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A Binuclear Copper(II) Complex of N,N′,N″,N‴-Tetra(2-aminoethyl)-1,1,5,5-pentanetetraamide. A Double Cavity Amide Ligand

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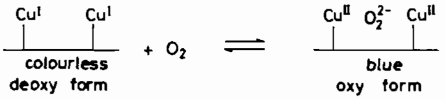
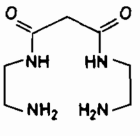
A number of dinucleating ligands have been used to bring two copper atoms into close proximity [1, 2]. Such complexes are of considerable interest as the biological function of many metalloproteins is believed to be associated with the occurrence of pairs of adjacent metal ions capable of mutual interaction via small bridging ligands. Thus in the O_2-carrying haemocyanins, the dioxygen uptake has been attributed [3] to the equilibrium (1), and a number of synthetic macrocyclic Cu(I) complexes having reversible O_2-binding activity with a $2Cu:O_2$ stoichiometry have been described [4, 5].

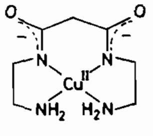


(1)

Hill and Raspin [6] first reported the preparation of the copper(II) complex of 1,9-diamino-3,7-diazanonane-4,6-dione (I) and established that deprotonation of both amide groups occurred on complexation with copper to give (II). Ligands of this type bear a structural resemblance to tripeptides which are well known to ionise two amide protons on coordination to metal ions such as copper(II). A large number of macrocyclic diamides have now been characterised [7].

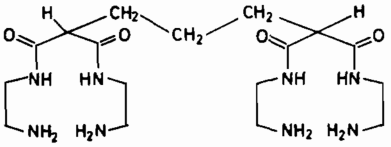


(I)



(II)

The present paper discusses the synthesis and physical properties of the double cavity amide ligand (III) and its copper complex.



(III)

Experimental

Tetraethyl 1,1,5,5-pentanetetracarboxylate was prepared by reaction of diethyl malonate with 1,3-dibromopropane in the presence of sodium ethoxide [8]. The product was fractionated through a Vigreux column, b.p. 198–202 °C at 2.5 mm, i.r. (liquid film) νCO 1735 cm^{-1} (br). ^1H n.m.r., CH_3 1.25 δ (12 H) triplet; OCH_2 4.15 δ (8 H) quartet; $CH_2\mathit{CH_2}CH_2$ 3.30 δ (2 H) triplet, CH_2 1.90 δ (4H) quartet. ^{13}C n.m.r. CH_3 14.11 δ; CH_2 25.14 δ, CH_2 28.41 δ, CH 51.86 δ, CH_2O 61.25 δ, CO_2R 169.14 δ ($CDCl_3$ solution). Calc. for $C_{17}H_{28}O_2$ m/e = 360.1785, found m/e = 360.1768.

The ligand, N,N′,N″,N‴-tetra(2-aminoethyl)-1,1,5,5-pentanetetraamide was prepared as follows. Tetraethyl 1,1,5,5-pentanetetracarboxylate (20 g, 0.055 mol) was added dropwise with stirring to 1,2-diaminoethane (73 g, 1.21 mol) at 0 °C. After completion of the addition, the mixture was allowed to stand at room temperature for 7 days. The excess 1,2-diaminoethane was removed under vacuum to give a brown glassy material. Trituration with ethanol gave a colourless hygroscopic solid (4.9 g). The copper(II) complex was prepared as follows. The ligand (0.5 g) was dissolved in water (7 cm^3) and added to a solution of copper(II) sulphate pentahydrate (0.69 g) in water (7 cm^3). A blue precipitate formed at this stage, which dissolved on slow addition of sodium hydroxide (0.22 g) in water (100 cm^3) The solvent was removed on a rotary evaporator and the residue extracted with methanol. Removal of the methanol gave a purple solid. The crude complex was dissolved in the minimum volume of water, the solution cooled in ice and the complex reprecipitated by the addition of ice-cold ethanol. The complex was filtered and washed with ethanol then ether and dried *in vacuo*. *Anal.* Calc. for $C_{17}H_{32}N_8O_4Cu_2 \cdot 6H_2O$: C, 31.4; H, 6.8; N, 17.2; H_2O, 16.7. Found: C, 31.2; H, 6.6; N, 16.9; H_2O 16.5. The water content was determined by thermogravimetric analysis. The i.r. spectrum (KBr disc) has a strong broad νOH band at *ca.* 3350 cm^{-1} and νNH at 3160 cm^{-1}. There is a strong amide band at 1580 cm^{-1} characteristic of deprotonated copper(II) complexes of this type [7].

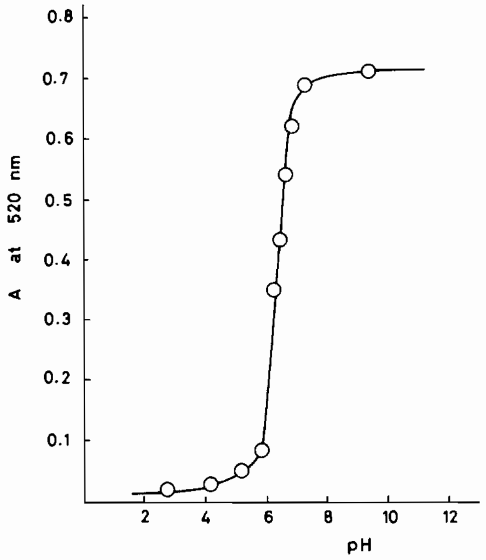


Fig. 1. Spectrophotometric titration of $Cu_2L{\cdot}6H_2O$ with hydrochloric acid.

Nmr measurements (^1H and ^{13}C) were carried out using a Bruker WP80 instrument, with $CDCl_3$ as solvent and TMS as internal standard. Ir spectra were determined on a Perkin Elmer 457 instrument using KBr discs, and visible spectra on a Perkin Elmer 402 spectrophotometer. Magnetic susceptibilities were determined by the Gouy method using $Hg[Co(CNS)_4]$ as calibrant.

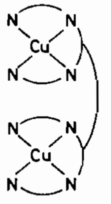
Results and Discussion

Reaction of an excess of 1,2-diaminoethane with 1,1,5,5-pentanetetracarboxylate gives an acceptable yield (*ca.* 25%) of the ligand(III). The tetraamide reacts with copper(II) in basic solution to give a purple complex in which four protons are lost from the ligand,

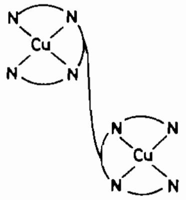
$$LH_4 + 2Cu(II) \rightleftharpoons Cu_2L + 4H^+$$

The binuclear copper(II) complex is neutral, and conductivity measurements confirmed that it was a non-electrolyte in aqueous solution. Spectrophotometric titration of the complex against hydrochloric acid (Fig. 1), indicates that ligand deprotonation begins at pH 5.5 and is complete at pH 8.0. The complex has a symmetrical d–d band at 525 nm (ϵ = 133) and a strong band at 205 nm (ϵ = 15,750). The d–d spectrum may be compared with that of the copper(II) complex of N,N′-di(2-aminoethyl)malondiamide-(II) where λ_{max} is 516 nm (ϵ = 63) [6]. The doubling of the band intensity is fully consistent with the incorporation of two copper(II) ions into the ligand. Molecular models indicate that as a result of the trimethylene bridge the complex is quite flexible and can adopt two extreme conformations which can be represented diagramatically as (IV) and (V).

The eclipsed conformation (IV) is expected to be less favoured than the staggered conformation (V).



(IV)



(V)

Magnetic susceptibility measurements confirm that the complex is paramagnetic with μ_{eff} = 3.52 B.M. at 18 °C (1.76 B.M. per copper(II)). There is no antiferromagnetic coupling of the type which might be expected with (IV). Attempts have been made to ring close the copper(II) complex by reaction with acetone to give two linked macrocycles. Such acetone condensation reactions have been used successfully on a number of occasions [9]. In the present case reddish-brown products are slowly formed on dissolving the complex in acetone, but it has not, as yet, been possible to characterise the products.

Acknowledgement

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