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Three 2-oxazolinyl rings on one quaternary carbon atom: preparation of a novel tripodal tris(oxazolinyl) ligand and the tetrameric molecular structure of its Cu^I complex

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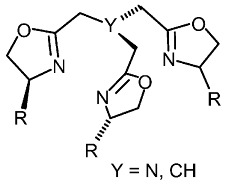
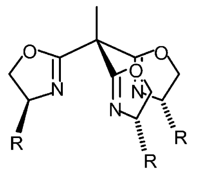
Reaction of the lithium salt of 1,1-bis[2-(4,4-dimethyl)oxazolinyl]ethane (1) with 2-bromo-4,4-dimethyloxazoline yielded the novel tripodal ligand, 1,1,1-tris[2-(4,4-dimethyl)-oxazolinyl]ethane (trisox-Me$_2$ 2) which was reacted with one mol equivalent of [Cu(NCCH$_3$)$_4$](BF$_4$) in dichloromethane to give [Cu(trisox-Me$_2$)]$_n$(BF$_4$)$_n$ (3); while monomeric in solution, an X-ray diffraction study of 3 established a cyclic, centrosymmetric tetramer in the solid state.

Neutral tripodal N-donor ligands have been studied as mimics of the tris(histidine) metal binding site in copper oxydases,[1] the principal aim being the development of novel oxidation catalysts.[2] The chiral environment at the reactive centre of a protein may be emulated by the presence of a chiral ligand periphery close to the N-donor functions. In the development of nitrogen ligand based homogeneous catalysis, oxazoline derivatives fulfil this condition and have emerged as a paradigmatic class of ligands in asymmetric catalysis.[3–4] Oxazolines are therefore obvious stuctural units in the quest for novel chiral N-tripods.

There are several reports in the literature of trisoxazoline ligands,[5–7] the most notable example being N(CH$_2$-ox)$_3$ and CH(CH$_2$-ox)$_3$ (ox = 2-oxazolinyl) systems (**I**), the copper complexes of which have been employed in asymmetric allylic oxidations.[5] However, there is as yet no report of 1,1,1-tris(oxazolinyl)methane or 1,1,1-tris(oxazolinyl)ethane ligands (**II**) which provide a geometry of the metal binding site which is in principle most adapted to tripodal coordination of the metal centre.



I



II

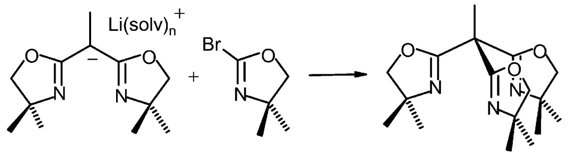
All previous attempts to synthesize these tripodal ligands, which contain three oxazoline units attached to a single carbon atom, by sequential formation of the three oxazoline rings failed due to decarboxylation and related decomposition of the precursors during the formation of the third ring.[8] We therefore reverted to a strategy in which a readily accessible bis(oxazoline) derivative was coupled with a preformed activated mono(oxazoline) ring. The synthesis of the first 1,1,1-tris(oxazolinyl)ethane derivative, 1,1,1-tris[2-(4,4-dimethyl)oxazolinyl]ethane (trisox-Me$_2$ **2**) was achieved by reaction of the lithium salt of 1,1-bis[2-(4,4-dimethyl)oxazolinyl]ethane (**1**)[9] with 2-bromo-4,4-dimethyloxazoline[10] (Scheme 1).[†]

In a first test into the complexation properties of this novel N-donor tripod in the context of copper based catalysis, we reacted **2** with one mol equivalent of [Cu(NCCH$_3$)$_4$](BF$_4$) in dichloromethane to give [Cu(trisox-Me$_2$)]$_n$(BF$_4$)$_n$ (**3**).[11] The formulation of this complex is based on the analytical data, the two ν(C=N) infrared bands at 1667 and at 1638 cm^{-1} of the oxazoline unit indicated the (albeit weak) coordination of the ligand to copper(I) while the ^{1}H NMR data recorded in CD$_3$CN are consistent with a threefold symmetrical monomer (n = 1: **3a**) on the time scale of the experiment in solution.[†] However, once isolated as a crystalline solid, the compound proved to be almost insoluble in all non-coordinating polar solvents, indicating a possible aggregation of the copper complex to form oligomers or polymers. A high resolution FAB mass spectrum displayed a molecular ion at 1799.6 which corresponds to the [Cu(trisox-Me$_2$)]$_4$(BF$_4$)$_3$ monocation along with a peak corresponding to the dication [Cu(trisox-Me$_2$)]$_4$(BF$_4$)$_2$ at m/z = 856.3 for the most abundant isotopomer in the characteristically half-amu spaced isotopomer distribution. This indicated the tetrameric nature of complex **3** in the solid state.

Crystals suitable for X-ray diffraction analysis were grown by slow diffusion of pentane in the dichloromethane solution.[‡] The cationic metal complex of **3** is a cyclic, centrosymmetric tetramer in the solid state (Fig. 1(a)) in which the trisoxazolines bridge two copper centres in a μ-{κ^2-*N*,*N′*:κ-*N″*} fashion. Each copper atom is in a distorted trigonal planar coordination environment [Σ(N–Cu–N) = 359°], connecting a chelating bisoxazoline unit of one ligand [N(1)–Cu(1)–N(2) 92.5(1), N(4)–Cu(2)–N(5) 93.3(1)°] and the remaining dangling oxazoline ring of a second tripod ligand. The apical methyl groups of the four tridentate ligands point to the inside of the tetrameric ring structure.

In the crystal, the metallamacrocycles are stacked to form tubes (Fig. 1(b)) which contain one counter ion BF$_4^-$ per tetramer while the other three anions lie outside the tubular arrays. The crystalline form of compound **3**, being only sparingly soluble in most aprotic polar organic solvents, only redissolves upon addition of CH$_3$CN to form the monomer [Cu(trisox-Me$_2$)(NCCH$_3$)(BF$_4$) (**3a**) which is C_{3v}-symmetrical on the NMR time scale even upon lowering the temperature to 230 K. While rapid exchange processes may not be ruled out in copper(I) chemistry, the low temperature spectra thus support our proposal of a symmetrical mononuclear complex in CD$_3$CN.

The modular {2 + 1} assembly of the new trisoxazolinines opens up the possibility of combining oxazoline rings with different substituents and thus reducing the threefold symmetry of the tripodal ligand. This and the development of chiral versions of this and related trisoxazolines, along with their application in oxidation catalysis is the object of our current and future activities.



1 **2**

Scheme 1 Synthesis of the 1,1,1-tris(oxazolinyl)ethane **2** by coupling of lithiated 1,1-bis[2-(4,4-dimethyl)oxazolinyl]ethane with 2-bromo-4,4-dimethyloxazoline.

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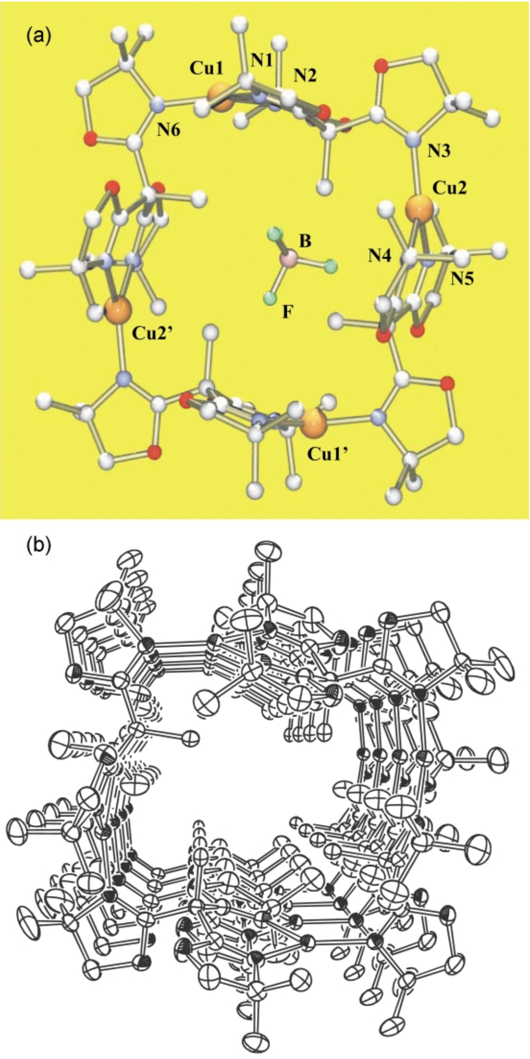

Fig. 1 (a) Molecular structure of the tetrameric copper complex $[\{Cu(trisox\text{-}Me_2)\}_4]^{4+}$ shown along with the BF_4 anion sandwiched between the cyclic units. The other three anions are located outside the cyclic structure in the unit cell. Principal bond lengths (Å) and angles (°): Cu(1)–N(1) 2.016(3), Cu(1)–N(2) 1.994(3), Cu(1)–N(6) 1.927(3), Cu(2)–N(3) 1.939(3), Cu(2)–N(4) 2.002(3), Cu(2)–N(5) 2.023(3); N(1)–Cu(1)–N(2) 92.5(1), N(1)–Cu(1)–N(6) 130.9(1), N(2)–Cu(1)–N(6) 135.5(1), N(3)–Cu(2)–N(4) 135.3(1), N(3)–Cu(2)–N(5) 130.3(1), N(4)–Cu(2)–N(5) 93.3(1). (b) Tubular stacking of the cyclic tetracationic $[Cu(trisox\text{-}Me_2)]_4$ units in the unit cell.

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Notes and references

† Compound (**2**) was prepared by deprotonation at −78 °C of the corresponding bisoxazoline (2.2 mmol) in THF using ^{t}BuLi (1.7 M in pentane) followed by the addition of 1.4 equivalents of 2-bromooxazoline. The resulting solution was refluxed for 5 days. Work-up by flash chromatography (50→100 ethyl acetate–hexanes) gave 120 mg of the desired product (17% yield).

Selected spectroscopic and analytical data: for **2**: ^{1}H NMR (300.16 MHz, CD_3CN, 295 K), δ 1.19 (s, 18H, $C(CH_3)_2$), 1.64 (s, 3H, CCH_3), 3.92 (s, 6H, CH_2); $^{13}C\{^1H\}$ NMR (50.32 MHz, $CDCl_3$, 295 K), δ 23.6 (CCH_3), 28.0 ($C(CH_3)(CH_3)$), 67.3 ($C(CH_3)_2$), 68.9 (CCH_3), 80.6 (CH_2), 165.9 (C=N); IR (KBr) cm^{-1}: 1659 (s, $\nu_{(C=N)}$) MS (EI): *m*/*z* (%): 321.2 (10) $[M]^+$, 306.2 (94), 225.1 (100); Anal. Calc. for $C_{17}H_{27}N_3O_3$: C 63.53, H 8.47, N 13.07; found: C 63.62, H 8.45, N 13.13%.

For **3**: IR (KBr) cm^{-1}: 2960.5 (m), 2926.1 (m), 2854.3 (w), 1666.8 (m), 1638.4 (s), 1460.9 (w), 1453.5 (w), 1369.7 (m), 1312.9 (m), 1288.9 (m), 1256.0 (w), 1217.9 (w), 1164.4 (m), 1109.0 (w), 1094.1 (w), 1053.2 (s), 1030.4 (s), 943.5 (m), 538.4 (m), 493.6 (w); FAB-MS (matrix NBA) *m*/*z*: 1799.6 ($[M - BF_4]^+$, calculated for the most abundant isotopomer: 1799.6), 856.3 ($[M - 2BF_4]^{2+}$, calculated for the most abundant isotopomer of the dication: 856.3), 705.4 ($[CuL_2]^+$), 384.1 ($[CuL]^+$); Anal. Calc. for $3(Cu_4L_4(BF_4)_4)\cdot 2CH_2Cl_2$: C 42.43, H 5.67, N 8.65; found: C 42.58, H 5.97, N 8.64%. ^{1}H NMR for **3a** (300.16 MHz, CD_3CN, 295 K), δ 1.30 (s, 18H, $C(CH_3)_2$), 1.71 (s, 3H, CCH_3), 4.08 (s, 6H, CH_2).

‡ *Crystal data* for (**3**): $C_{34}H_{54}Cu_2N_6O_6\cdot 2BF_4\cdot 2CH_2Cl_2$, colorless, crystal dimensions 0.20 × 0.16 × 0.16 mm, M = 1113.40, monoclinic, space group $P2_1/n$, a = 11.3723(2), b = 22.4765(4), c = 19.4660(3) Å, β = 94.367(5)°, U = 4961.3(1) Å^3, Z = 4, D_c = 1.49 g cm^{-3}, μ = 1.150 mm^{-1}, $F(000)$ = 2288, number of measured data: 18734 ($2.5 < \theta < 27.48°$) at 173 K, number of data with $I > 3\sigma(I)$: 6698, number of variables: 577, R = 0.046, R_w = 0.063, GOF = 1.398, largest peak in final difference map: 0.816 e Å^{-3}. CCDC reference number 183395. See http://www.rsc.org/suppdata/cc/b2/b202846h/ for crystallographic data in CIF or other electronic format.

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