

Oxidations of Primary Alcohols with a Copper(II) Complex as a Possible Galactose Oxidase Model

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N,N'-(2-Hydroxy-propane-1,3-diyl)bis(salicylaldiminato)copper(II) was found to be an effective catalyst for the oxidation of ethanol, n-propanol, or hydroxyacetone in the presence of KOH under O₂; the X-ray crystal structure shows that the co-ordination geometry of the copper is significantly distorted toward tetrahedral from square planar with two oxygens and two nitrogens from salicylaldimine moieties.

Galactose oxidase (EC 1.1.3.9) is a copper containing enzyme which catalyses two-electron oxidation of not only D-galactose but also a variety of primary alcohols (equation 1).^{1,2} Since galactose oxidase is the only known enzyme that contains one

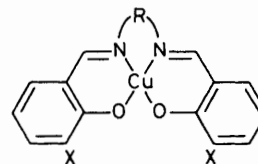


type II copper and no other prosthetic group, the structure of the copper site as well as the reaction mechanism has received considerable attention. However, there are only limited data on the protein ligands around the copper available, although co-ordination of 2 to 4 imidazole groups and some oxygens in tetragonal or square pyramidal geometry has been proposed.³⁻⁵ As one approach toward understanding the role of copper in the catalysis, we have attempted to develop a model system which mimics oxidation of a primary alcohol with a copper(II) complex having a N, O, or S donor set.

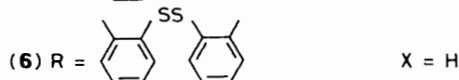
The catalytic activities of the copper(II) complexes, (1)–(7), were examined for EtOH oxidation. Without an additive, no reaction proceeded with any of these complexes. In the presence of KOH, however, (1)[†] showed catalytic activity;

[†] (1) was prepared by the reaction of 1,3-bis(salicylideneamino)propan-2-ol with 1 equiv. of copper(II) acetate monohydrate in ethanol. Satisfactory elemental analyses were obtained. When the ligand is reacted with 2 equiv. copper(II) acetate monohydrate a different colour species, a dinuclear copper(II) complex, is formed.⁶

when 21.6 mg of (1) (0.06 mmol) was stirred in 30 ml of 0.1 M KOH ethanolic solution under 1 atm O₂ for 10 h at 40 °C, 0.35 mmol of acetaldehyde was formed. Under comparable conditions, 0.04 mmol of propionaldehyde and 0.70 mmol of



- | | |
|---|---------|
| (1) R = CH ₂ CH(OH)CH ₂ | X = H |
| (2) R = CH ₂ CH ₂ | X = H |
| (3) R = CH ₂ CH ₂ | X = OMe |
| (4) R = CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ | X = H |



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| (7) R = CH ₂ CH ₂ CH ₂ NHCH ₂ CH ₂ CH ₂ | X = H |
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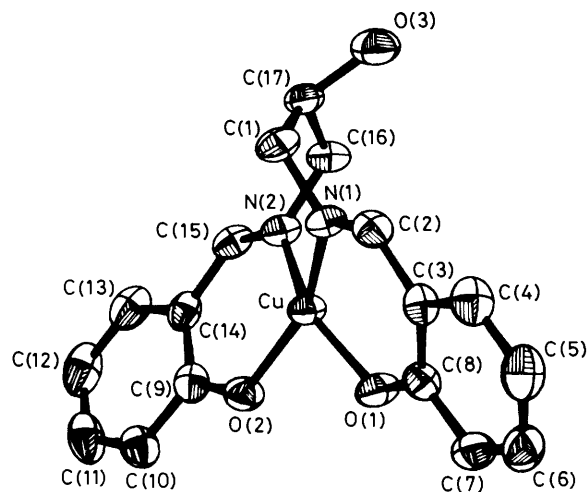


Figure 1. Perspective view (ORTEP, 50%) of (1). Selected bond lengths (Å) and angles (°): Cu–O(1), 1.901(2); Cu–O(2), 1.900(2); Cu–N(1), 1.937(3); Cu–N(2), 1.946(3); O(1)–C(8), 1.313(4); O(2)–C(9), 1.326(4); N(1)–C(2), 1.281(5); N(2)–C(15), 1.293(4); O(3)–C(17), 1.419(5); O(1)–Cu–O(2), 91.6(1); O(1)–Cu–N(1), 94.0(1); O(1)–Cu–N(2), 153.5(1); O(2)–Cu–N(1), 154.5(1); O(2)–Cu–N(2), 94.5(1); N(1)–Cu–N(2), 91.5(1); C(1)–N(1)–C(2), 119.8(3); C(15)–N(2)–C(16), 119.1(3); O(3)–C(17)–C(1), 104.3(3); O(3)–C(17)–C(16), 112.7(3); N(1)–C(1)–C(17), 112.9(3); N(2)–C(16)–C(17), 113.9(3).

pyruvic aldehyde were formed with (1), from *n*-propanol and hydroxyacetone, respectively. Nickel(II), cobalt(II), or zinc(II) complexes with 1,3-bis(salicylideneamino)propan-2-ol were inactive, as was copper(II) acetate.

Complex (1) in dimethylformamide (DMF) (dark green) exhibits an electronic spectrum with two absorption bands at 370 (ϵ 11300 mol⁻¹ dm³ cm⁻¹) and 611 nm (263) in the 300–1100 nm region, whereas galactose oxidase (light murky green) has bands at 445 (1155), 630 (1015), 775 nm (905).⁷ The e.s.r. spectrum of (1) measured in CHCl₃ at -196°C [g_{\parallel} = 2.247, g_{\perp} = 2.053, A_{\parallel} = 173.2 G, $a(N_{\perp})$ = 27.5 G] bears close similarity to that of galactose oxidase⁶ [g_{\parallel} = 2.277, g_{\perp} = 2.055, A_{\parallel} = 175.0 G, $a(N_{\perp})$ = 15.1 G; $1G = 10^{-4}$ T].

Although the detailed mechanism has not been elucidated yet, the *X*-ray crystal structure of (1)[‡] implies that the suitable co-ordination geometry and ligand donor set may be the key

[‡] Crystal data for (1): C₁₇H₁₆CuN₂O₃, $M = 359.9$, triclinic, space group $P\bar{1}$, $a = 9.620(2)$, $b = 10.685(3)$, $c = 7.782(1)$ Å, $\alpha = 104.66(2)$, $\beta = 95.50(2)$, $\gamma = 91.66(3)^{\circ}$, $U = 769.1(3)$ Å³, $Z = 2$, $D_c = 1.56$ g cm⁻³, $D_m = 1.55$ g cm⁻³, $F(000) = 370$, graphite monochromated Mo- K_{α} radiation, $\lambda = 0.71069$ Å, $\mu(\text{Mo-}K_{\alpha}) = 13.70$ cm⁻¹. The data were collected on a Rigaku four-circle diffractometer using the ω - 2θ scan mode in the range $3 < 2\theta < 50^{\circ}$. The structure was solved by direct method using the program MULTAN 78 and refined by full-matrix least squares. All the H atoms were found on a difference map. The final refinement was made with anisotropic and isotropic thermal parameters for non-hydrogen and H atoms, respectively, with the $R = 0.040$ ($R_w = 0.039$) from 2518 unique reflections for which $F_o > 3\sigma(|F_o|)$. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic data Centre. See Notice to Authors, Issue No. 1, 1986.

factor of the catalytic activity. § The structure of (1) is shown in Figure 1. The co-ordination geometry of the copper is described as square planar significantly distorted toward tetrahedral with two oxygens and two nitrogens from salicylaldehyde moieties; the dihedral angle between O(1)–Cu–N(1) and O(2)–Cu–N(2) planes is 35.7°. The oxygen of the hydroxy group on the 1,3-diaminopropan-2-ol backbone does not interact with the copper. This forms a hydrogen bond with the oxygen in salicylaldehyde moieties of a molecule related by translation along the *c* axis $x, y, -1.0 + z$ [H(16)–O(2'), 1.82(6) Å; O(3)–O(2'), 2.744(4) Å].

It is established that copper(II) complexes with *N*-alkylsalicylaldehydes can occur in square planar or tetrahedral configuration, depending on the bulkiness of the alkyl group and of the ring substituents.⁸ In the case of tetra- or penta-dentate Schiff base copper(II) complexes like (1), however, only a few examples^{9,10} of tetrahedral distortion from square planar are known. Among the complexes (2)–(7), the crystal structures are known for (2),¹¹ (3),¹² (5);^{11b,13} the co-ordination geometry of the copper is regular square planar with an N₂O₂ ligand donor set. ¶ The configurations of (6) and (7) are anticipated to be square pyramidal with N₂O₂S and N₃O₂ ligand donor sets, respectively, from the crystal structures of the corresponding nickel(II)¹⁴ and iron(III)¹⁵ complexes.

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§ Hydrolysis (or ethanolsis) of (1) under reaction conditions does not occur considerably, since e.s.r. and visible spectra of (1) in 0.1 M KOH ethanolic solution are completely consistent with the ones in ethanol.

¶ The co-ordination geometry of copper in (4) is suggested to be regular square planar from the e.s.r. spectrum.