

A functional model of galactose oxidase: catalytic oxidation of primary alcohols with a one-electron oxidized copper(II) complex

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The electrochemically one-electron oxidized copper(II) complex of *N, N'*-bis(2-hydroxy-3,5-di-*tert*-butylbenzyl)-1,2-ethylenediamine catalyses, in the presence of KOH at room temperature, the oxidation of primary alcohols into aldehydes (turnovers > 30); secondary alcohols are not oxidized under the same conditions.

Galactose oxidase (GOase), a mononuclear copper(II) enzyme with a N_2O_2 coordination sphere that harbours a tyrosyl radical in its oxidized active form (Fig. 1), catalyzes the two-electron oxidation of primary alcohols into aldehydes.¹ Copper(II) complexes of tetradentate ligands have been described as structural models of the active site in GOase,^{2–8} but only a limited number of data are available concerning functional models exhibiting activity towards the oxidation of primary alcohols.^{9–11} A functional model of GOase has been recently described,¹¹ involving the one-electron oxidized copper(II) complex of a salen-type ligand. This model allows the catalytic oxidation of benzylic alcohol into benzaldehyde (9.2 turnovers, 5 hours, 20 equivalents of $[TPA]^+ [SbCl_6]^-$, 20 equivalents of BuLi, substrate as solvent). These data prompted us to present our first results concerning the activity of the electrochemically one-electron oxidized copper(II) complex of the ligand H_2L^\dagger (Fig. 1), which allows the catalytic oxidation of primary alcohols into the corresponding aldehydes with more than 30 turnovers.

The electrochemical behaviour of $Cu^{II}L$ was studied by cyclic voltammetry in dimethylformamide (DMF) using the Ag/AgNO₃ 10 mmol dm⁻³ system as reference electrode. The

CV curve is characterized in the anodic region by three successive electrochemical systems [Fig. 2(a) and (b)]. The first one is quasi-reversible ($E_{1/2} = 0.11$ V; $\Delta E_p = 80$ mV; $v = 0.1$ V s⁻¹), the two others appear irreversible ($E_{pa} = 0.45$ and 0.76 V respectively). Exhaustive potentiostatic oxidation at a potential slightly greater than 0.11 V gives $n = 1$ exchanged electron for the first electrochemical system. Due to the moderate stability of the one-electron oxidized species at room temperature, the spectroscopic properties were obtained at -60 °C after addition of a stoichiometric amount of

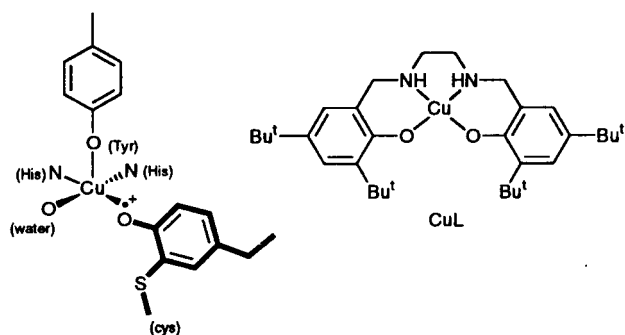


Fig. 1 Active site in GOase (oxidized active form) and the complex $Cu^{II}L$

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[†] The free ligand H_2L was synthesized according to reference 12. The dark green $Cu^{II}L$ complex was obtained as a powder from $H_2L + CuClO_4 + 2 NEt_3$ in CH_2Cl_2 ; FAB⁺MS: 559 $[M + 1]$. In DMF: $\lambda = 604$ and 407 nm (486 and 1940 dm³ mol⁻¹ cm⁻¹). EPR reveals a square-planar complex: $A_{||} = 175$ G, $g_{||} = 2.23$, $g_{\perp} = 2.01$, $g_{||}/A_{||} = 130$ cm.

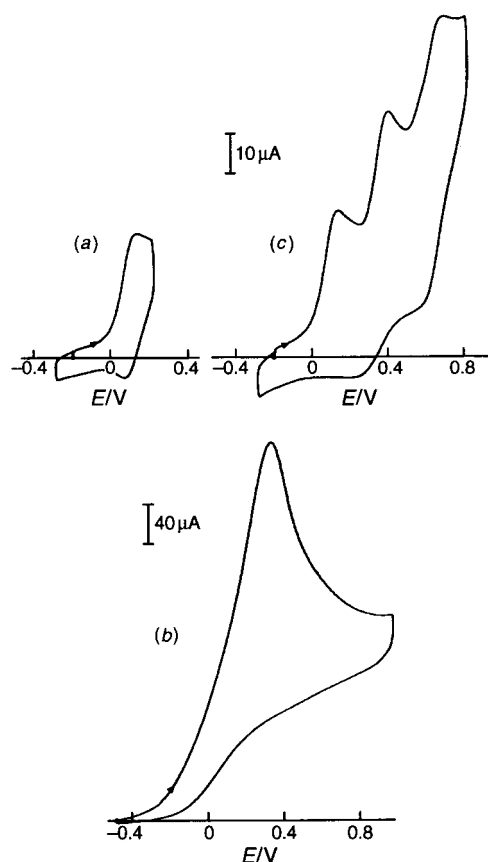


Fig. 2 CV curves on a Pt electrode ($\Phi = 5$ mm) of $Cu^{II}L$ (9.7 mmol dm⁻³ in DMF) + TPAB (0.1 mol dm⁻³, 4 ml); scan rate: 0.1 V s⁻¹; E/V vs. Ag/AgNO₃ (10 mmol dm⁻³); recorded up to 0.20 (a), 0.80 (b) and after addition of EtOH (1.6 ml) + KOH (7.2×10^{-2} mol dm⁻³), up to 1.0 V (c)

$\text{Ce}(\text{NO}_3)_6(\text{NH}_4)_2$ to $\text{Cu}^{\text{II}}\text{L}$ in DMF. These properties are comparable to previously reported analogs.⁸ The one-electron oxidized solution at -60°C reveals an EPR-silent species characterized by an electronic spectrum with main features at 610 (4800), 440 (2500) and 403 nm ($2500\text{ dm}^3\text{ mol}^{-1}\text{ cm}^{-1}$).[‡] Upon warming, $\text{Cu}^{\text{II}}\text{L}$ is reformed quasi-quantitatively. Thus the first electrochemical step of the oxidation of $\text{Cu}^{\text{II}}\text{L}$ in DMF electrolyte leads to the formation of a coupled radical cation species at a potential close to that of GOase¹³ ($E_{\frac{1}{2}} = 0.23\text{ V vs. SCE}$) and at a significantly lower potential than for the salen-type complexes described by Stack and Wang.¹¹

In the presence of a primary alcohol in basic medium, a strong modification of the CV curve is observed [Fig. 2(c)]. After addition of a KOH alcoholic solution, the CV curve presents only one large anodic irreversible peak overlapping the three electrochemical systems observed without an additive. The peak potential depends on the primary alcohol considered: $E_{\text{pa}} = 0.47, 0.42, 0.25, 0.20\text{ V}$ in the presence of MeOH, EtOH, 1-PrOH or 1-BuOH respectively. This behaviour is characteristic of an electrocatalytic process. In contrast, under comparable conditions, no modifications in the CV curve are observed in the presence of 2-BuOH and only a slight cathodic shift of the first electrochemical system is observed in the presence of 2-PrOH.

Only the primary alcohols are thus involved in the catalytic process. This result has been confirmed by exhaustive potentiostatic electrolysis performed at a potential corresponding to the peak current determined by CV under the same experimental conditions. The electrolyses on a Pt grid have been conducted in DMF-alcohol (2:1, v/v) electrolyte in the presence of $\text{Cu}^{\text{II}}\text{L}$ (1 mmol dm^{-3}) and KOH (40 mmol dm^{-3}), at room temperature, up to the obtention of a residual current corresponding to 1% of the initial current. At this stage, the CV curve shows that the complex is fully degraded. Analysis of the resulting solution by HPLC shows that the electrocatalytic oxidation of each primary alcohol (MeOH, EtOH, 1-PrOH or 1-BuOH) leads to the formation of the corresponding aldehyde with a Faradaic yield close to 90%. The number of turnovers performed by the complex during the electrolysis is close to 32 whatever the surveyed primary alcohol, showing that the degradation rate of the complex is independent of the alcohol. The efficiency of $\text{Cu}^{\text{II}}\text{L}$ as catalyst for electrooxidation of primary alcohols appears somewhat better than that found with related Cu^{II} complexes^{10,11} and electrooxidation can be performed at low potentials. It has to

be emphasized that potentiostatic electrolysis performed under the same experimental conditions in the presence of secondary alcohol (2-PrOH and 2-BuOH) did not result in the corresponding ketone confirming the selectivity of the electrocatalytic process. Also, no electrooxidation of the surveyed alcohol occurs in the range of the explored potentials in the absence of $\text{Cu}^{\text{II}}\text{L}$. Accessibility of the alcohol to the catalytic site and co-ordination geometry of the copper (tetrahedral distortion has been found to be necessary^{10,11}) may be factors of prime importance in the efficiency of the catalyst. At -60°C , in the presence of KOH and of a large excess of ethanol, the one-electron oxidized species gives a new electronic spectrum: 585 (3600) and 398 nm ($5000\text{ dm}^3\text{ mol}^{-1}\text{ cm}^{-1}$). Such a blue shift is in agreement with the ethoxide binding into the one-electron oxidized species.

Further studies are in progress concerning the mechanism of the catalytic process.

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‡ These features were also observed in the UV/VIS spectra with withdrawal of the electrolytic solution during electrolysis.

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