Nuclear Magnetic Resonance Spectra of Dimeric Cupric Compounds

By **William Byers** and **Robert J. P. Williams**,* Inorganic Chemistry Laboratory, University of Oxford, Oxford OX1 3PN

The proton magnetic resonance spectra of some dimeric cupric complexes which are models for copper dimer units in proteins have been examined. The spectra are discussed in terms of a simple theory. The possibility of being able to describe the nature of dimeric copper units in proteins by the temperature-dependence of their proton magnetic resonance spectra is discussed.

As part of our interest in the role of metal ions in biologically important systems we have been investigating the role of copper atoms in oxidase metalloenzymes.[1] The recent suggestion [2,3] that the e.p.r. non-detectable copper atoms in such enzymes as laccase and caeruloplasmin exist in the form of spin-paired cupric dimeric units has led us to consider what properties might be associated with such a unit. Our initial studies are restricted to possible model complexes with the expressed hope that they might reveal methods for distinguishing between such dimers and copper(I) complexes. We now report the solution ^1H n.m.r. of some cupric dimer compounds.

Tetragonal monomeric complexes of the copper(II) ion normally exhibit very broad ill defined ^1H n.m.r. resonances owing to the slow electron spin relaxation of the cupric ion.[4] It seems reasonable to expect however that if copper(II) interactions occur, a mechanism for mutual

---

[1] W. Byers and R. J. P. Williams, unpublished work.

[2] R. Malkin, B. G. Malmström, and T. Vänngård, *European J. Biochem.*, 1969, **10**, 324.

[3] J. A. Fee, R. Malkin, B. G. Malmström, and T. Vänngård, *J. Biol. Chem.*, 1969, **244**, 4200.

[4] B. R. McGarvey, *Transition Metal Chem.*, 1966, **3**, 90.

fast relaxation, which could lead to paramagnetic shifts in ^{1}H n.m.r. spectra, would exist. The possibility that some copper(II) dimers may act as shift probes has therefore been investigated by looking both at the ligands themselves and at molecules forming loose intermolecular complexes with these dimers. It should be recognised that very strong coupling in a dimer of copper(II) could produce a copper(II) complex which would not give a paramagnetic shift. We give an example of this case. After our work was completed a paper reporting ^{1}H n.m.r. shifts for dimeric copper(II) benzoates was published.[5] We shall refer to this work later.

Choice of Systems for Study.—Although a larger number of cupric dimer compounds exhibiting antiferromagnetic coupling have been reported in the solid state, these compounds seem to be of low solubility or to dissociate considerably in solution and are therefore unsuitable for our purposes.

Recently the compound di-μ-methoxy-bis(acetylacetonato)dicopper(II) was reported to be dimeric with methoxy-bridges.[6] It was therefore decided to prepare and study a series of alkoxy bridged β-dicarbonyl complexes and study their nuclear magnetic properties.

EXPERIMENTAL

The alcohols and base used in the syntheses of the dimers were AnalaR. All other chemicals were reagent grade, used without further purification. The preparation of salicylaldehyde compounds is described below. Other dimeric derivatives were prepared by similar means.

Preparation of Bis(salicylaldehydato)copper(II).—Copper(II) acetate monohydrate (0·05 mol) was dissolved in refluxing methanol (200 ml) and the hot solution was filtered. Salicylaldehyde (0·1 mol) in ethanol (100 ml) was added dropwise to the above stirred solution. A green precipitate was filtered off from the cooled solution. Attempts to recrystallise it gave poorer analytical data than obtained for the original precipitate. The precipitate was washed twice with ethanol, thrice with ether, air-dried, and used without further purification.

Preparation of Di-μ-methoxy-bis(salicylaldehydato)dicopper(II).—Bis(salicylaldehydato)copper(II) (0·01 mol) was dissolved in refluxing methanol (400 ml) and the hot solution was filtered. Potassium hydroxide (0·01 mol) in ethanol (20 ml) was added dropwise to the stirred solution. The solution gradually became cloudy and a light green precipitate was observed. The solution was filtered and the filtrate discarded. The precipitate was washed with methanol and ether, and air-dried.

Preparation of Di-μ-ethoxy-bis(salicylaldehydato)dicopper(II).—Bis(salicylaldehydato)copper(II) (0·01 mol) was dissolved in refluxing ethanol (400 ml). Potassium hydroxide (0·01 mol) in ethanol (20 ml) was added dropwise to the stirred solution. The solution was refluxed for a further 2 h and filtered hot. A deep green precipitate was obtained on cooling. The precipitate was washed with ethanol and ether, and air-dried.

Preparation of Bis(diazoaminobenzene)copper(II).—Diazoaminobenzene was prepared by the method of Mann and Saunders.[7] The copper(II) complex was prepared by the method of Dwyer.[8]

Physical Methods.—N.m.r. spectra were recorded on a JEOL–JNM–C–60HL spectrometer operating at 60 MHz. Standard 5 mm tubes were used containing an internal standard in a total of at least 0·5 ml of solution.

Electronic absorption spectra were measured on a Pye Unicam SP 800 double-beam spectrometer with standard silica cells.

I.r. spectra as Nujol mulls between sodium chloride plates were recorded on a Perkin-Elmer model 457 grating spectrometer.

Analytical Data.—C, H, and N analyses (Table 1) were determined in the Department's microanalytical laboratory.

TABLE 1

Analytical data for complexes

Compound	C (%) Found	C (%) Calc.	H (%) Found	H (%) Calc.
Cu(acac)$_2$	45·5	45·8	5·3	5·3
Cu(acac)OMe	36·6	37·1	5·0	5·15
Cu(salic)$_2$	54·4	54·8	3·2	3·3
Cu(salic)OMe	44·2	44·8	3·5	3·7
Cu(salic)OEt	46·9	47·0	4·1	4·3
Cu(*o*-HOacet)$_2$	56·8	57·6	4·3	4·2
Cu(*o*-HOacet)OMe	46·9	47·1	4·2	4·3
Cu(*o*-HOacet)OEt	48·0	49·1	5·2	4·9
Cu(hfa)OMe	23·5	23·8	1·2	1·3
Cu(hfa)OEt	25·8	26·5	1·7	1·9
[Cu(Ph$_2$N$_3$)$_2$] *	62·2	61·8	4·4	4·4

acac = acetylacetone monoanion, salic = salicylaldehyde monoanion, *o*-HOacet = *o*-hydroxyacetophenone monoanion, hfa = hexafluoroacetylacetone monoanion, Ph$_2$N$_3$ = diazoaminobenzene monoanion.

* Found: N, 17·8; Calc., N, 18·0%.

RESULTS AND DISCUSSION

(a) *Nature of Compounds*.—Violet compounds of the aliphatic β-diketones acetylacetone and ethyl acetoacetate were prepared but were considered unsuitable for n.m.r. studies as they give rise to green solutions in non-conducting solvents from which it has not proved possible to re-isolate the dimers. It seems likely that dissociation in solution resulting in alkoxy-polymer formation is occurring but this has not been investigated.

It proved possible to prepare the methoxy- and ethoxy-bridged dimers, the yield of the former being several times greater than that of the latter. It had been hoped to prepare dimers with the bulky alkoxides as bridging ligands. This could well have resulted in the formation of pseudotetrahedrally co-ordinated dimeric copper atoms which would have added to the interest of this study. Unfortunately we have been unable to obtain any such compound. Modification of the preparation method described invariably failed to give the desired products. In particular bis(acetylacetonato)copper(II) did not appear to react with tertiary butoxide ion in refluxing dioxan.

The dimers arising from the ligands salicylaldehyde, hexafluoroacetylacetone, and *o*-hydroxyacetophenone are stable in solution for several hours and these com-

---

[5] R. A. Zelonka and M. C. Baird, *Inorg. Chem.*, 1972, **11**, 134.

[6] J. A. Bertrand and R. I. Kaplan, *Inorg. Chem.*, 1965, **4**, 1657.

[7] G. F. Mann and B. C. Saunders, ' Practical Organic Chemistry,' 4th edn., Longmans, London, 1960.

[8] F. P. Dwyer, *J. Amer. Chem. Soc.*, 1941, **63**, 78.

pounds have been studied. Reaction of chloro- and nitro-substituted salicylaldehydes with cupric acetate gave insoluble solids which gave no reaction with base.

Bis(diazoaminobenzene)copper(II) is the only well documented simple diamagnetic cupric compound [9] and we have therefore studied this as an example of strong interaction behaviour.

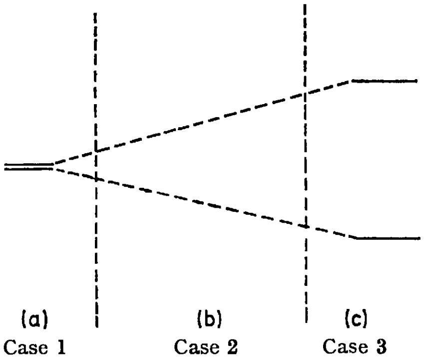

FIGURE 1 Effect of interaction on the energy levels for discreet pairs of copper atoms

(b) *Characterisation of Complexes.*—*X*-ray structural data are not yet available for the dimers discussed and therefore the suggested structure of square planar copper ions bridged by alkoxy-groups is based on magnetic data only. It is difficult to envisage any other model consistent with the experimental data.

It has been suggested that the $\geq$C–O– stretch of a bridging methoxide will fall below 1040 cm^{-1} while that for a terminal methoxide will lie above 1060 cm^{-1}.[6,10] This does not appear to be a very useful general method of structural assignment in our compounds as the absorptions in this region are generally weak, broad, and close to 1050 cm^{-1}. The i.r. spectrum of the alkoxy-compounds however are very similar to those of the parent monomers. Changes, particularly in the carbonyl stretching region, would be expected if the diketonate changed its mode of bonding and became the bridging group.

The absorption spectra of the dimers are also very similar to those of the parent monomers. The visible spectra support the formulation of pseudosquare planar arrangement of four oxygen donors around each copper atom. The near-u.v. spectra have bands in identical positions for both the monomers and their alkoxy-derivatives. This is again a strong indication that no change in the bonding of the dicarbonyl ligand has occurred.

Before discussing the n.m.r. spectra of the complexes we outline the relevant theory.

Theoretical Outline of N.m.r. Spectra of Dimers.—Three cases for the interaction of discrete pairs of copper(II) atoms are conceivable (see Figure 1). (a) The interaction between the two metal ions is negligible and the properties of the compounds can be explained by considering the atoms separately. This system offers no advantage over normal monomeric complexes and will not be discussed further.

(b) Weak interaction between the two metal ions results in a singlet ground state and a triplet state of somewhat higher energy. This case is characterised by the experimental observation of a diminished magnetic moment at low temperature as for cupric acetate. The stronger the interaction, the more effective should be the relaxation mechanism. It is this case in which we have been mainly interested.

(c) The interaction between the two metal ions is large, again giving rise to a singlet ground state and a triplet excited state. Here however the triplet state is at too high an energy to be populated. This strong antiferromagnetism will give a susceptibility corresponding to that of normal diamagnetic copper(I) complexes; no temperature-dependence will be observed but the resonances should be sharp. We have observed this behaviour, in the one case of the bis(diazoaminobenzene)-copper(II) dimer.

Golding has discussed the theory of temperature-dependent shifts for the complexes containing single paramagnetic ions for a variety of ground states.[11,12] Some additional considerations are required for the case of exchange-coupled ions but the basic method of calculation remains the same.

The major interaction between the two copper atoms in cupric dimers is the spin-exchange Hamiltonian $-J \, . \, S_1S_2$. This interaction gives rise to a singlet $Si' = 0$ and a triplet $Si' = 1$ state at relative energies 0 and $-J$. For complexes with proton-containing ligands the proton may interact with the impaired electron density. The paramagnetic contact (Knight) shift is given by equation (1) (where $\langle Sz \rangle$ is the time-averaged value of the z-component of the total spin S and A is in Hz).

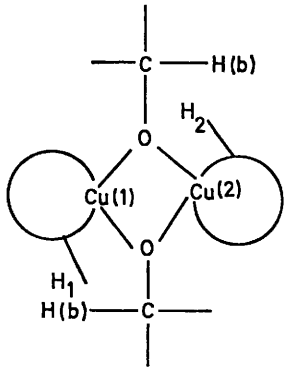

FIGURE 2

$$\Delta H = \frac{Ah\langle Sz \rangle}{g_nB_n} \qquad (1)$$

For an exchange-coupled system as in Figure 2 it is

---

[9] C. M. Harris and R. L. Martin, *Proc. Chem. Soc.*, 1958, 259.

[10] C. G. Barraclough, D. C. Bradley, J. Lewis, and I. M. Thomas, *J. Chem. Soc.*, 1961, 2601.

[11] R. M. Golding, *Mol. Phys.*, 1964, **8**, 561.

[12] R. M. Golding, 'Applied Wave Mechanics,' D. van Nostrand, London, 1969.

necessary to consider the contributions to the Knight shifts of a given proton from both ions.

Thus the Knight shift experienced by a proton can be written as the sum (2) of the shifts due to Cu(1) and Cu(2). For the terminal protons [H(1) and H(2) in

$$\Delta H = \frac{h}{g_n B_n}\left(A_1\langle S_{1z}\rangle + A_2\langle S_{2z}\rangle\right) \tag{2}$$

Figure 2] contributions from the copper ion more distant from a particular proton can be considered small and the approximation (3) will be justified. Assuming a

$$\Delta H_1 = \frac{A_1 h\langle S_{1z}\rangle}{g_n B_n} \tag{3}$$

Boltzmann distribution, we obtain equation (4) where

$$\langle Sz'\rangle = \frac{\Sigma(Sz')Si' \exp -(Esi/kT)}{\Sigma \exp -(Esi/kT)} \tag{4}$$

$\langle Sz'\rangle$ is the time-averaged value of the z component of S' in spin state Si' of energy Esi. Equations (5) and (6) follow.

$$\Delta H = -\frac{AhgBH}{g_n B_n kT}\left(\frac{\exp (J/kT)}{1 + 3 \exp (J/kT)}\right) \tag{5}$$

$$= -\frac{AhgBH}{g_n B_n kT}\left(\frac{1 + (J/kT)}{1 + 3[1 + (J/kT)]}\right) \tag{6}$$

In theory equation (6) tells us that the contact shift of a proton associated with an interacting pair of copper ions will not have the inverse linear temperature dependence predicted for a monomeric complex by assuming fast electron spin relaxation to be achieved in the monomer. Examination of the expression $(1 + J/kT)$, however, reveals that it can only take values between 0·33 and 0·25. In practice it would be necessary to vary the temperature over a very wide range to obtain clear-cut evidence for such a small change. We expect that it will be very difficult to observe deviation from linearity in the temperature dependence of proton shifts in copper dimers although the susceptibility of these dimers may be low.

In the case of the protons associated with the bridging ligands, H(b), there will be contributions to the shift from both metal ions of roughly equal weight. The Knight shift on such a proton could now be larger than that attributable to a single copper(II) ion and we might expect larger shifts of the protons of bridging ligands than those on the terminal ligands. However the pseudo-contact shift from the two copper ions will not be additive in all cases, depending upon the exact geometry of the proton relative to the magnetic axes of the two copper centres.

Nuclear Magnetic Resonance Spectra.—The ^{1}H n.m.r. spectra of the compounds prepared were studied in the temperature range +30 to −30 °C. Only in the case of the di-μ-ethoxy-bis(salicylaldehydato)dicopper(II) were large temperature-dependent shifts observed. A broad band at low field assigned to the aldehydic proton is observed to sharpen and move to low field as the temperature is decreased, and bands assignable to the methylene and methyl protons are observed to high field and to undergo very small shifts to low field as temperature is decreased (Table 2). Integration of the signal gave an intensity ratio of 1 : 2 : 3 as expected for the aldehydic, methylene, and methyl protons respectively. The protons of the aromatic nucleus lie on top of the proton signal of the reference chloroform, and could not be located precisely. This region has been carefully studied on a Bruker HFX spectrometer operating at 270 MHz and the aromatic peak is seen to consist of at least two and probably three resonances. Unfortunately the spectrum could be run at only a single temperature and we cannot comment on the mechanism of electron transfer to the aromatic nucleus. Our results on the J.E.O.L. spectrometer did show that at least part of the aromatic signal moves clear of the solvent peak to higher field as the temperature decreases.

TABLE 2

Temperature dependence of the chemical shifts (in p.p.m.) of the protons of di-μ-ethoxy-bis(salicylaldehydato)dicopper(II) with respect to tetramethylsilane

T/K	10^3K/T	δ[−C(O)H]	δ(−CH$_2$−)	δ(−CH$_3$)
300	3·333	14·7	3·65	1·23
298 (return)	3·356	14·8	3·6	1·23
289	3·460	14·95	3·7	1·20
273	3·663	15·6	3·7	1·25
258	3·876	15·95	3·7	1·25
248	4·023	16·35	3·75	1·25

It is no surprise that the aldehydic proton should be the one giving large shifts as this proton has been observed to give large shifts with other paramagnetic ions.[13] This proton is also nearer to the paramagnetic centre than any other of the salicylaldehyde protons. The fact that the α-protons on the alkoxide ligand show much smaller temperature-dependent shifts than the aldehydic proton is somewhat surprising on the basis of our model. The bridging ligand protons may experience opposing pseudo-contact effects from the two copper atoms.

The n.m.r. spectrum of bis(salicylaldehydato)copper(II) shows no absorption at very low field assignable to the aldehydic proton. This could result either from excessive broadening or to unfavourable overlap of orbitals giving no contact effect from the unpaired electron. In the methoxy-dimer the band has not been observed owing to the low solubility of this compound. Small temperature-dependent shifts were again observed for the methyl protons. The n.m.r. spectrum of di-μ-ethoxy-bis(σ-hydroxyacetophenonato)dicopper(II) showed bands assignable to the α- and β-protons of the ethoxy-group and to the methyl protons of the dicarbonyl ligand to high field of solvent peaks. No band corresponding to the aldehydic proton was observed to low field, supporting the previous assignment.

---

[13] K. E. Schwarzhans, *Angew. Chem. Internat. Edn.*, 1970, **9**, 946.

The possibility that these dimers might act as shift probes in molecular complexes has been investigated for this would correspond to an interaction between a dimeric copper(II) unit in a protein and protein-side-chains not in the co-ordination sphere. The spectra of several steroids and ethyl acetate were found to give selective broadening but no shift with varying concentrations of di-μ-ethoxy-bis(salicylaldehydato)dicopper(II). The possibility of π-complexation was investigated with the latter molecule by use of trinitrobenzene as acceptor. Some broadening of the acceptor spectrum was observed but no shift was obtained.

We refer again to the work of Zelonka and Baird.[5] We are unable to assess the value of this work in full as the authors did not publish details of their n.m.r. spectra. The proton shifts for the copper(II) dimers are reported with respect to diamagnetic zinc complexes. This could only be justifiable if the zinc compounds contain bridging benzoate groups. The authors report contact shifts for the *ortho*-protons on the benzoate rings of much smaller magnitude than for *meta*- and *para*-protons. This apparent anomaly leads us to believe that the zinc compounds were not suitable standards. The work was done at one temperature only so that its interpretation was extremely tenuous.

A plot of shift from tetramethylsilane against the reciprocal of the temperature [for the aldehydic proton of di-μ-ethoxy-bis(salicylaldehydato)dicopper(II)] gave a straight line (Figure 3, Table 2) as predicted in the theoretical section. The magnetic susceptibility of this compound was measured by the method of Evans.[14] A graph of the splitting of the standard peaks against reciprocal temperature is a straight line (Figure 4, Table 3). It is clearly seen by this method that the magnetic moment of the complex is much lower than expected for non-interacting metal ions. An uncorrected magnetic moment per copper atom of 1·1 B.M. is calculated from the experimental data. It does not seem reasonable to make any attempt at diamagnetic corrections as these are not accurately known.

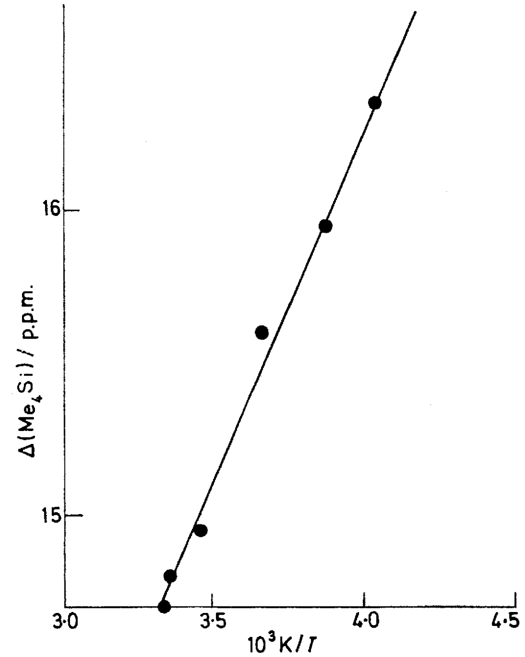

FIGURE 3

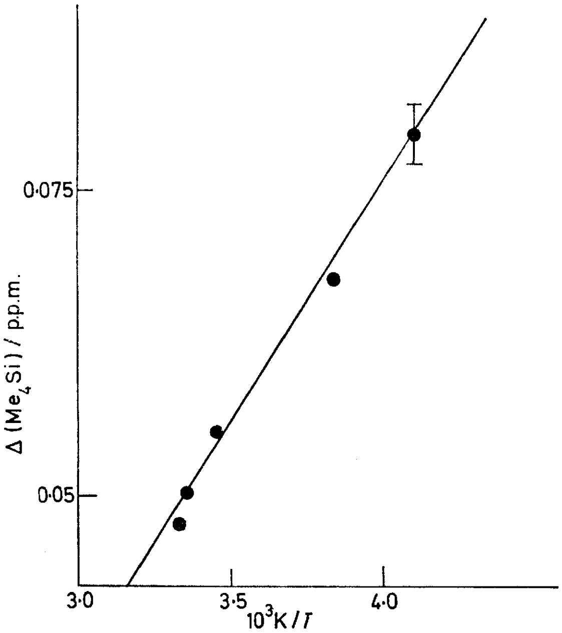

FIGURE 4

TABLE 3

Temperature dependence of the tetramethylsilane peaks in the magnetic susceptibility determination of a 0·0077 g cm^{-3} solution of di-μ-ethoxy-bis(salicylaldehydato)dicopper(II) by the Evans method

T/K	10^{3}K/T	Splitting/p.p.m.*
300	3·34	0·047
296 (return)	3·36	0·050
292—287	3·46	0·055
259—261	3·85	0·067
245—242	4·11	0·077—0·082

* Of the tetramethylsilane peak.

The n.m.r. spectrum of bis(diazoaminobenzene)copper(II) gave reasonably sharp peaks which show no temperature dependence. This molecule shows behaviour typical of a strongly interacting dimeric pair of cupric ions (case **3**, Figure 1).

Conclusion.—In principle it is clearly possible to distinguish copper(II) dimers from copper(I) systems by the temperature dependence of their n.m.r. spectra provided interaction between the paramagnetic ions is not too strong. How easily this can be achieved in the case of very large molecules remains to be seen. The situation in a protein may be complicated by the occurrence of several different types of copper ion and by the

---

[14] D. F. Evans, *J. Chem. Soc.*, 1959, 2003.

presence of aromatic residues generating ring currents. The presence of monomeric copper(II) centres will lead to broadening of the proton resonances and ring currents will give rise to shifts: in neither case though would any temperature dependence of the shifts be observed. Even in the presence of monomeric cupric ions and ring currents in the same molecule it is therefore theoretically possible to detect a magnetically coupled cupric dimer.

We thank Dr. F. Hayes for discussion. The work is supported by the Medical Research Council; one of us (W. B.) held a Senior S.R.C. Fellowship.

[2/1820 *Received, 1st August,* 1972]