

Type 3 Copper Model Chemistry. Dioxygen Activation by Binuclear Two-co-ordinate Copper(I) Complexes derived from L-Histidine and L-N^t-Methylhistidine

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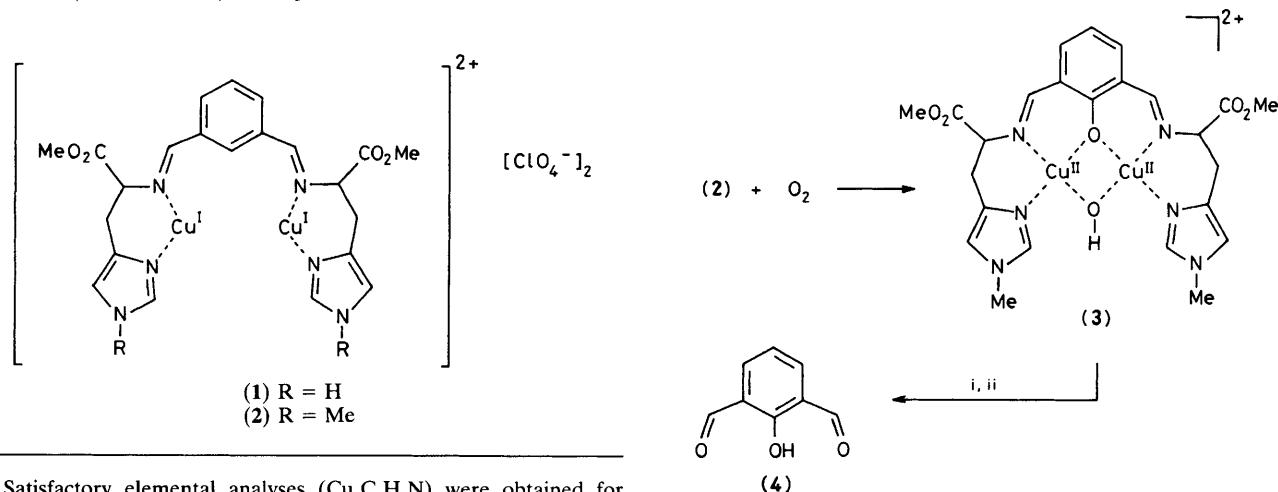
The reaction of dioxygen with the binuclear two-co-ordinate copper(I) complexes derived from the condensation of benzene-1,3-dicarbaldehyde and two molecules of L-histidine methyl ester or L-N^t-methylhistidine methyl ester occurs with hydroxylation of the aromatic nucleus at position 2, producing binuclear phenoxy-bridged copper(II) complexes.

Much current interest in copper biomimetic chemistry focuses on the synthesis of copper(I) systems as mimics for the reduced state of Type 3 active sites of copper proteins.¹⁻⁵ Very little information is available on the structures of these protein copper(I) sites except for the possible involvement of imidazole groups in metal binding and the necessity of co-ordinative unsaturation of the metal ions.⁶ Two-co-ordination is a likely possibility for copper(I) in these binuclear sites, although other protein ligands may become involved during activity.⁶ Only a few synthetic two-co-ordinate copper(I) complexes containing nitrogen donors have been reported;³ these display somewhat unusual behaviour, since they are apparently reluctant to react with carbon monoxide, while their reactions with dioxygen have not been understood. We report here binuclear two-co-ordinate copper(I) complexes containing L-histidine or L-N^t-methylhistidine residues for which dioxygen reactivity has been characterized.

The binuclear complexes (1) and (2) were prepared by condensation of benzene-1,3-dicarbaldehyde and 2 equiv. of free L-histidine methyl ester, or L-N^t-methylhistidine methyl ester (prepared according to ref. 7), respectively, in the presence of Cu(MeCN)₄ClO₄ (2 equiv.) in refluxing methanol under an inert atmosphere. The resulting yellow precipitates were recrystallized from methanol.[†] The i.r. and ¹H n.m.r. spectra of the complexes indicate that the ester groups are not co-ordinated to copper(I). The structure of the metal centres in (1) and (2) is thus assumed to be two-co-ordinate, although molecular models show that the fragments N-Cu-N cannot achieve a perfectly linear arrangement. As expected, neither (1) nor (2) form stable carbonyl adducts. Only weak CO adducts are formed in solution [$\nu(\text{CO})$ at 2093–2096 cm⁻¹], but these readily lose CO on evaporating the solvent under vacuum.

When solutions of (1) or (2) in dry MeCN or dimethylformamide (10⁻³–10⁻⁴ M) are exposed to dioxygen (1 atm; room

temp.) the colour of the solution gradually turns green (~1 h). For (1) the electronic spectra of the oxygenated solutions show the growth of a modest, poorly defined absorption in the range 300–400 nm ($\epsilon \sim 1500 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for the shoulder near 360 nm) and a weak band near 650 nm ($\epsilon \sim 150$). Bands near these wavelengths appear also in the corresponding c.d. spectra, while the frozen-solution e.s.r. spectra display only broad signals near $g = 2.1$. The near-u.v. spectral changes are indicative of the formation of imidazolate-bridged copper(II) compounds,⁸ while the amount of dioxygen absorbed by the solutions, measured manometrically, corresponds to 1 O₂ molecule per 4 Cu atoms and shows that dioxygen is reduced to water or hydroxide ion rather than hydrogen peroxide. The oxygenation of (2) produces an intense near-u.v. absorption band near 355 nm ($\epsilon \sim 6000 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) and a much weaker visible band near 600 nm ($\epsilon \sim 110$); manometric measurements of dioxygen uptake correspond to 1 O₂ molecule per 2 Cu atoms. The i.r. spectrum of the product (3) isolated upon evaporation of the oxygenated solutions is practically superimposable on that of (2) but contains two additional bands near 1560 and 3500 cm⁻¹. The spectral characteristics of (3) are thus very similar to those of phenoxy- and hydroxy-bridged binuclear copper(II) complexes of the imines derived from 2-hydroxy-5-methylbenzene-1,3-dicarbaldehyde.⁹ In particular, the near-u.v. band at ~355 nm and the i.r. band at ~1560 cm⁻¹ are associated with the low-energy $\pi \rightarrow \pi^*$ electronic transition and a typical vibration, respectively, of the 2-hydroxyphenylimino chromophores,^{9,10} while the i.r. band at ~3500 cm⁻¹ involves formation of a hydroxy group. Therefore, the oxygenation of (2) occurs with hydroxylation of the aromatic nucleus according to the reaction outlined in Scheme 1. This is confirmed by the analytical data of (3)[†] and the isolation of 2-hydroxybenzene-1,3-dicarbaldehyde, (4), on treatment of (3) with



[†] Satisfactory elemental analyses (Cu, C, H, N) were obtained for these compounds.

Scheme 1. Reagents: i, HCl-H₂O; ii, CHCl₃.

aqueous acid followed by extraction with chloroform.‡ Interestingly, when the oxygenation of (1) and (2) is carried out in methanol solution, the spectral features of (3) develop in both cases, but for (1) the product corresponding to (3) is formed either in part or at a much slower rate. Also, the amount of O₂ absorbed by (1) in methanol is higher than that observed in the nonprotic media and we are currently trying to establish the full distribution of the products of this reaction.

The copper-mediated hydroxylation of the aromatic ring of (1) and (2) is formally similar to that effected by copper mono-oxygenases.^{6a} Although this reaction has precedent in synthetic copper systems,^{1a,11} the present results show the feasibility of binuclear, two-co-ordinate copper(I) centres bound to histidine imidazole groups for the reduced state of Type 3 active sites of copper proteins.

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‡ Spectroscopic data for (4): ¹H n.m.r. (CDCl₃, 60 MHz): δ 11.6 (~s, 1 H, OH; exchanges with D₂O), 10.2 (~s, 2 H, CHO), 7.6–8.2 (m, 2 H, 4-H + 6-H), 6.7–7.2 (m, 1 H, 5-H). I.r. (CHCl₃): 1687; 1662 cm⁻¹ [ν(C=O)]. m/z: 150 (M⁺), 134, 133 (M–17), 122 (M–28), 121 (M–29).