Copper(I) Complex-catalysed Reduction of Dioxygen to Water and Oxidation of Alcohols: a Model of Copper(I)-containing Oxidase

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Summary Binary copper(I) complexes with 2,2′-bipyridine, 4,4′-dimethyl-2,2′-bipyridine, 2,2′,2″-terpyridine, and ethylenediamine and ternary copper(I) complexes containing 2,2′-bipyridine and β-diketonates catalyse the reduction of O_2 to H_2O and the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively

COPPER proteins are metalloenzymes which play an important role in oxidation–reduction, oxygenation, and oxygen carrying [1] Most of the proteins contain copper(II) ions Tyrosinase is a typical copper(I)-containing protein and catalyses both the reduction of O_2 to H_2O and the reduction of one atom of O_2 to H_2O with hydroxylation of the other atom Few copper(I) complexes having enzyme-like activity have been reported [2] We report here some copper(I) complexes which catalyse the reduction of O_2 to H_2O together with oxidation of alcohols, *i e*, a model of copper(I)-containing oxidase, and our studies on the reaction mechanism The copper(I) complexes were obtained in two forms a, as the chlorides $[CuL_2]Cl$, and b, as the mixed ligand complexes Cu(L)A To obtain the complexes $[CuL_2]Cl$ copper(I) chloride crystals were added to alcoholic solutions of the ligands (L) under N_2 in the mole ratio 1:2 and after 3 h stirring the copper(I) complexes, $[CuL_2]Cl$, were formed quantitatively In the preparation of the mixed ligand copper(I) complexes, Cu(L)A, the mole ratio of CuCl:L:A used was 1:1:1, where L is 2,2′-bipyridine(bpy), 4,4′-dimethyl-2,2′-bipyridine (4,4′-Me_2-bpy), and ethylenediamine (en) and A is lithium acetylacetonate (Li-acac) and lithium thenoyltrifluoroacetonate (Li-tta) Dioxygen was passed into alcoholic solutions of $[CuL_2]Cl$ and Cu(L)A to give ketones or aldehydes as products, as confirmed by g l c The products could also be precipitated as their 2,4-dinitrophenylhydrazones which were then identified by i r spectroscopy and satisfactory elementary analyses The quantity of water produced in the oxidation was determined by Karl–Fischer titration

TABLE Acetaldehyde formed on copper(I) complex-catalysed oxidation of ethanol [a]

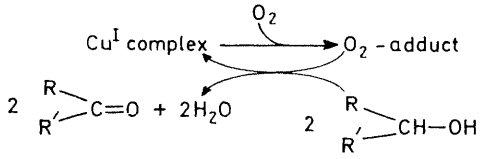
Copper(I) complex[b]	Acetaldehyde/10^{-3}M
$[Cu(4,4'\text{-}Me_2\text{-bpy})_2]Cl$ (**1**)	36
$[Cu(bpy)_2]Cl$ (**2**)	28
[Cu(bpy) (tta)]	15
[Cu(bpy) (acac)]	10
$[Cu(en)_2]Cl$	5·3
[Cu(tpy)Cl] (**3**)	1·5
$[Cu(phen)_2]Cl$ (**4**)	Not detected
$[Cu(5\text{-}NO_2phen)_2]Cl$ (**5**)	Not detected
$[Cu(5\text{-}Cl\text{-}phen)_2]Cl$ (**6**)	Not detected
$[Cu(2,9\text{-}Me_2\text{-}phen)_2]Cl$ (**7**)	Not detected
$[Cu(biq)_2]Cl$ (**8**)	Not detected
$[Cu(4\ 7\text{-}Me_2\text{-}phen)_2]Cl$ (**9**)	Not detected

[a] Flow rate of O_2 : 190 ml min^{-1} [b] Concentration of copper(I) complex in ethanol = 5×10^{-4} M

The Table shows the concentration of acetaldehyde formed from the copper(I) complex-catalysed oxidation of ethanol under O_2 for 1 h at 15 °C The catalysis of $[Cu(4,4'\text{-}Me_2\text{-bpy})_2]Cl$ (**1**) and $[Cu(bpy)_2]Cl$ (**2**) is large compared to that of [Cu(tpy)Cl]Cl (**3**) [(tpy)Cl = 2,2′,2″-terpyridine] and $[Cu(en)_2]Cl$ which are easily oxidized to the corresponding copper(II) complexes Complexes (**1**) and (**2**) are very slowly oxidized to the corresponding copper(II) complexes and show no catalytic activity after *ca* 10 h reaction under the oxygenation conditions Copper(II) complexes such as $[Cu(bpy)_2]Cl_2$, [Cu(tpy)Cl]Cl, [Cu(bpy)-(acac)]Cl, and $[Cu(4,4'\text{-}Me_2\text{-bpy})_2]Cl_2$ do not catalyse the oxidation Also $[Cu(phen)_2]Cl$ (**4**), $[Cu(5\text{-}NO_2\text{-phen})_2]Cl$ (**5**), $[Cu(5\text{-Cl-phen})_2]Cl$ (**6**), $[Cu(2,9\text{-}Me_2\text{-phen})_2]Cl$ (**7**), and $[Cu(biq)_2]Cl$ (**8**), the copper(I) states which are more stable than those of (**1**) and (**2**), show no catalysis (phen, acac, and biq are 1,10-phenanthroline, acetylacetonate, and 2,2′-biquinoline, respectively) Since (**1**) and (**2**) possess appropriate redox potentials for this oxidation (Cu^I/Cu^{II}), catalysis may be extensive This is supported by the redox potentials of (**1**) (+91 mV) and (**2**) (+120 mV) being between those of (**3**) (−80 mV) and (**4**) (+174 mV) [3] The dependence of the catalytic activity of the copper(I) complexes on their redox potentials suggests the formation of the O_2-adduct of the complex as an intermediate [4] This is supported by the fact that exposure of the reddish brown ternary copper(I) complexes in alcoholic solution to oxygen yields a pale blue species and the solution is reconverted into the reddish brown form by deaeration with N_2 for 3 h Formation of the O_2-adduct of (**2**) has been suggested by a kinetic study on the oxidation of (**2**) in aqueous solution [5]

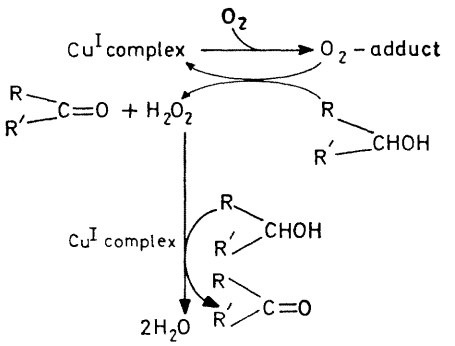
Another important factor in the catalysis is the flexibility of the copper(I) complexes The Cu^I complex which has a tetrahedron structure must change to a five-co-ordinated structure in order to combine with dioxygen The steric barrier to the conformational change of (**1**) and (**2**) is smaller than that for $Cu(4,7\text{-}Me_2\text{-phen})_2Cl$ (**9**), since the 2,2′-bipyridine skeleton, in which the two pyridine groups are bound by a single bond, is more flexible than the 1,10-phenanthroline skeleton [6] Therefore, (**9**) does not combine with O_2 and shows no catalytic properties though its oxidation potential is between that of (**1**) and (**2**) † The mole ratio of aldehyde/water produced in the oxidation of ethanol and propan-1-ol is 1 Primary alcohols are not oxidized to carboxylic acids in the catalysis The mole ratios of ketone/water obtained for the oxidation of propan-2-ol and butan-2-ol were *ca* 0·9 and 0 8, respectively If the copper(I) complexes catalysed a four-electron transfer converting 1 mol of O_2 into 2 mol of H_2O during the oxidation of 2 mol of alcohol to 2 mol of the corresponding aldehyde or ketone (Scheme 1), the mole ratio of the aldehyde or ketone to water should be 1:1 Therefore, the mole ratio obtained for the oxidation of the secondary alcohols cannot be explained by Scheme 1

† Redox potentials (Cu^{II}/Cu^I) of (**1**), (**2**), and (**9**) in 50% dioxan–water are 204, 251, and 220 mV, respectively (see ref 3)



SCHEME 1

We found that copper(I) complexes also catalyse the reduction of H_2O_2 to H_2O during the oxidation of primary and secondary alcohols. In the oxidation of ethanol and propan-1-ol the quantity of aldehyde obtained was equal to the amount of H_2O_2 added but in the oxidation of propan-2-ol and butan-2-ol less ketone was obtained giving acetone and ethyl methyl ketone in 75 and 50% yield, respectively. H_2O_2 in alcohols with a lower dielectric constant may be partially decomposed to H_2O and O_2 by the copper(I) complexes. This suggests the mechanism shown in Scheme 2 for copper(I) complex-catalysed oxidations of alcohols, as it explains the difference in the mole ratio of the oxidation product to water. The possibility of formation of H_2O_2 with the reduction of the O_2-adduct of (**2**) in aqueous solutions has been reported.[5] Copper(I) complexes also catalyse the oxidation of catechol and ethane-1,2-diol. Tyrosinase, which has 4 g atoms of copper(I) per mole, catalyses the reduction of O_2 to H_2O. Those copper(I) complexes which catalyse this reduction are thus models of



SCHEME 2

tyrosinase although in a two-step reduction (O_2 to H_2O_2 then H_2O_2 to H_2O) and the turnover numbers ($\leqslant 0{\cdot}02$) are very small.

In conclusion the catalytic activity of copper(I) complexes depends upon their redox potentials and flexibility which govern the formation of O_2-adducts of the complexes. Work on the copper(I) complex-catalysed oxygenation of monophenols, the oxidation of *o*-diphenols, and the structure of the O_2-adduct is in progress.

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