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H-bonding and steric effects on the properties of phenolate and phenoxyl radical complexes of Cu(II)†

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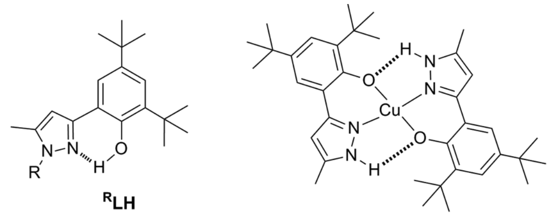
Herein, the N–R substituted N,O-phenol-pyrazole redox-active pro-ligands, ^{R}LH (R = Me, Pr) are reported together with their corresponding *bis*-Cu^{R}L$_2$ complexes (2 and 3, respectively). The latter are reversibly oxidised to the corresponding stable Cu(II)-phenoxyl radical complexes 2$^+$ and 3$^+$. The properties of the tetrahedrally distorted complexes 2 and 3 (and those of 2$^+$ and 3$^+$) are being compared to those of the square-planar H-bonded complex 1 (*bis*-Cu^{H}L$_2$) and those of 1$^+$. These studies have permitted H-bonding and steric effects on the redox, spectroscopic and chemical properties of Cu(II)-phenolate and Cu(II)-phenoxyl radical species to be established.

Galactose Oxidase (GO)[1] is a unique enzyme amongst the new emerging class of so-called "radical enzymes".[2] Its active site contains a catalytically active Cu(II)-tyrosyl radical moiety, which has triggered current research interest in the preparation and studies of metal-phenoxyl radical complexes.[3] These studies have provided an enhanced understanding on the unique spectral properties and structural attributes of the active form of GO. However, the local factors that modulate the redox properties of the Cu(II)–Tyr/Cu(II)–Tyr$^{\bullet}$ redox couple are not yet fully understood.

Suitably protected N,O-phenol-imidazole pro-ligands have been successfully used to model the active form of GO, as they have permitted the isolation and full characterisation of stable Cu(II)-phenoxyl radical complexes.[4] Recently, we have extended this chemistry to the phenol-pyrazole analoguous pro-ligand **^{H}LH** (Scheme 1).[5] The latter behaves like its imidazole analogue, in that its *bis*-Cu^{H}L$_2$ (**1**; Scheme 1) complex can be reversibly oxidised to the corresponding stable Cu(II)-phenoxyl radical.[5] However, thanks to the pyrazole-NH group, the square planar copper complex **1** represents a unique example in which the two coordinated phenolate ligands are involved in intramolecular H-bonding interactions (Scheme 1). Herein, we introduce the new N–R substituted ligand ^{R}LH (R = Me, Pr; see Scheme 1), which are unable to establish H-bonds when coordinated to the Cu(II) ion. The properties of the corresponding *bis*-Cu^{R}L$_2$ complexes **2** and **3** (Scheme 1) are being compared to those of **1**; permitting H-bonding and steric effects to be established.



^{R}LH

Cu^{R}L$_2$: R = H (1); R = Me (2); R = Pr (3)

1

Scheme 1

^{H}LH is readily deprotonated using NaH and further reacted with MeI or PrI to yield **^{Me}LH** and **^{Pr}LH** respectively (see ESI†). Despite the introduction of N-substituents, the **^{Me}LH** and **^{Pr}LH** possess similar properties to those of their unsubstituted parent **^{H}LH** in solution. Firstly, both display a relatively strong intramolecular OH···N hydrogen bonding between the phenol OH and the adjacent N-pyrazole as evidenced by a down field phenol-OH ^{1}H NMR resonance at *ca.* 11 ppm in CDCl$_3$ (see ESI†).[4,5] Secondly, as for other similar intramolecularly H-bonded phenol compounds,[6] **^{H}LH**, **^{Me}LH** and **^{Pr}LH** each exhibit a quasi-reversible one-electron PCET oxidation process (at E$_{1/2}$ = 0.660, 0.710 and 0.719 V *vs.* Fc/Fc$^+$, respectively, (Fig. S4–S5†)) that is attributed to the formation of a phenoxyl radical cation hydrogen bonded to a pyrazolium.

^{Me}LH and **^{Pr}LH** react with Cu^{II}(BF$_4$)$_2$·6H$_2$O in a 2 : 1 ratio in the presence of triethylamine in methanol to afford the purple *bis*-Cu^{R}L$_2$ complexes (**2** and **3** respectively). Slow evaporation of a DMF solution of **3** affords single crystals suitable for X-ray crystallography.‡ The molecular structure of **3** reveals that the Cu(II) ion possesses a N$_2$O$_2$ coordination environment in a tetrahedrally distorted geometry (the dihedral angle between the two CuNO planes is 37.45°), formed by the ligation of two L$^-$ ligands in a N,O bidentate fashion (Fig. 1 and Table S1†).

The significant distortion from a square planar geometry results from the presence of sterically demanding propyl groups, which prevent the two ligands from being on the same plane. This is in

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† Electronic supplementary information (ESI) available: Experimental part and Physical methods; ^{1}H NMR spectra for **^{Me}LH** and **^{Pr}LH** (Figs. S1–S2); Cyclic voltamograms of **^{Me}LH** and **^{Pr}LH** (Fig. S3–4); IR spectra of **1**, **2** and **3** (Fig. S5); X-band EPR spectra (exp. and sim) of **2** and **3** (Figs. S6–7); Decay curve of **1$^+$**, **2$^+$** and **3$^+$** (Figs. S8–10). CCDC reference number 846432. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1dt11868d

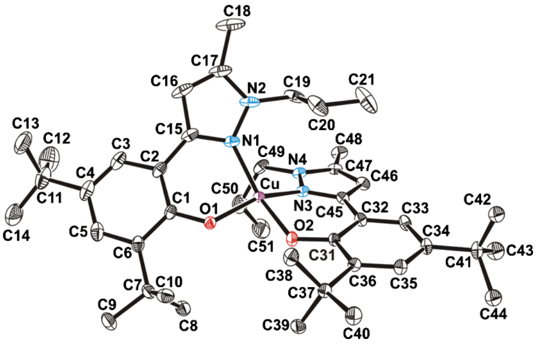

Fig. 1 The molecular structure of **3** (the displacement ellipsoids are shown at the 30% probability level).

great contrast with $Cu^{II}L_2$ (**1**), which possesses a perfect *trans*-square planar geometry, associated with the establishment of intramolecular inter-ligand O···HN H-bonding between phenolate and pyrazole groups (see Scheme 1). These H-bonds appear to affect significantly Cu–O and Cu–N bond distances. Thus, the average Cu–O bond is significantly longer in **1** than in **3** (1.9233(14) Å *vs.* 1.8806(16) Å) and the average Cu–N bond is significantly shorter in **1** than in **3** (1.9092(19) Å *vs.* 1.9549(19) Å).[5] Importantly, the phenolate C–O bond appears to be slightly lengthened upon H-bonding as evidenced by the longer average C–O bond in **1** than in **3** (1.329(3) Å *vs.* 1.317(3) Å).

The EPR spectra of **1**, **2** and **3** in frozen CH_2Cl_2 solution at 77 K exhibit an axial signal characteristic of that of Cu^{II}–N_2O_2 complexes possessing a $(dx^2-y^2)^1$ or $(dxy)^1$ ground state ($S = 1/2$) with $g_{zz} \gg g_{xx} \sim g_{yy} > g_e$ (Fig. 2).[7] The parallel region of the spectra (*i.e.* the g_{zz} and $A_{zz}\{^{63,65}Cu\}$) is known to be sensitive to the geometry around the Cu(II) ion.[8] Thus, a distortion from a square planar to a tetrahedral geometry induces an increase of g_{zz} and a decrease of A_{zz}.[8] In that respect, the simulated A_{zz} values for **2** (165 G) and **3** (160 G) are found to be similar but both are significantly smaller than that of **1** (195 G); whereas the g_{zz} value for **2** and **3** (2.258) is significantly higher than that of **1** (2.210). Thus, clearly the difference in EPR parameters for **2** and **3** as compared to **1**[4] in solution reflects their difference in geometry: *i.e.* whilst **1** is square planar, **2** and **3** are significantly distorted.

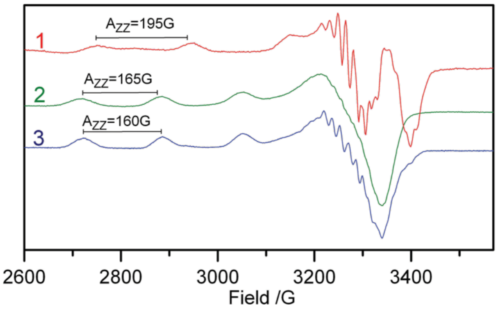

Fig. 2 X-band EPR spectra of **1**, **2** and **3** (~1 mM) in CH_2Cl_2 recorded at 77 K.

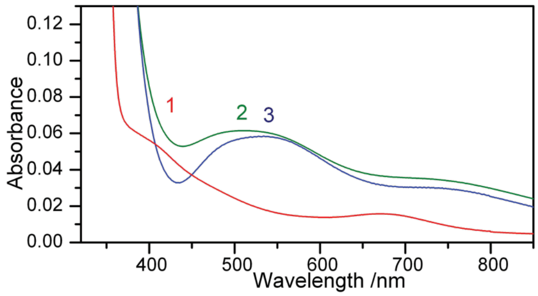

Fig. 3 UV-vis spectra of **1**, **2** and **3** (~1 mM) in CH_2Cl_2 at 298 K [λ_{max}/nm (ε/M^{-1} cm^{-1}) recorded using a 0.1 cm cell: 407 nm (539); 684 nm (150) **1**, 520 (610), 755 sh (350) **2**; 535 (580), 745sh (300) **3**].

Similarly, the UV-vis spectra (CH_2Cl_2 at 298 K, Fig. 3) of the purple coloured complexes **2** and **3** are similar but distinct from that of the brown complex **1**. The spectra of **2** and **3** resemble those of other distorted square planar Cu–N_2O_2 complexes; displaying a relatively intense phenolate to Cu(II) charge transfer band at 520–535 nm (ε = 610–580 M^{-1} cm^{-1}) and weaker ligand field transition at 755–745 nm (ε = 350–300 M^{-1} cm^{-1}); Fig. 3.[4] Importantly, the phenolate to Cu(II) charge transfer transition appears at much higher energy for **1** (407 nm (ε = 539 M^{-1} cm^{-1}) than for **2** and **3** (Fig. 3). This most likely evidences the effect of the H-bonding on the coordinated phenolate in **1**, particularly in pulling electron density from the coordinated phenolate ring.

The CV of **1**,[5] **2** and **3** in CH_2Cl_2 at room temperature, all display two reversible one-electron oxidation processes at $E_{1/2}$/V *vs.* Fc/Fc$^+$: 0.430/0.580 (**1**);[5] 0.317/0.594 (**2**); 0.267/0.618 (**3**); Fig 4. These are assigned to the successive ligand-based oxidation to the corresponding *mono*-, and *bis*-phenoxyl radical complexes. Remarkably, the first oxidation occurs at much lower potential for the tetrahedrally distorted **2** and **3** than for the H-bonded square planar **1** ($\Delta E_{1/2}$ = 110 mV and 160 mV, respectively). Thus, H-bonding to a coordinated phenolate increases its oxidation potential.

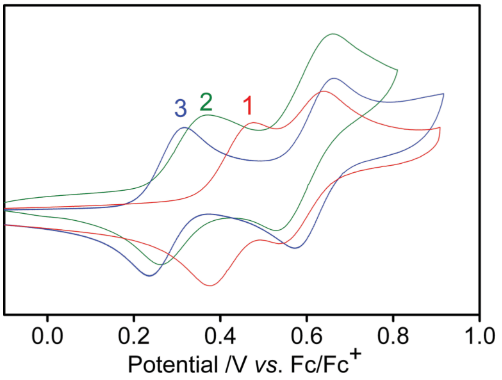

Fig. 4 The cyclic voltammograms of **1** , **2** and **3** (~1 mM) in CH_2Cl_2 at 298 K containing $[NBu_4{}^n][PF_6]$ (0.15 M) as supporting electrolyte, at a scan rate of 100 mV s^{-1}.

The electrochemical, one-electron oxidation of **1**, **2** and **3** at 263 K under N_2 in CH_2Cl_2 containing $[NBu_4{}^n][PF_6]$ (0.15 M) as the background electrolyte, led to a significant colour change from purple to dark brown. The corresponding oxidised species **1**$^+$, **2**$^+$ and **3**$^+$ were proved to be relatively stable at room temperature with half-lives of 255, 71 and 478 min, respectively. The highest stablity obtained for **3**$^+$ suggests that steric hindrance around the radical prevent decomposition pathways.

The UV-vis spectra of 1^+, 2^+ and 3^+ are very similar, and all exhibit an intense absorption band at *ca.* 440 nm; together with a less intense low energy broad NIR band at *ca.* 950 nm [λ_{max}/nm (ε/M^{-1}cm^{-1}): 440 nm (2420), 970 nm (590) 1^+; 438 (3400), 920 (1200) 2^+; 442 (3800), 910 (1240) 3^+] (Fig. 5). Both these bands are characteristic of those of phenoxyl radical complexes, the former being assigned to the π–π* transition of the coordinated phenoxyl radical.[3] The similarity of the spectra of 1^+, 2^+ and 3^+ indicates that, as opposed to those of their parent complexes, the absorption spectra of the Cu(II)-phenoxyl radical complexes are less sensitive to geometrical change and/or H-bonding interaction. Although one should note that whilst the *ca.* 440 nm band in 1^+ displays a gaussian shape, those of 2^+ and 3^+ are unsymmetrical and display a quasi-plateau in the 400–440 nm region. These subtle changes may help to differentiate Cu(II)-phenoxyl radicals with varying local environments.

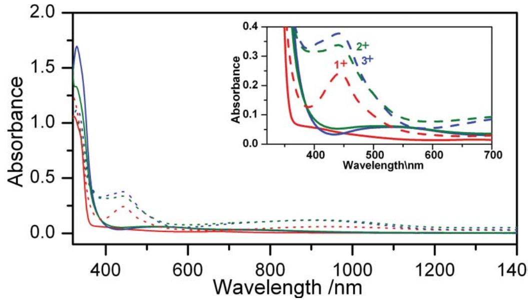

Fig. 5 UV-vis spectra (straight line) of **1** (red), **2** (green) and **3** (blue) and the electrochemically generated (dotted line) $\mathbf{1}^+$ (red), $\mathbf{2}^+$(green) and $\mathbf{3}^+$ (blue) in CH_2Cl_2 (*ca.* 1 mM) containing [NBu_4^n][PF_6] (0.15 M) at 298 K. Inset: enlarged 300–700 nm region.

The electrochemical one-electron oxidations of **2** and **3** are accompanied by a significant reduction in the intensity of their EPR signals, *i.e.* 2^+ and 3^+ in CH_2Cl_2 at 77 K are essentially EPR silent, only a residual Cu(II) signal, ∼<5% of the intensity of the parent complex, was observed for **2** and **3** (see ESI†). The lack of an EPR signal for 2^+ and 3^+ is consistent with an $S = 0$ or 1 (with a very large zero-field splitting) ground state, resulting from magnetic coupling between an $S = \frac{1}{2}$ Cu(II) centre and an $S = \frac{1}{2}$ coordinated radical ligand, as observed for 1^+ and other Cu(II)-phenoxyl radical complexes [Cu(II)(^{R}L)(^{R}L$^•$)]$^+$.[3]

Conclusions

We herein have demonstrated that the redox, spectroscopic and chemical properties of Cu(II)-phenolate and its corresponding oxidised Cu(II)-phenoxyl radical species are modulated by steric and H-bonding effects. These biomimetic studies are relevant to understand the factors that govern the reactivity of the Cu(II)-Tyrosyl radical moiety of GO.

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Notes and references

‡ *Crystal data* for **3**. $C_{42}H_{62}CuN_4O_2$, $M_r = 718.50$, monoclinic, space group $P2_1/c$ (no. 14), $a = 25.4688(7)$, $b = 9.5148(3)$, $c = 16.9516(5)$ Å, $\beta = 91.368(10)°$, $U = 4106.7(2)$ Å^3, $Z = 4$, $\rho_{cald} = 1.162$ g cm^{-3}, μ(Mo-Kα) = 0.569 mm^{-1}, 46 126 reflections measured, 9913 unique, $T = 120$ K, final $R_1 = 0.0514$ (for 7891 reflections with $I > 2\sigma(I)$), wR_2 (all data) = 0.1342. CCDC number 846432.

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