

An *N*-Ligated Trinuclear Copper(I) Cation Structurally Reminiscent of the Active Site of Ascorbate Oxidase

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The trinuclear copper(I) cation, $[\text{Cu}(\mu\text{-ppdBu})_2\{\text{Cu}(\text{cnge})(\text{MeCN})\}_2](\text{BF}_4)_3\cdot\text{MeCN}$ (ppdBu = 3,6-bis[*N*-(3-*tert*-butyl)pyrazolyl]pyridazine, cnge = 2-cyanoguanidine), which comprises three copper atoms held together in an isosceles triangle ($\text{Cu}\cdots\text{Cu}$ = 3.62, 3.63 and 5.01 Å) by two approximately perpendicular (dihedral angle 86.9°) planar ppdBu bridging ligands, is synthesised by addition of a dichloromethane solution of ppdBu to an acetonitrile solution of $[\text{Cu}(\text{MeCN})_4](\text{BF}_4)$ containing cnge.

Trinuclear copper clusters are essential functional units in multicopper blue oxidases, such as laccases and ascorbate oxidases, which catalyse the $4e^-/4\text{H}^+$ reduction of dioxygen to water with concomitant one-electron oxidation of a variety of substrates.¹ Messerschmidt *et al.* have determined the structures of the reduced² and oxidised³ forms of ascorbate oxidase, isolated from green zucchini. The enzyme comprises two similar subunits, each of which contains four copper atoms in mononuclear and trinuclear active sites, minimum Cu–Cu distance between sites 12.2 Å. In the reduced form, studied to a resolution of 2.2 Å,² the latter sites are based on a 'type 3' copper pair and one 'type 2' copper atom arranged in a near isosceles triangle ($\text{Cu}\cdots\text{Cu}$ = 4.1, 4.4, 5.1 Å) and *N*-ligated by histidine moieties.³

Recognising the Cu \cdots Cu separation (3.566, 3.582 Å) generated by the tetradentate ligand 3,6-bis(2'-pyridyl)pyridazine (dppn) in the tetramer $[\text{Cu}_4(\text{dppn})_4]^{4+}$ and the stabilisation of copper(I), often coordinatively unsaturated, by 2-cyanoguanidine (cnge),⁵ we have turned our attention to the synthesis of bi- and tri-nuclear copper(I) complexes bridged by analogous 3,6-bis(*N*-pyrazolyl)pyridazine ligands 1–3. In the reaction of the unsubstituted ligand (ppd) with cnge and $[\text{Cu}(\text{MeCN})_4](\text{BF}_4)$, the only product obtained thus far is the tetrameric cation, $[\text{Cu}_4(\text{ppd})_4]^{4+}$ 4.⁶ For the 3,5-dimethyl (ppdMe) and 3-*tert*-butyl (ppdBu) substituted pyrazole derivatives, however, we have generated novel copper(I) trimeric cations, $[\text{Cu}(\text{L})_2\{\text{Cu}(\text{cnge})(\text{MeCN})\}_2]^{3+}$ (L = $\mu\text{-ppdMe}$ or $\mu\text{-ppdBu}$). Although attempted recrystallisation of the ppdMe compound resulted in the formation of the tetrameric cation $[\text{Cu}_4(\mu\text{-ppdMe})_4]^{4+}$ 5,⁶ crystals of the ppdBu complex suitable for single crystal X-ray studies were obtained. It is the synthesis and structure of $[\text{Cu}(\mu\text{-ppdBu})_2\{\text{Cu}(\text{cnge})(\text{MeCN})\}_2](\text{BF}_4)_3\cdot\text{MeCN}$ 6 which are here described.

The tetradentate ligand, ppdBu, was synthesised⁷ by treatment of 3,6-dichloropyridazine with the potassium salt of 3-*tert*-butylpyrazole.⁸ It was characterised by MS, IR and ¹H NMR spectroscopy and elemental analysis.† Addition of a dichloromethane solution (40 cm³) of ppdBu (0.51 g, 1.57 mmol) to a stirred acetonitrile solution (40 cm³) of $[\text{Cu}(\text{MeCN})_4](\text{BF}_4)$ (1.106 g, 3.52 mmol) in the presence of powdered cnge (0.264 g, 3.14 mmol) gave a yellow solution which darkened to orange over 24 h. Solvent–solvent interface diffusion of an aliquot of the solution with toluene gave red crystals, which elemental analysis and vibrational spectroscopy showed to have the formulation of compound 6.‡

The structure of compound 6 was determined by single crystal X-ray diffraction.§ It comprises $[\text{Cu}(\mu\text{-ppdBu})_2\{\text{Cu}(\text{cnge})(\text{MeCN})\}_2]^{3+}$ cations, uncoordinated BF_4^- anions and lattice acetonitrile molecules. The trinuclear cation (Fig. 1), which has approximate twofold symmetry, is based on a near

isosceles triangle of copper atoms, held together by two approximately perpendicular (dihedral angle 86.9°) planar ppdBu ligands (maximum deviation from the least squares best plane 0.13 Å) ppdBu ligands. All three copper atoms are coordinated by four

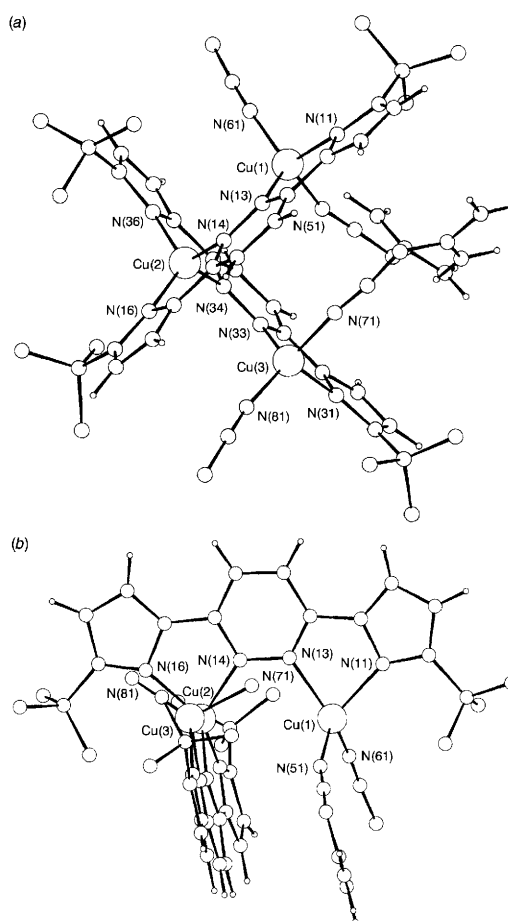
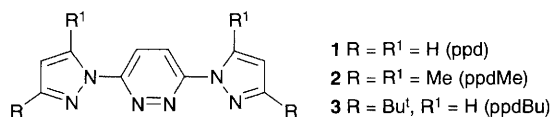


Fig. 1 Views of the molecular structure of the $[\text{Cu}(\mu\text{-ppdBu})_2\{\text{Cu}(\text{cnge})(\text{MeCN})\}_2]^{3+}$ trinuclear cation (a) perpendicular to the Cu_3 plane, and (b) slightly offset from the $\text{Cu}(3)\cdots\text{Cu}(2)$ axis [to aid clarity, only the ligating nitrogen atoms of the cnge [N(71)] and acetonitrile [N(81)] molecules attached to $\text{Cu}(3)$ are shown]. Significant interatomic distances (Å) and angles (°): $\text{Cu}(2)\cdots\text{Cu}(1)$ 3.634(15), $\text{Cu}(2)\cdots\text{Cu}(3)$ 3.624(16), $\text{Cu}(1)\cdots\text{Cu}(3)$ 5.011(15), $\text{Cu}(1)\text{---}\text{Cu}(2)\text{---}\text{Cu}(3)$ 87.3(5), $\text{Cu}(2)\text{---}\text{Cu}(3)\text{---}\text{Cu}(1)$ 46.4(5), $\text{Cu}(1)\text{---}\text{Cu}(2)\text{---}\text{Cu}(3)$ 46.3(5); $\text{Cu}(1)\text{---}\text{N}(11)$ 2.103(16), $\text{Cu}(1)\text{---}\text{N}(13)$ 2.042(16), $\text{Cu}(1)\text{---}\text{N}(51)$ 1.941(20), $\text{Cu}(1)\text{---}\text{N}(61)$ 1.949(22), $\text{N}(11)\text{---}\text{Cu}(1)\text{---}\text{N}(13)$ 77.8(7), $\text{N}(11)\text{---}\text{Cu}(1)\text{---}\text{N}(51)$ 114.8(7), $\text{N}(11)\text{---}\text{Cu}(1)\text{---}\text{N}(61)$ 114.3(8), $\text{N}(13)\text{---}\text{Cu}(1)\text{---}\text{N}(51)$ 114.5(7), $\text{N}(13)\text{---}\text{Cu}(1)\text{---}\text{N}(61)$ 127.5(7), $\text{N}(51)\text{---}\text{Cu}(1)\text{---}\text{N}(61)$ 105.8(8); $\text{Cu}(2)\text{---}\text{N}(14)$ 1.971(16), $\text{Cu}(2)\text{---}\text{N}(16)$ 2.024(16), $\text{Cu}(2)\text{---}\text{N}(34)$ 2.008(15), $\text{Cu}(2)\text{---}\text{N}(61)$ 1.924(22), $\text{N}(14)\text{---}\text{Cu}(2)\text{---}\text{N}(16)$ 82.4(7), $\text{N}(14)\text{---}\text{Cu}(2)\text{---}\text{N}(34)$ 120.5(6), $\text{N}(14)\text{---}\text{Cu}(2)\text{---}\text{N}(61)$ 123.3(7), $\text{N}(16)\text{---}\text{Cu}(2)\text{---}\text{N}(34)$ 125.0(7), $\text{N}(16)\text{---}\text{Cu}(2)\text{---}\text{N}(61)$ 130.0(7), $\text{N}(34)\text{---}\text{Cu}(2)\text{---}\text{N}(61)$ 81.3(7); $\text{Cu}(3)\text{---}\text{N}(31)$ 2.158(18), $\text{Cu}(3)\text{---}\text{N}(33)$ 2.065(16), $\text{Cu}(3)\text{---}\text{N}(71)$ 1.928(24), $\text{Cu}(3)\text{---}\text{N}(81)$ 1.934(23), $\text{N}(31)\text{---}\text{Cu}(3)\text{---}\text{N}(33)$ 78.2(7), $\text{N}(31)\text{---}\text{Cu}(3)\text{---}\text{N}(71)$ 104.1(8), $\text{N}(31)\text{---}\text{Cu}(3)\text{---}\text{N}(81)$ 117.9(8), $\text{N}(33)\text{---}\text{Cu}(3)\text{---}\text{N}(71)$ 108.1(8), $\text{N}(33)\text{---}\text{Cu}(3)\text{---}\text{N}(81)$ 123.6(8), $\text{N}(71)\text{---}\text{Cu}(3)\text{---}\text{N}(81)$ 117.7(9).



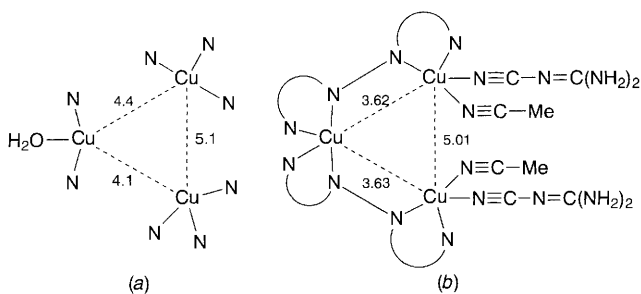


Fig. 2

nitrogen atoms with approximately tetrahedral geometry; the pivotal copper {Cu(2)} by nitrogens from two tetradentate ligands in a similar fashion to that in the tetramer,⁴ the two terminal coppers {Cu(1), Cu(3)} by two nitrogens from the tetradentate ligand and one each from the nitrile moieties of cnge and acetonitrile. The cnge molecules are located in the space between the two terminal copper atoms, the acetonitrile molecules in external positions [Fig. 1(a)]. Although the cnge molecule attached to Cu(1) is parallel to the ppdBu molecule bridging Cu(2) and Cu(3) (dihedral angle 6.0°) [Fig. 1(b)], that attached to Cu(3) is twisted through 140.5° to form a weak hydrogen bond to the other cnge molecule {N(73)–H(731)···N(52); N(73)···N(52) = 3.15 Å, N(73)–H(731)–N(52) 130.1°}.

Trinuclear copper(I) clusters are not uncommon.⁹ However, with the exception of two complexes¹⁰ based on trinucleating ligands, they are structurally analogous with approximate threefold symmetry and either μ^2 -bridging, μ^3 -bridging or terminal anionic ligands. Thus, compound **6** is the first reported example of an unsymmetrical trinuclear cationic copper(I) complex with approximate twofold symmetry and without coordinated anions.

Biomimetic studies to elucidate the function of trinuclear copper clusters are few in number. Structural analogues have proved to be elusive. Fenton *et al.*¹¹ have recently reported the structure of a trinuclear copper(II) complex, based on a functionalised bibracchial tetra-imine Schiff-base macrocycle, with Cu···Cu separations of 3.6, 4.9 and 5.9 Å. Using complex trinucleating ligands, Karlin *et al.*¹⁰ have described the synthesis of two trinuclear copper(I) complexes; structural analysis of one has revealed rather large Cu···Cu separations (6.06, 7.43 and 7.67 Å). Compound **6** has several structural features more reminiscent of the trinuclear site of ascorbate oxidase. The two structures are compared schematically in Fig. 2. They both contain two different types of copper atom and have approximate twofold symmetry, *N*-ligation predominates in both structures, and the distances between the copper atoms are similar (Fig. 2). As a functional model, compound **6** may prove to be limited owing to the spatial arrangement of the labile monodentate ligands on Cu(1) and Cu(3). However, the fact that the arrangement of the two cnge molecules is distorted to allow hydrogen bond formation suggests sufficient flexibility to permit incorporation of bridging ligands between Cu(1) and Cu(3).

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Footnotes

† Found (calc. for C₁₈H₂₄N₆): C 66.80 (66.65), H 8.00 (7.45), N 24.90 (25.90). MP 130–132 °C. MS (*m/z*, relative intensity): 324 (M⁺, 38%), 309 [(M – CH₃)⁺, 100%], 147 [(M – 2CH₃)/2]⁺, 10%, 133 [(M – 2CH₃)/2]

– N]⁺, 4%), 57 ([C₄H₉)⁺, 6%). ¹H NMR [CDCl₃, 250 MHz, standard SiMe₄, *J*/Hz]: δ 8.58 (d, *J* 2.66, 2H), 8.27 (s, 2H), 6.40 (d, *J* 2.66, 2H), 1.36 (s, 18H). IR ν /cm⁻¹: 3103(m), 2961(m), 1525(s), 1456(s), 1361(s), 1268(m), 1025(m), 946(s), 777(s).

‡ Found (Calc. for [Cu(C₁₈H₂₄N₆)₂{Cu(C₂H₄N₄)(C₂H₃N)}₂](BF₄)₃·C₂H₃N): C 39.25 (39.70), H 4.65 (4.70), N 23.60 (23.15). IR ν /cm⁻¹: 2965(m, ppdBu), 2223(s, cnge), 2179(m, cnge), 1643(s, cnge), 1480 (s, ppdBu), 1370(s, ppdBu), 1264(m, ppdBu), 1050(br s, BF₄⁻), 947(s, ppdBu) 767(m, ppdBu).

§ *Crystal data* for: [Cu(μ-ppdBu)₂{Cu(cnge)(MeCN)}₂](BF₄)₃·MeCN, C₄₆H₆₅B₃Cu₃F₁₂N₂₃, *M* = 1391.22, monoclinic, space group *P*2₁/*n*, *a* = 13.467(6), *b* = 23.371(3), *c* = 20.993(2) Å, β = 91.47(2)°, *U* = 6605.1 Å³, *Z* = 4, *F*(000) = 2848, *D*_c = 1.399 g cm⁻³, Mo-Kα radiation, λ = 0.71069 Å, μ = 10.4 cm⁻¹, crystal size 0.07 × 0.18 × 0.145 mm. *Data collection and processing.* A suitable crystal was mounted in a dry Lindemann tube under nitrogen. After initial determination of cell dimensions and space group, diffraction data were collected at 298 K using a Delft Instruments FAST TV area detector diffractometer situated at the window of a rotating molybdenum anode generator operating at 50 kV, 45 mA.¹² Somewhat more than one hemisphere of data was collected for which 30643 reflections were recorded giving 9696 unique reflections. The data were corrected for Lorentz and polarisation effects and also for absorption effects (DIFABS).¹³ *Structure analysis and refinement.* The structure was solved by direct methods using SIR92¹⁴ and refined by full matrix least-squares methods on *F*² {2838 reflections with *F*_o > σ(*F*_o²)} using CRYSTALS,¹⁵ to final *R* and *wR* values (unit weights) of 7.24 and 16.90% for 552 parameters. The BF₄⁻ anions based on B(2) and B(3), the *tert*-butyl group based on C(42) and the uncoordinated acetonitrile molecule all exhibited disorder. The copper, nitrogen, carbon (except those of the ppdBu ligand) and fluorine (except those of the disordered B(3)F₄⁻ anion) atoms were anisotropic; the remaining fluorine and carbon atoms and the boron atoms were isotropic. Hydrogen atoms were placed on the cnge nitrogens and ppdBu ring carbons and allowed to ride on their parent atoms in the calculated position (C···H = 1.00 Å, *U*[ISO] = 0.05). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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