra data showing concentration-dependent variation in % relative intensity of the major cationic species present in 1:1 solutions of **3** and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ in acetonitrile; the m/z ratio is indicated below each cation in parentheses; **1** = $[\text{Cu}_4\text{3}_4]^{8+}$, **2** = $[\text{Cu}_6\text{3}_6]^{12+}$, $\text{X} = \text{CF}_3\text{SO}_3^-$.

Conc. Cu^{2+} [mol dm^{-3}]	$[\text{Cu}_3\text{2}]^{2+}$ (366)	$[\text{1X}_3]^{5+}$ (407)	$[\text{1X}_4]^{4+}; [\text{2X}_6]^{6+}$ (547)	$[\text{2X}_7]^{5+}$ (686)	$[\text{1X}_5]^{3+}$ (779)	$[\text{Cu}_3\text{2X}]^+$ (881)	$[\text{2X}_8]^{4+}$ (895)	$[\text{1X}_6]^{2+}; [\text{2X}_9]^{3+}$ (1243)	$[\text{2X}_{10}]^{2+}$ (1939)
3.2×10^{-2}	14	7	100	36	42	18	72	61	4
3.2×10^{-3}	17	29	100	21	50	7	25	24	1
3.2×10^{-4}	100	12	85	9	15	23	8	4	0
3.2×10^{-5}	100	0	0	0	0	10	0	0	0

Table 2. Electronic absorption spectral data of Cu²⁺ complexes with pyridine-type donor ligands showing the variation of absorption maxima with the metal ion coordination number.

Coordination number	Complex ^[a]	λ [nm] (ϵ [mol ⁻¹ dm ³ cm ⁻¹])		reference
		MeNO ₂	MeCN	
6	[Cu(bipy) ₃](CF ₃ SO ₃) ₂	675(59)	675(56)	This work ^[c]
6	[Cu(terpy) ₂](CF ₃ SO ₃) ₂	687(63)	687(61)	this work ^[c]
6	[CuPTC](BF ₄) ₂		687(100)	[19]
5	[Cu(bipy)(terpy)](CF ₃ SO ₃) ₂	634(93)	640(85)	this work ^[c]
5	[Cu(bipy)(terpy)](ClO ₄) ₂		636(91)	[18]
5	[Cu ₃ BT](CF ₃ SO ₃) ₆		626(363)	[18]
4	[Cu(dmb) ₂](CF ₃ SO ₃) ₂	734 (129)	726(123)	this work ^[c]
4	[Cu(tmb) ₂](ClO ₄) ₂		740, 1000 ^[b]	[17a]
4	[CuPTC](PF ₆) ₂		670(830)	[17d]
4	[CuPC](ClO ₄) ₂		666(820)	[17c]
4	[Cu(phen) ₂](ClO ₄) ₂		666(820)	[17c]
4	1 -(CF ₃ SO ₃) ₈ + 2 -(CF ₃ SO ₃) ₁₂		680(313), 804(469)	this work ^[c]
4	1 -(CF ₃ SO ₃) ₈	700(375), 789(417)		this work ^[c]

[a] bipy = 2,2'-bipyridine, terpy = 2:2',6':2''-terpyridine, dmb = 6,6'-dimethyl-2,2'-bipyridine, tmb = 4,4',6,6'-tetramethyl-2,2'-bipyridine, phen = 2,9-bis-(p-methoxyphenyl)-1,10-phenanthroline, PC = di(phenanthroline)catechane, PTC = di(phenanthroline)terpyridine)catenane, B = tritopic tris-(bipyridine), T = tritopic tris-(terpyridine). [b] 1:1 H₂O/1,4-dioxane. [c] [Cu²⁺] = 3.2 × 10⁻² mol dm⁻³.

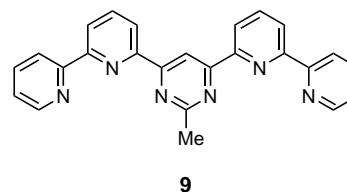
Figure 3. Electrospray mass spectrum of the CuX₂/3 system in nitromethane; [Cu²⁺] = 3.2 × 10⁻³ mol dm⁻³, X = CF₃SO₃⁻.

al of solvent under reduced pressure and replacement by an equivalent volume of acetonitrile yielded a green solution whose ES mass spectrum was identical to that of 3.2 × 10⁻³ mol dm⁻³ [Cu²⁺] solution in Table 1, and which showed that the hexamer **2** had been regenerated. Replacement of the acetonitrile by nitromethane resulted in reformation of the initial ES mass spectrum in which **1**-(CF₃SO₃)₈ was the only species present in solution. These results show that the self-assembly of the hexamer **2** is solvent-environment dependent and can be reversibly switched on or off depending upon whether the surrounding medium is acetonitrile or nitromethane.

The influence of chloride counterions was also investigated in order to explore the possible existence of anion templating effects upon the self-assembly of **1** and **2**, as in the case of circular helicates^[7a,b] However, mixing CuCl₂ and **3** in 1:1 ratio in acetonitrile or nitromethane resulted only in the formation of sparingly soluble coordination polymers. Insoluble solids were also the only products obtainable upon addition of varying proportions of N(*n*Bu)₄Cl to solutions of Cu(CF₃SO₃)₂ and **3** in acetonitrile or nitromethane.

Previous investigations into ligand-recognition fidelity within helicate mixtures demonstrated that in the presence of the correct stoichiometric ratio of metal ions, helicates form only from identical ligand strands, which contain the same number of 2,2'-bipyridine complexation subunits, and metal ions of tetrahedral or octahedral coordination geometry.^[21] On the other hand, a mixture of a tris-bipyridine (L₁) and of a tris-terpyridine (L₂) ligand selectively formed a mixed-ligand [Cu₃L₁L₂]⁶⁺ helicate in the presence of Cu²⁺.^[18] The main contributory factor to this hetero-ligand recognition process is the preference of Cu²⁺ to be five-coordinate with pyridine-

type nitrogen-donor ligands. It was therefore decided to explore the possibility of using the propensity of Cu²⁺ to be five-coordinate as a design principle for the generation of a mixed ligand [2 × 2] grid of type [Cu₄3,9]₂(CF₃SO₃)₈. Accordingly, a mixture **3**, **9**,^[22] and Cu(CF₃SO₃)₂ in a 1:1:2 stoichiometric ratio in acetonitrile resulted in dissolution of the



ligands to give a green solution. Instead of selective formation of the mixed-ligand entity [Cu₄3,9]₂(CF₃SO₃)₈, an ES-MS analysis of the reaction solution indicated the additional presence of a range of species resulting from counterion loss from homoligand products.^[23] Therefore, selective hetero-ligand recognition appears not to be operative in this system; this indicates that, in addition to coordination geometries, the structural features of the ligands play an important role in determining the outcome of the self-assembly process.

Crystal structure of the hexameric complex 2: Layering a 1:1 solution of ligand **3** and Cu₂(CF₃SO₃)₂ in acetonitrile at a [Cu²⁺] of 3 × 10⁻² mol dm⁻³ onto 1,4-dioxane resulted in the development of green prismatic crystals, which were investigated by X-ray crystallography. The crystal structure (Figure 4) revealed that the selected crystal contained the cyclic species formulated as **2**. The cation **2** is shaped into a beautiful hexameric ring composed of six Cu²⁺ ions and six ligand **3** components. The ligand **3** units are positioned alternately above and below the mean plane through the six Cu²⁺ ions to give an overall arrangement in which three are above and three below. The Cu²⁺ ions are situated in the form of a

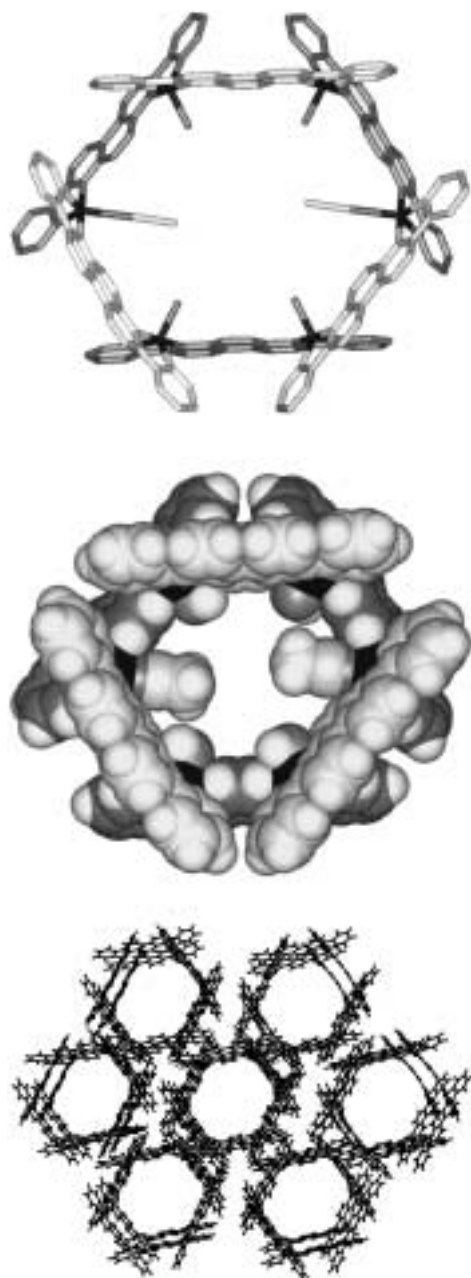


Figure 4. Crystal structure of the hexameric complex **2**. Top: stick representation. Center: space-filling representation. Bottom: representation of the packing perpendicular to the plane of the hexagon.

hexagonal ring, with average distances of 7.8 Å between the metals along each ligand axis. Cation **2** is, however, not a perfect hexagon, but has a C_2 axis perpendicular to the plane of the copper ions. Two Cu^{2+} ions are separated by a greater distance (15.678 Å) than the remaining two pairs of Cu^{2+} ions (14.784 Å). This feature also gives rise to two sets of inner angles between the mean planes of three consecutive ligands **3** (two angles of 106.1° and four angles of 120.0°). The Cu–N bond lengths and N–Cu–N (intraligand) and N–Cu–N (interligand) angles fall within the ranges 1.995–2.182 Å, 80.6–81.9°, and 97.2–121.0°, respectively. The cyclic cation **2** possesses a large hexagonal-box-shaped cavity of 15.7–16.2 Å internal diameter and 9.1 Å depth, in which are

included six guest species, two acetonitrile solvent molecules coordinated to two diagonally located Cu^{2+} ions, and four hydroxo anions (one of which is at 70% occupancy and shared with a triflate at 30% occupancy) coordinated to the remaining four Cu^{2+} ions.

All Cu^{2+} ions therefore display a distorted five-coordinate geometry. The overall external dimensions of the hexamer **2** are 21.6 Å (diameter) and 9.1 Å (height), which places it within the nanostructural domain. In the crystal lattice the cations pack into parallel layers, which are alternately stratified above each other in an ABAB arrangement such that the outer edges of the hexagons between each layer are within van der Waals contact. The alternate alignment of the cation layers results in the development of continual tubular voids penetrating the crystal lattice as viewed down the central axes of the **2** cations. Triflate anions, acetonitrile, methanol, tetrahydrofuran, and 1, 4-dioxane solvent molecules fill the interstices between the cations so that all available void space is filled.

Discussion

Self-assembly and dynamic combinatorial libraries: The reaction of suitable linear ligands, which contain several subunits, with metal ions can in principle yield a set of interconverting complexes, representing a dynamic combinatorial library.^[11] In particular, a dynamic library of cyclic oligomeric complexes can thus be generated, as occurs for circular helicates^[7a,b] (see also Figure 4 in ref. [11]). One or several of the constituent complexes may be expressed or amplified depending on the conditions. Thus, for example, the anion-dependent formation of circular helicates,^[7a,b] the process of crystallisation,^[12] and the presence of a suitable substrate^[24] have been shown to lead to the preferential expression of a specific member of the equilibrating set of complexes.

In the present case, 1:1 stoichiometric combinations of $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ and the rigidly preorganised ditopic ligand **3** react in acetonitrile to give equilibrium mixtures that contain the tetranuclear $[2 \times 2]$ grid **1** and the hexameric ring **2**. The self-assembled cations **1** and **2** were formulated on the basis of ES mass spectrometric measurements, the spectra of which were found to be free of accompanying pentameric, heptameric, and higher oligomers as well as of polymeric species. The structure of cation **2** was unambiguously characterised by X-ray crystallography, which showed it to be that of a cyclic hexamer composed of six **3** ligands cemented together by a hexagonal array of six Cu^{2+} ions. The cavity of **2** is large enough to potentially incorporate a variety of small molecules, and indeed contains two acetonitrile molecules and four hydroxo anions each coordinated to a copper ion within the wall of the hexagon. Since the mass spectral data (see above) did not indicate the presence of bound hydroxo groups, these were probably introduced in the course of the lengthy crystallization process. When assembled in acetonitrile solution, species **2** may be expected to contain in its cavity rather weakly bound acetonitrile molecules and eventually triflate counteranions.^[25] The formation of this multicomponent

entity represents a case of self-assembly of a receptor molecule with simultaneous binding of several substrates, that is, *multiple guest inclusion*.

It is the presence of adequate guests and the dynamic accessibility of the complementary receptor molecule that leads to the expression of the unique entity $[(\mathbf{3})_6(\text{Cu}^{\text{II}})_6(\text{CH}_3\text{CN})_6]^{12+}$. One may note that the cation $\mathbf{2}$ itself is indeed a constituent of a virtual combinatorial library, since it is only potentially available in the system and is brought into existence by the guest species in a multisubstrate molding event.^[11, 26]

The ES-MS data also showed cations $\mathbf{1}$ and $\mathbf{2}$ to coexist with varying quantities of the mononuclear species $(\text{Cu}_3\text{O})\text{-(CF}_3\text{SO}_3)_2$, which presumably acts as a dominant intermediate along the formation/dissociation and interconversion pathways of the two cyclic architectures (Scheme 1).

Adaptive self-assembly and switchable superstructures: Of special interest is the fact that the interconversion of $\mathbf{1}$ and $\mathbf{2}$ can be reversibly switched by changes in the external environment, that is, by variation of the solvent medium and of the solution concentration. The ES-MS analysis of the relationship between the concentration of the reaction mixture and the product distribution (Table 1) revealed that dilution to $3.2 \times 10^{-5} \text{ mol dm}^{-3}$ in acetonitrile causes destruction of the cations $\mathbf{1}$ and $\mathbf{2}$. However, concentration of the reaction mixture results in regeneration of $\mathbf{1}$ and $\mathbf{2}$ with a preference for the formation of hexamer $\mathbf{2}$ at the high-concentration limit. This process is reversible and can be repeated many times without any apparent change in the overall speciation composition.

More interestingly, the formation of $\mathbf{1}$ and $\mathbf{2}$ can be controlled by the nature of the solvent. Thus, while in nitromethane only $\mathbf{1}$ is present, hexamer $\mathbf{2}$ is generated preferentially to $\mathbf{1}$ when acetonitrile is used. The interconversion is completely reversible on changing solvent.

The solvent-dependent existence of $\mathbf{2}$ may originate from the inclusion of acetonitrile molecules within the cavity of the hexagon, as observed in the crystal structure of the cation. An expansion of the Cu^{2+} coordination polyhedron from four to five upon further binding to an acetonitrile molecule would be expected to result in an angle increase of $>90^\circ$ between the two $\mathbf{3}$ ligands bound to each metal ion. A species of the type $[\text{Cu}_3\text{MeCN}]^{2+}$ would therefore be unable to close into a rectangular entity upon reaction with additional Cu^{2+} and acetonitrile, but may instead assemble into a hexameric structure as the assembly with the least internal strain. On the other hand, the square grid $\mathbf{1}$ is the only cyclic species formed in solution in the absence of suitable coordinating entities (other than $\mathbf{3}$), as is the case in nitromethane. One may speculate whether larger rings or other architectures could be generated in presence of ligand species of other sizes and shapes. Butyronitrile did not lead to any identifiable product, but other units might be more adapted.

In addition to its interest as a structural switching process, the interconversion of $\mathbf{1}$ and $\mathbf{2}$ as a function of medium nature and/or composition has special significance in view the character of adaptation of the system to the environment that it presents.

Conclusion

The 1:1 stoichiometric reaction between $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ and $\mathbf{3}$ in acetonitrile solution affords the tetranuclear grid $\mathbf{1}$ and the hexameric inorganic cyclophane $\mathbf{2}$. The self-assembly of $\mathbf{1}$ and $\mathbf{2}$ can be reversibly switched on and off by imposing external environmental changes upon the system, that is, by changing the nature of the surrounding solvent medium or by varying the concentration of the reagents. This system therefore represents an intriguing example of environmentally switchable metal-ion-mediated self-assembly. Reversible chemical reactions which yield product distributions that can be addressed and manipulated by controlled environmental changes form a particularly interesting category of supramolecular processes. Systems of this type may provide means for the externally controllable uptake, transport, and release of included guest substrates, features of much potential interest, for example, in medicine and materials science. The development of environmentally addressable self-assembling supramolecular architectures such as $\mathbf{1}$ and $\mathbf{2}$ may be considered to represent a step towards *adaptive materials*,^[27] that is, dynamic combinatorial materials responding to environmental pressure. Further investigations into the physicochemical properties of the above and related systems are currently underway in order to gain a deeper understanding of the principles required for the designed generation and control of switchable self-assembly.

The present process thus displays three remarkable features of general interest: 1) self-assembly with substrate binding, 2) dynamic combinatorial diversity with multisubstrate receptor molding, and 3) environment-sensitive behavior resulting in a process of *adaptive self-assembly*. Such systems being instructed, dynamic and combinatorial contribute to the exploration of the emerging field of *adaptive chemistry*.^[27]

Experimental Section

General: ES-MS studies were performed on a VG BioQ triple quadrupole mass spectrometer upgraded in order to obtain Quattro II performance (Micromass, Altrincham, UK). Samples were dissolved in acetonitrile or nitromethane and were continuously infused into the ion source at a flow rate of 6 mL min^{-1} , through a Harvard Model 551111 syringe pump (Harvard Apparatus, South Natick, MA, USA). The extraction cone voltage (Vc) was at 10–20 V to avoid fragmentations. Elemental analyses were performed by the Service de Microanalyse, Institut de Chimie, Université Louis Pasteur.

4,7-N,N-Dimethyl-4,7-phenanthroline-3,8-dione (6): Compound $\mathbf{5}$ (5.00 g , $1.077 \times 10^{-2} \text{ mol}$) was dissolved in hot distilled water (350 ml), and the solution allowed to cool to ambient temperature. Two drops of an aqueous solution of NaOH (3.142 g , $7.86 \times 10^{-2} \text{ mol}$) in distilled water (80 ml) followed by one drop of a solution of $\text{K}_3\text{Fe}(\text{CN})_6$ (16.76 g , $5.09 \times 10^{-2} \text{ mol}$) in distilled water (167 ml) were added alternately to the stirred solution over 1.5 h. The mixture was thereby continually maintained just at an alkaline pH throughout the reaction. A suspended orange-brown solid formed towards the end of the addition. Aqueous NaOH (50 ml of a 20% solution) was then added to precipitate more solid, and the mixture stirred for a further 1.5 h. The solids were isolated by filtration under vacuum, washed with water, and recrystallised from boiling water (40 ml). The product was then further purified by two successive recrystallisations from acetonitrile to give $\mathbf{6}$ (1.75 g ; 68%) as granular yellow crystals. $^1\text{H NMR}$ (CDCl_3 , 400 MHz, 25 °C): $\delta = 8.23$ (d, $^3J_{1,2,10,9} = 9.9 \text{ Hz}$, 2H; H1,10), 7.64 (s, 2H; H5,6), 6.90 (d, $^3J_{2,19,10} = 9.9 \text{ Hz}$, 2H; H2,9), 3.79 (s, 6H; H-Me);

^{13}C NMR (CDCl_3 , 100.6 MHz, 25 °C): δ = 161.5, 135.9, 132.5, 123.6, 117.5, 116.4, 29.9 (Me); EIMS: m/z (%): 240.2 (100); elemental analysis calcd (%) for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2$ (240.2): C 69.99, H 5.03, N 11.66; found C 69.85, H 5.04, N 11.64.

3,8-Dibromo-4,7-phenanthroline (7): POBr_3 (40 g, 0.14 mol), PBr_3 (7.49 g, 2.77×10^{-2} mol), and **6** (1.75 g, 5.18 mol) were weighed into a 100 ml round-bottomed flask fitted with an air condenser and CaCl_2 drying tube. The mixture was then heated in a bath at 180 °C and the viscous dark liquid was magnetically stirred at this temperature for 36 h. After cooling to about 60 °C, the black residue was added to excess ice/water and was vigorously stirred until hydrolysis of the remaining phosphorus halides was complete. Further ice was added, the mixture adjusted to pH 14 by dropwise addition of 20% aqueous NaOH, and stirring continued for 3 h. The precipitated gray solid was isolated by filtration under vacuum, washed with distilled water, air dried, and sublimed under vacuum (210 °C, 2×10^{-6} mm Hg) to yield **7** (2.316 g; 94%) as a cream powder. ^1H NMR ($\text{CDCl}_2\text{CDCl}_2$, 400 MHz, 100 °C): δ = 8.67 (d, $^3J_{1,2;10,9}$ = 8.6 Hz, 2H; H1,10), 8.25 (s, 2H; H5,6), 7.80 (d, $^3J_{2,1;9,10}$ = 8.7 Hz, 2H; H2,9); ^{13}C NMR ($\text{CDCl}_2\text{CDCl}_2$, 100.6 MHz, 100 °C): δ = 148.2, 142.8, 132.7, 132.2, 126.7, 123.6; EIMS: m/z (%): 337.9 (100), 257.0 (39) $[\text{M} - \text{Br}]^+$, 177.0 (79) $[\text{M} - 2\text{Br}]^+$; FAB⁺ HRMS: calcd m/z for $[\text{C}_{12}\text{H}_6\text{N}_2\text{Br}_2]^+$; found: 336.89766 (336.89760).

3,8-Bis-(2-pyridyl)-4,7-phenanthroline (3): Toluene (15 ml) was added by syringe to a mixture of **7** (0.212 g, 6.27×10^{-4} mol), **8** (0.538 g, 2.22×10^{-3} mol), and $[\text{Pd}(\text{PPh}_3)_4]$ (0.059 g, 5.11×10^{-5} mol) under a nitrogen atmosphere, and the mixture refluxed and stirred at 140 °C for 48 h. All solvent was then removed under reduced pressure, and the residue column chromatographed on basic alumina (activity IV), with CHCl_3 as the eluent. The product thus obtained was briefly ultrasonicated in MeOH (15 ml), filtered under vacuum, washed with MeOH and air dried to yield **3** (0.187 g; 89%) as a white fibrous microcrystalline solid. ^1H NMR (CDCl_3 , 500 MHz, 25 °C): δ = 9.05 (d, $^3J_{2,1;9,10}$ = 8.7 Hz, 2H; H2,9 (phenanthroline)), 8.76 (m, 4H; H1,10 (phenanthroline), H6 (pyridine)), 8.71 (dm, $^3J_{3,4}$ = 7.9 Hz, 2H; H3 (pyridine)), 8.33 (s, 2H; H5,6 (phenanthroline)), 7.91 (td, $^3J_{4,3;4,5}$ = 7.5 Hz, $^4J_{4,6}$ = 1.8 Hz, 2H; H4 (pyridine)), 7.38 (qd, $^3J_{5,4}$ = 7.5 Hz, $^3J_{5,6}$ = 4.8 Hz, $^4J_{5,3}$ = 1.2 Hz, 2H; H5 (pyridine)); ^{13}C NMR (CDCl_3 , 125.8 MHz, 25 °C): δ = 154.6, 154.2, 147.5, 145.8, 135.2, 130.7, 129.9, 122.9, 122.4, 120.0, 117.6; FAB⁺ MS: m/z (%): 335.3 (100) $[\text{M}+1]^+$; elemental analysis calcd (%) for $\text{C}_{22}\text{H}_{14}\text{N}_4$ (334.3) C 79.02, H 4.22, N 16.76; found C 78.98, H 4.47, N 16.99.

Generation of the complexes 1-(CF₃SO₃)₈ and 2-(CF₃SO₃)₁₂: Acetonitrile (5 ml) was added to a mixture of **3** (0.0132 g, 3.95×10^{-5} mol) and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ (0.0144 g, 3.98×10^{-5} mol), and the reaction mixture was briefly ultrasonicated and then gently heated to give a grass-green solution. Aliquots of the reaction solution were then concentrated or diluted to the appropriate $[\text{Cu}^{2+}]$ (Table 1). In order to obtain the solid reaction product, the above procedure was repeated and the solution reduced in volume to 2 ml under reduced pressure; 1,4-dioxane was then added dropwise until precipitation was complete. The product was then washed twice with 1,4-dioxane, isolating by centrifugation each time, air dried, and further dried under dynamic vacuum to yield 0.026 g of a microcrystalline green solid which may be composed of **1**-(CF₃SO₃)₈, **2**-(CF₃SO₃)₁₂, or a mixture of both complexes. Elemental analysis calcd (%) for $[\text{Cu}_3](\text{CF}_3\text{SO}_3)_2 \cdot 0.75$ 1,4-dioxane (762.15): C 42.55, H 2.65, N 7.35; found C 42.59, H 2.62, N 7.54.

X-ray crystal structure determination of 2: Green prismatic crystals of **2**, suitable for a single-crystal X-ray diffraction study, were obtained by slow diffusion of a saturated acetonitrile solution of the 1:1 reaction product between **3** and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ into 1,4-dioxane at room temperature. Crystal data: $\text{C}_{132}\text{H}_{84}\text{Cu}_6\text{N}_{24} \cdot 6.6(\text{CF}_3\text{SO}_3)_2$ with the following located counterions $6(\text{CH}_3\text{CN}) \cdot 3.4(\text{OH}^-) \cdot (\text{C}_4\text{H}_8\text{O}) \cdot 1.5(\text{CH}_3\text{OH}) \cdot (\text{C}_4\text{H}_8\text{O}_2)$, $M = 3883.84$, $a = 15.470(3)$, $b = 21.610(4)$, $c = 22.190(4)$ Å, $\alpha = 68.07(3)^\circ$, $\beta = 72.29(3)^\circ$, $\gamma = 69.98(3)^\circ$, $V = 6332(2)$ Å³, $T = 173$ K, space group = $P\bar{1}$, $Z = 2$, $\rho_{\text{calcd}} = 2.030$ g cm⁻³, $\mu(\text{MoK}\alpha) = 1.23$ mm⁻¹, $F(000) = 3941$. Data were collected on a STOE-IPDS diffractometer, $3.82 \leq 2\theta \leq 51.92^\circ$, $\text{MoK}\alpha$ radiation (graphite monochromator). 22898 independent reflections were measured and of these, 14611 were unique ($R_{\text{int}} = 0.052$) with $I > 2\sigma(I)$. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The hydrogen atoms were placed in calculated positions, the isotropic temperature factor was coupled with the U_{eq} from the parent carbon atom. The refinement was by full-matrix least-squares based on F^2 to give $R = 0.0836$, $wR = 0.2478$ with $F > 6\sigma(F_0)$ and $R = 0.1216$, $wR = 0.2773$ with all data for 1365

parameters. The maximum and minimum residual electron densities in the final DF map were 1.366 and -1.155 e Å⁻³. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-141245. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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