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A stereodynamic and redox-switchable encapsulation-complex containing a copper ion held by a *tris*-quinolinyl basket[†]

Sandra Stojanović,^{*a*} Daniel A. Turner,^{*a*} Andrew I. Share,^{*b*} Amar H. Flood,^{*b*} Christopher M. Hadad^{*a*} and Jovica D. Badjić^{**a*}

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We investigated the coordination of Cu(I)/Cu(II) ions to chiral basket (S_3)-1. The results of both experimental and computational studies suggest the formation of a copper redox-switchable system capable of entrapping CH₃CN.

Improving the characteristics of transition-metal catalysts¹ may require placement of the metal ion within a concave host.² Despite the potential of such encapsulation catalysis, there has been a paucity of functional cavitands³ available for investigating the concept. We recently introduced a family of cavitands, gated molecular baskets,^{3b-f} for controlling the kinetics of molecular encapsulation^{3b} and promoting chemical reactions in gated environments.^{3d} These hosts comprise a bowl-shaped platform with revolving aromatic rings as gates at the rim of the basket (Fig. 1). The gates were designed to (a) interact via hydrogen bonding^{3f} or (b) coordinate to Cu(I)/IAg(1) cations.^{3c,e} In particular, the coordinated cation resides in either tetrahedral or trigonal ligand fields whereby the propeller-like gates are constrained to assume either left- (Λ) or right-handed (Δ) orientations (Fig. 1). We recently demonstrated^{3e} that the helicity in this stereodynamic coordination environment⁴ is controllable: a stereogenic center (with R or S configuration) at the "hinge" position directs the twisting of the gates at the rim, thereby ensuring the preponderance of one diastereomeric form (Fig. 1). The current study builds on these observations and we initiated it to (a) investigate the coordination of Cu(II) to basket (S_3) -1 (Fig. 1),⁵ (b) evaluate the scope of static-to-dynamic chirality transfer as monitored by exciton-coupled circular dichroism (ECCD), 6a,b and (c) examine the Cu(I)/Cu(II) conversion in this coordination system.⁴ Furthermore, the impetus for the work is ultimately to learn about the structure and dynamics of copper-containing molecular baskets in order to facilitate studies of their catalytic function, *e.g.*, the activation of molecular oxygen⁷ in a dynamic confined space.



Fig. 1 Chemical structure of (S_3) –1 basket and its ¹H NMR spectrum (400 MHz, 298.0 K) in CDCl₃ (top). Top view of energy-minimized Cu(1)– (S_3) –1 (MMFF, Spartan) with quinolinyl gates, assuming Δ handedness.

On the basis of Karlin and co-workers' systematic study of cupric ion coordinating to tetradentate tripodal ligands,⁵ we envisaged that basket (S_3)–1 should bind to Cu(II) to form a complex with three, or perhaps two, quinolines coordinating to the metal. In this scenario, acetonitrile (as the solvent) would occupy the remaining coordination sites relative to the complex's coordination number (CN) of 5–6. Importantly, the quinoline chromophore has a strong transition electric moment ($\lambda = 233$ nm, $\varepsilon = 57000$ M⁻¹ cm⁻¹) polarized along the long axis of the aromatic ring (Fig. 2A),^{6c} which should give rise to bisignate ECCD^{6a,b} spectra for these chiral complexes.

First, we used an established synthetic methodology for preparing enantiomerically pure (*S*)-1-(quinolin-3-yl)ethanamine **8** (Scheme S1, ESI[†]). This amine was condensed with a previously reported *tris*-anhydride 9^{3c} in toluene to give basket (*S*₃)–1 (Scheme S2, ESI[†]). ¹H NMR analysis of (*S*₃)–1 (Fig. 1) reveals a *C*₃ symmetric molecule with gates revolving at a sufficiently high rate (198–300 K, Fig. S15, ESI[†]) about the asymmetric H–C(CH₃) unit. On the basis of our previous study, ^{3e} we hypothesized that the coordination of Cu(II) to the quinoline moieties in (*S*₃)–1 would drive these chromophores into a right-handed (Δ) propeller. Thus, in each Cu(II)–(*S*₃)–1 quinoline arm, the C–H bond should become eclipsed with the

^a Department of Chemistry, The Ohio State University, 100 W. 18th Avenue, Columbus, OH 43210, USA.

E-mail: badjic@chemistry.ohio-state.edu; Tel: +1 11 614 247 8342 ^b Department of Chemistry, Indiana University, Bloomington,

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Fig. 2 (A) The interaction of the transition electric moments from the quinoline arms should give a negative ECCD couplet⁶ in Cu(11)–(S_3)–1. (B) Circular dichroism spectra of (S_3)–1 (2.63 μ M) obtained upon an incremental addition (0.1–4.0 molar equivalents) of Cu(BF₄)₂·6H₂O.

adjacent O=C-N bond for, perhaps, relieving some steric strain^{3e} and a favourable alignment for the C=O group^{3c,e} (Fig. 1). Under these circumstances, the transition electric moments ($\lambda \approx 233$ nm) of the quinolines would interact through space (Fig. 2A) and give rise to a bisignate ECCD curve: the counter-clockwise disposition of the projected exciton axes should result in a negative coupling, hence with the appearance of a positive Cotton effect (CE) at shorter and a negative CE at longer wavelengths.^{6b} Indeed, incremental addition of Cu(BF₄)₂. $6H_2O$ to (S_3) -1 in acetonitrile revealed the formation of a strong and negative excitonic couplet centered at 239 nm (Fig. 2B); specifically, the CD spectrum of such formed $Cu(II)-(S_3)-1$ comprised a positive CE at 230 nm ($\Delta \varepsilon_1 = 467 \text{ M}^{-1} \text{ cm}^{-1}$) followed by a negative CE at 249 nm ($\Delta \varepsilon_2 = -373 \text{ M}^{-1} \text{ cm}^{-1}$). Importantly, the large A ($|\Delta \varepsilon_1| + |\Delta \varepsilon_2|$) value of 840 indicates a through-space interaction of the quinoline chromophores with a contribution from all three ECCD couplets.⁴ The changes in the UV-vis spectrum of (S_3) -1, obtained upon the addition of Cu(BF₄)₂·6H₂O, were much less dramatic (Fig. S16, ESI[†] and/or Fig. 5). In particular, a broad band appearing at 234 nm is likely a composite of $\pi - \pi^*$ transitions corresponding to the phthalimide platform (~225 nm, $\varepsilon \approx 2.5 \times 10^5 \,\mathrm{M^{-1} \, cm^{-1}}$ and ~245 nm, $\varepsilon \approx$ 1.7×10^5 M⁻¹ cm⁻¹)^{3e} and the quinolinyl groups (~233 nm).^{6c}

Importantly, the presence of an isosbestic point at 234 nm (CD titration, Fig. 2B) is a good indication of two chiral species contributing to the equilibrium. Indeed, the binding isotherm (Fig. S17, ESI†) is in line with the formation of a 1 : 1 complex: multivariate factor analysis of the CD data (ReactLab software) suggests a strong affinity of Cu(II) for complexation by (S_3) –1 $(K_a > 10^7 \text{ M}^{-1}, \text{ Fig. S17}, \text{ ESI†})$. The stoichiometric 1 : 1 ratio of Cu(II) and (S_3) –1 was also confirmed by mass spectrometric measurements (ESI-TOF, Fig. S18, ESI†) whereby the highest intensity peak appeared at 577.63 amu corresponding to the doubly-charged Cu(II)– (S_3) –1 without any CH₃CN.

What is the coordination number of the Cu(II) cation within the Cu(II)–(S_3)–1 complex? With all three quinolines coordinated to the metal, one anticipates Cu(II)–(S_3)–1 to correspond to either trigonal bipyramidal 2 (CN = 5) or square-pyramidal 3 (CN = 5, Fig. 3A).⁵ We performed some geometry minimizations, with density functional theory (DFT)⁸ at the RI-BHLYP/ SV(P),TZVP⁸ level of theory, for the C_3 symmetric 2 and C_1 symmetric 3 (Fig. 3A) and noted that the square-pyramidal complex has a greater thermodynamic stability (2.0 kcal mol⁻¹). In square-pyramidal 3, the basal plane is comprised of three quinolinyl groups and one acetonitrile, while another encapsulated CH₃CN completes the coordination sphere around the copper



Fig. 3 (A) Five-coordinate complexes 2 and 3 (M= Cu^{2+}) were energy minimized with density functional theory (RI-BHLYP/SV(P), TZVP) to reveal a greater thermodynamic stability of the square-pyramidal 3 (see ESI†). (B) CPK representation of square-pyramidal 3 (top-view) showing three juxtaposed hydrogens H_f (in green) at position 8 of the quinolinyl rings. (C) Energy-minimized RI-BHLYP/SV(P),TZVP complex 4 (M= Cu^+).

(Fig. 3A). Importantly, the quinolines in **3** are tilted ($\phi = 42^\circ$, Fig. 3A), forming a small hydrophobic pocket at the top of Cu(II) with the quinolines' **H**_f atoms (Fig. 3B) being separated by only 2.4–2.8 Å. Placing an acetonitrile ligand at the top position would, however, require a greater separation of the **H**_f atoms⁵ and thereby additional tilting of the aromatic rings, relative to what was obtained for trigonal bipyramidal **2** (d = 4.4 Å and $\phi = 69^\circ$, Fig. 3A). It is worth mentioning that the Cu–N_{quin} bonds in **3** are shorter (2.076–2.103 Å) than in **2** (2.181 Å), which perhaps, among other factors, contributed to the computed difference in stability.

The pattern and the intensity of d-d absorptions (650-1000 nm region), in the electronic spectrum of Cu(II) complexes, are diagnostic for the coordination geometry around the metal center.⁵ These bands were, however, absent in the UV-vis spectrum of our Cu(II)– (S_3) –1 (Fig. S19, ESI[†]). Alternatively, we anticipated that the electron paramagnetic resonance (EPR) spectrum of Cu(II) (d⁹ electronic state, S = 1/2), within the Cu(II)– (S_3) –1 complex, should report on the nature of the coordination sphere.9 Indeed, if the geometry around the cupric ion is square pyramidal, then the spin-orbit interaction between its ground $d_{x^2-y^2}$ and excited states gives rise to a normal/axial EPR signature with equivalent x and y axes and two g tensor values: $g_{II} = g_z > 2.1 > g_{\perp} = g_x, g_y > 2.0.^{9c}$ As a result of the unpaired electron in Cu(II) interacting with the nuclear magnetic spin of Cu(II) (I = 3/2), there should also appear four hyperfine lines (2I + 1) with the coupling constant (A_{II}) in the range of 158–200 G. Clearly, our EPR experimental data (Fig. 4A) suggest the sole formation of complex 3 in solution $(g_{\text{II}} = 2.31 > g_{\perp} = 2.07 \text{ and } A_{\text{II}} = 166 \text{ G}).^{9b}$

The affinity of soft Cu(1) for coordinating (S_3) –1 is comparatively small: a nonlinear least-squares analysis of the ¹H NMR titration data revealed K_a of 4.1 \pm 0.3 \times 10⁴ M⁻¹ (Fig. S21, ESI†) for the formation of 4 (Fig. 3C). As expected, ^{3c} the cuprous ion resides in a



Fig. 4 (A) EPR spectrum of square-pyramidal complex 3 in CH₃CN at 77 K. (B) Cyclic voltammograms (two subsequent scans at a rate of 0.2 V s^{-1}) of complex 3 (1.0 mM) in degassed CH₃CN; each measurement was conducted with 0.1 *n*-BuNPF₆ and a glassy carbon working electrode.



Fig. 5 Experimental (black) and computed TD-BHLYP/SV(P),TZVP (red)⁸ UV-vis (left) and CD (right) spectra of compound **3**. The blue sticks are computed electronic transitions that were subjected to Gaussian broadening (0.3 eV) and wavelength shift (-0.7 eV) for generating the theoretical spectra (see ESI⁺).

tetrahedral ligand field with a coordinated molecule of acetonitrile pointing to the basket's interior (Fig. S23 and S24, ESI[†]). The chirality transfer is operating in this system as well ($\phi = 57^{\circ}$, Fig. 3C), with a strong and negative excitonic couplet centered at 239 nm (Fig. S22, ESI[†]).

Redox-driven interconversion between complexes 3 and 4 (Fig. 3) should involve a reorganization of the coordination sphere about the copper ion¹⁰ and, perhaps, the formation of two unstable complexes square-pyramidal-Cu(I) and tetrahedral-Cu(II) in accordance with a square-scheme mechanism.^{10b} The cyclic voltammetry (CV) of square-pyramidal 3 (1.0 mM, CH₃CN) showed four primary waves **a**-**d** (0.2 V s⁻¹, Fig. 4B); for more details, see primary copper-based redox processes and switching between 3 and 4 in ESI.[†] The phthalimide moieties are reduced/oxidized at waves \mathbf{b}/\mathbf{c} to their radical anions (Fig. 4B), ^{10c} and the peak intensities and shapes do not differ from CVs of the empty basket (Fig. S25, ESI[†]). Waves a/d are, however, associated with the copper ions, as seen in the titration of Cu(II) into a solution of the cage (Fig. S25^{\dagger}). Peak **a** is assigned to a Cu(II) reduction^{9b} of complex 3 while peak d corresponds to the oxidation of the cuprous ion of complex 4. The peak potentials ($E_{pc}^{a} = -0.96$ V and $E_{\text{pa}}^{\text{d}} = -0.27$ V) are similar to Cu(1) complexes of tris-(2-pyridyl)methanamine^{9b} and are more cathodic than for funnellike complexes.^{10a} The large difference in redox potentials of 690 mV between peaks a and d is, however, consistent with the changes in geometry and coordination number seen for other 4-coordinate Cu(I) and 5-coordinate Cu(II) complexes.^{10a} The formation of intermediate complexes^{10b} was not observed at faster scan rates (0.5-20 V s⁻¹, Fig. S28, ESI[†]). The a/d peak intensities are less than 1/3 those of the b/c peaks, suggesting slower heterogeneous electron transfer to and from the copper ions than the walls of the cage, nevertheless, the first and second cycles of the CVs are identical (Fig. 4B), indicating a chemically reversible process.

Finally, we computed the UV-vis and CD spectra of DFTminimized **3** (Fig. 5) using time-dependent density functional theory (TD-BHLYP/SV(P),TZVP).⁸ There is excellent agreement between the experimental and computed spectra of **3**, thereby corroborating the complex's absolute configuration as predicted by the exciton chirality method.^{6a} In particular, the accurate prediction of the optical rotatory strengths of this large (145 atoms) and C_1 symmetric complex indicates a high quality of the wave function generated with this level of theory¹¹ as well as conformational stability of the complex.

Given the proclivity of baskets for forming both Cu(I) and Cu(II) complexes, there is a potential for examining these compounds as encapsulation catalysts.¹² Our studies are now directed toward investigating the activation of O_2^{7b} in a controllable and confined environment that these baskets provide.

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