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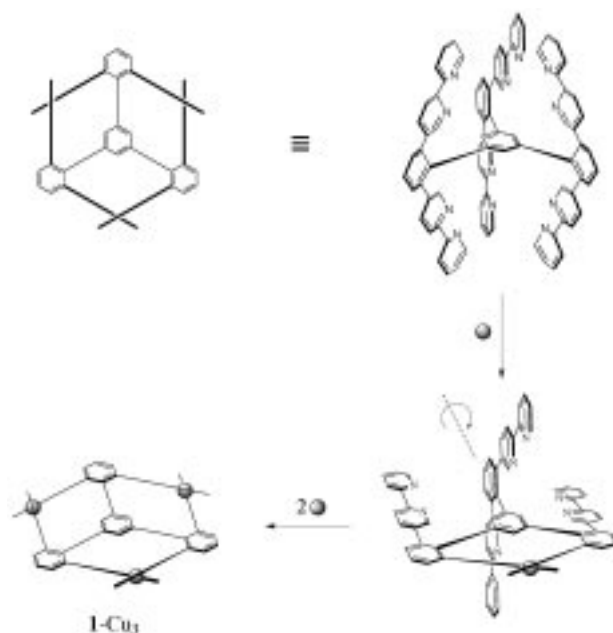
Trinuclear Copper(I)-bipyridine Triskelion: Template/Bascule Control of Coordination Complex Stereochemistry in a Trefoil Knot Precursor**

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Projection of a knotted structure in the plane can be oriented to reveal a principal core “crossing structure” and a periphery of connecting arcs. From that perspective, the retrosynthesis of molecular knots and links can be divided into problems related to the control of a) macrocyclizations and b) stereochemistry of “crossing structures”. Molecular designs that capitalize on symmetry and cooperativity lead to

efficient control of stereochemistry.^[1,2] In the double helicates, the regular helical structure provides cooperative reinforcement for each new metallostereocenter to be of uniform configuration.^[3] The identification of the double helix motif in a representation of the trefoil knot is key to understanding the rational synthesis where stereochemical control of helicity dictates the product identity, chirality, and yield.^[4–9] An alternative representation of the trefoil knot has a D_3 -symmetric core embedded within.^[10] This core is also common to the Borromean link motif.^[11–14] As such, synthesis and stereochemical control of an appropriate D_3 triskelion would provide a new class of stereoregular polynuclear coordination complexes and set the path to high-symmetry molecular knots and links.

Templating is a tried-and-true method for regulating the juxtaposition of molecular substructures.^[15–20] A bascule mechanism pivots about the midpoint of a beam and couples the motion of the two ends such that as one end raises the other lowers.^[21] Combining a tripodal template with tangential bascule beams readily evokes a D_3 -symmetric construct in which neighboring beam-ends can cross. If these beam-ends were bidentate ligands, their crossing points would constitute binding sites for metals with tetrahedral ligand fields. Thus, emerges a design for a trinuclear copper(I)–bipyridine triskelion (**1**) (Scheme 1). The triskelion comes from three equivalents of a crescent-shaped polyaryl (**2**) and a 1,3,5-triethynyl core.



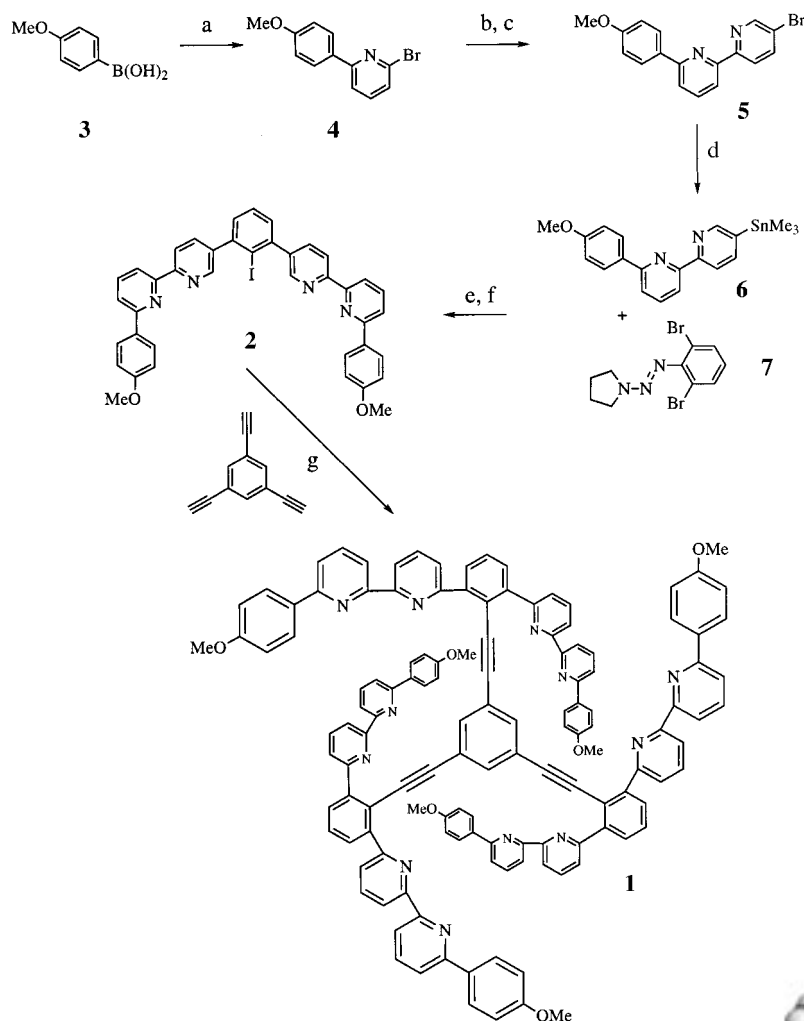
Scheme 1. Bascule mechanism for binding three metals in a triskelion. ● = Cu^I.

Synthesis of **1** depends heavily on the application of palladium-based Suzuki,^[22–24] Stille,^[25] and Sonogashira^[26] type aryl couplings (Scheme 2).^[27–29] Although one begins from anisyl boronic acid (**3**) and 2,6-dibromopyridine to form 6-anisyl-2-bromopyridine (**4**), the coupling strategy rapidly builds much larger products. The stannylation of **4** occurs by reaction with butyllithium at -78°C followed by quenching with trimethylchlorostannane. This stannyl reagent reacts

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Scheme 2. Synthesis of **1**: a) 2,6-dibromopyridine, $[\text{Pd}(\text{PPh}_3)_4]$, Na_2CO_3 , toluene, reflux, 74 %; b) 1) BuLi , Et_2O , -78°C , 2) Me_3SnCl , 85 %; c) 2,5-dibromopyridine, $[\text{Pd}_2(\text{dba})_3]$, AsPh_3 , DME, reflux, 57 %; d) $\text{Me}_3\text{SnSnMe}_3$, $[\text{Pd}(\text{PPh}_3)_4]$, DME, reflux, 57 %; e) $[\text{Pd}(\text{PPh}_3)_4]$, DME, reflux, 66 %; f) I_2 , dichloroethane, reflux, 78 %; g) $[\text{PdCl}_2(\text{PPh}_3)_2]$, Et_3N , THF, reflux, 51 %. dba = dibenzylideneacetone.

regioselectively with the 2 position of 2,5-dibromopyridine to give 6'-anisyl-5-bromobipyridine (**5**). Problems with the stannylation of **5** led to the development of a direct stannylation procedure, which employs hexamethyldistannane and catalytic amounts of palladium in dimethoxyethane (DME).^[30] The 5-stannyl derivative **6** coupled cleanly with the dibromophenyltriazene **7**, and, after conversion of the triazene functionality to the iodide with iodine in refluxing dichloroethane,^[31] **2** was obtained. Sonogashira coupling of three equivalents of **2** with 1,3,5-triethynylbenzene yielded the desired D_3 -symmetric ligand,^[26] which readily bound copper(I) in acetonitrile solution (**1**- Cu_3).

The characteristic deep red color of **1**- Cu_3 was the first sign of successful complexation, and electrospray mass spectrometry confirmed molecular mass and composition, but neither could prove our goal: control of stereochemistry. Additional evidence came from the ^1H and ^{13}C NMR spectra that display the limited set of signals one would associate with D_3 symmetry. The X-ray crystal structure of **1**- Cu_3 complemented

the solution work and showed the successful template/basculc construction (Figure 1).^[32] Thus, barring anomalous crystal forces in combination with dynamic averaging in the solution NMR spectra, the idealized structure of **1**- Cu_3 is D_3 -symmetric in all chemical phases, as designed.^[33, 34]

Inspection of the structural details reveals that the bipyridine arms from neighboring units cross to form the envisioned tetrahedral metal binding sites. The overall structure is distorted away from D_3 symmetry; but this distortion is most likely the result of crystal packing forces. The bond lengths and bond angles are in good agreement with standard values.

The bascule mechanism ensures that the stereochemical configuration set during the binding of the first metal ion dictates the same configuration for the remaining sites. A related question is whether that initial metal binding also promotes subsequent metal bindings (positive cooperativity).^[35] Titration of **1** with Cu^{I} ions leads to clean isosbestic behavior consistent with an intermediate-free transformation. Indeed, when observing the process by NMR spectroscopy, addition of a given fraction of the complement of three Cu^{I} ions leads to that fraction of **1**- Cu_3 and free **1** with no other species or intermediates (Figure 2). These two sets of data provide strong

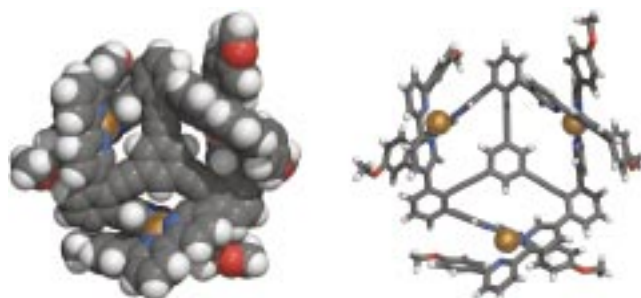


Figure 1. Space-filling (left) and framework (right) representation down the C_3 axis of the crystal structure of **1**- Cu_3 .

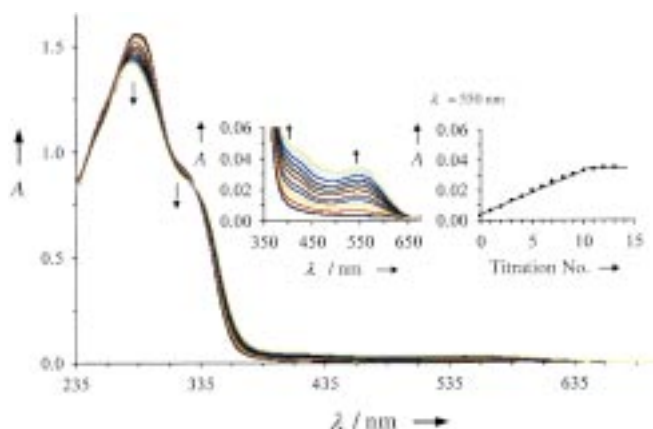


Figure 2. UV/Vis titration of **1** with copper(I) tetrafluoroborate. Left inset: enlargement of 350–650 nm; right inset: Scatchard plot of absorbance vs. metal equivalents at 550 nm.

evidence for positive cooperativity among the metal binding sites in **1**-Cu₃.

Thus, metal-binding properties of **1** and the high symmetry of **1**-Cu₃ illustrate a high degree of control over the degree and regularity of molecular entwinement. In combination with an appropriate macrocyclization method, the stage is set for the directed synthesis of complex topological stereoisomers of high symmetry, specifically, a molecular trefoil knot.^[36]

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remaining non-H atoms by LS – ΔF syntheses, refinement against F^2 (SHELXL) with all H atoms included in idealized positions, all Cu, O, and F atoms refined anisotropically. Structure solution, refinements, graphics, and tables calculations performed with SHELXTL/PC. **1**: C₁₃₂H₉₀B₃Cu₃F₁₂N₁₂O₆, M_r 2391.21, monoclinic, space group $P2_1/c$ (no. 14), $a = 24.879(2)$, $b = 14.4764(12)$, $c = 37.097(3)$ Å, $\beta = 102.912(1)^\circ$, $V = 13023(2)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.220$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.558$ mm⁻¹, crystal dimensions ca. $0.15 \times 0.06 \times 0.06$ mm³, $2\theta_{\text{max}} = 38.6^\circ$, 37667 reflections measured, 9851 unique reflections ($R_{\text{int}} = 0.149$), 770 parameters, 3 restraints, $R_1(wR_2) = 0.1163$ (0.2624) for 5498 reflections with $I > 2\sigma(I)$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-148313. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Tetranuclear Copper(II)-Biphenanthroline Gridwork: Violation of the Principle of Maximal Donor Coordination Caused by Intercalation and CH-to-N Forces**

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The amelioration of “hot spots” in a molecule through specific molecular association is a general chemical principle, which has been recently highlighted as a driving force for “supramolecular” reactions.^[1] The instability of unpaired radicals, uncoordinated metal ions and ligands, and unasso-

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