# Electronic Studies of Copper Complexes of Nucleic Acid Components. Part 10.† The Copper(II)–Guanosine 5′-Dihydrogenphosphate System

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The polymeric complex $[\{Cu_3(guop)_3(OH_2)_8{\cdot}5H_2O\}_n]$ (guop = guanosine monophosphate) has been studied by i.r., e.s.r., and electronic spectroscopy and by magnetic-susceptibility measurements. The $PO_4$ bonding to $Cu^{II}$ in this complex does not differ much from that of other oxygen donors, and there are two sets of magnetically coupled copper(II) ions with $-2J$ values of 130 and 15 cm$^{-1}$, respectively. Corresponding coupling paths are proposed. A value of the zero-field splitting, $|D| = 0.15$ cm$^{-1}$, has been obtained for the strongly coupled species.

As part of our continuing study of the bonding, electronic, and magnetic properties of the copper(II) co-ordination compounds with nucleic acid components,[1] we have completely elucidated these properties for the copper(II)–guanosine monophosphate (guop) complex. For several years it has become increasingly evident that these co-ordination compounds could be used as models of many important biological processes,[2] such as the observed poisoning of the RSV cancer virus by $Cu^{II}$.[3] The $[\{Cu(guop){\cdot}4.5H_2O\}_n]$ complex was previously prepared and the i.r. spectrum studied by Ogawa and Sakaguchi.[4] They concluded that the guop molecule co-ordinated at O(6). Recently, $X$-ray structural information has appeared from two different laboratories [5,6] which indicates [5] the occupation of the axial position at $Cu^{II}$ by N(7) of the guop molecule and that the five-co-ordination at the metal is completed in two thirds of the cases [(*a*) in Figure 1] by three water molecules and one $PO_4$ group, while the remaining third [(*b*) in Figure 1] possess two water molecules and two $PO_4$ groups. A further point of interest is that the molecular species consists of a polymeric chain structure with repeating sequences every three Cu–guop–$H_2O$ units, that is $[\{Cu_3(guop)_3(OH_2)_8{\cdot}5H_2O\}_n]$. Here we present a reinterpretation of the i.r. spectrum as well as electronic, e.s.r, and magnetic-susceptibility data for this complex. These are the first magnetic and electronic data published for a copper(II)–nucleotide co-ordination compound.

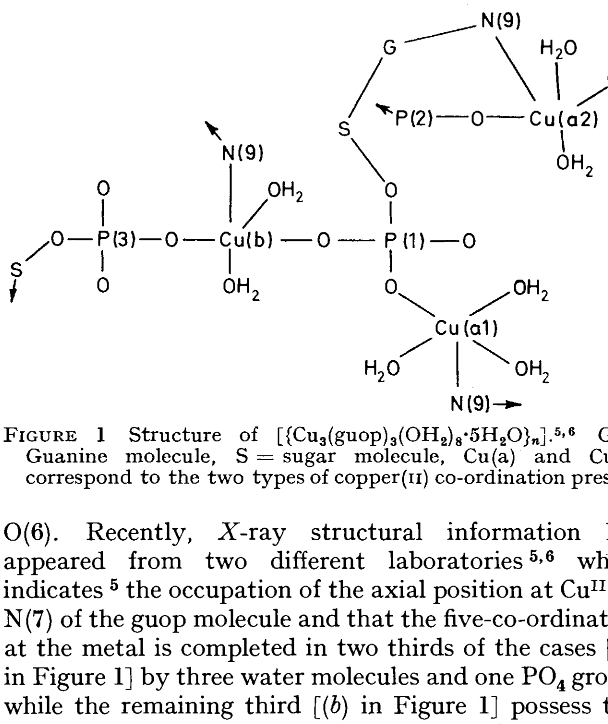

FIGURE 1 Structure of $[\{Cu_3(guop)_3(OH_2)_8{\cdot}5H_2O\}_n]$.[5,6] G = Guanine molecule, S = sugar molecule, Cu(a) and Cu(b) correspond to the two types of copper(II) co-ordination present

## EXPERIMENTAL

All the starting materials were commercially available and used without further purification. The complex was isolated from a neutral aqueous solution of guanylic acid (guanosine 5′-dihydrogenphosphate, guo-5′-p) and copper(II) nitrate by slow partial evaporation. Elemental analysis by PCR, Inc. agreed well with the $Cu(guop){\cdot}4.5H_2O$ (basic monomeric unit) stoicheiometry (Found: C, 23.0; H, 4.05; N, 13.9. Calc. for $C_{10}H_{21}CuN_5O_{12.5}P$: C, 23.65; H, 4.15; N, 13.85%).

The i.r. spectra of the free and co-ordinated ligand were obtained as KBr pellets in a Perkin-Elmer 21 spectrometer, the e.s.r. spectra for polycrystalline samples in a Varian HFE-12 $X$-band spectrometer at room temperature and 77 K, and the electronic spectrum in Beckman DK-2A and McPhearson 300 spectrophotometers. The static magnetic-susceptibility measurements [7] were made in a Faraday system using a Cahn 4700 microbalance, an Alpha 2000 electromagnet with a current-regulated power supply, and an Air Products refrigerator and shroud to cool the sample with regulation down to 12 K.

## RESULTS AND DISCUSSION

The i.r. spectra of the co-ordination compound were compared with that of the free ligand as well as those of normal and deuteriated guanine derivatives obtained from the literature.[8,9]

Specificially, the carbonyl frequency assigned at 1 690—1 700 cm$^{-1}$ in the free ligand remains in the same region on co-ordination (Table). This assignment is made with the aid of the i.r. work on deuterioguanine, which exhibits carbonyl bands in the 1 680—1 690 region.[8] The slight shift in intensity (from strong to medium) can be assigned to H-bonding changes on co-ordination.

The $NH_2$ deformation is assigned at 1 640 cm$^{-1}$ on the basis that it disappears on deuteriation of the guanine molecule.[8] This band remains constant throughout and is indicative of no $NH_2$ involvement in co-ordination. The bands associated with the ribose moiety are assigned to the 963—1 130 cm$^{-1}$ region and also remain unchanged in the free and complexed nucleotide. The phosphate bands do change; the single band at 1 235 cm$^{-1}$, assigned in the free ligand to the P=O stretch, changes to two strong bands at 1 109 and 984 cm$^{-1}$ which can be assigned to $[PO_4]^{2-}$ bands. This change is

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† Part 9; H. C. Nelson, N. Khoe, and J. F. Villa, presented at the A.C.S. National Meeting, San Francisco, California, September 1, 1976, paper INOR 119.

qualitatively the same as that observed in the disodium,[9] magnesium,[10] and cadmium [11] salts of guanylic acid and adenylic acid. The magnitude of the metal–$PO_4$ interactions can be followed quantitatively by the shift towards higher energies on complexation of the band at *ca.* 980 $cm^{-1}$. In the present case this band lies at 984 $cm^{-1}$, intermediate between highly ionic and covalent in character.

Pertinent i.r. bands ($cm^{-1}$) of the free and co-ordinated guop molecule. s = Strong, m = medium, w = weak, sh = shoulder, sp = sharp, and br = broad

| Compound | $\nu$(C=O) | $\delta(NH_2)$ | $\nu$ (Rings) | $\nu$ (Ribose) | $\nu$ (Phosphate) |
|---|---|---|---|---|---|
| Guanylic acid | 1 704s<br>1 689s | 1 639m (sh) | 1 597w<br>1 462m (sh)<br>1 408m<br>1 355s,br | 1 130m (sh)<br>1 075s<br>1 040(s)<br>963 (s) | 1 235s,br |
| Copper(II)–guanylic acid | 1 704m (sh)<br>1 689s | 1 639w,sp | 1 597sh<br>1 462w,sp<br>1 408w<br>1 365w (sh) | 1 145w (sh)<br>1 075s<br>1 045m (sh)<br>975w | 1 109s<br>984s |

It can also be seen from the Table that there are some changes in the ring stretches on co-ordination. These shifts can be assigned to co-ordination *via* N(7) since N(1) is protonated and the Lewis basicity of N(7) is greater than N(3).[12]

The e.s.r. spectrum of the complex consisted of a parallel and a perpendicular band at $g$ 2.38 and 2.11, respectively (Figure 2). From the general shape, $g$ values, and intensity measurements at different temperatures, it was concluded [13] that the bands can be interpreted as originating in a doublet species of approximate $D_{4h}$ symmetry (lowest $g > 2.04$). A closer study of the $g$ values is revealing. The $G$ function,[13] defined as $(g_{\parallel} - 2)/(g_{\perp} - 2)$, is equal to 3.5, somewhat lower than 4.0. This indicates that exchange coupling is present among copper(II) ions. Because of the similarity to a $S = \frac{1}{2}$ spectrum, these bands undoubtedly originate in the weakly coupled (a2) copper(II) ions (Figure 1).

A magnified scan at lower fields revealed the presence [14] of a band which from its lineshape, intensity, and position can be identified as $H_{min}$, the spin-forbidden transition for $S = 1$ species, at 1 580 G (Figure 3).* This is evidence of the presence of Cu–Cu interactions in this polymer. A zero-field splitting, $|D|$, value [15] of 0.15 $cm^{-1}$ can be estimated from equation (1) where $\boldsymbol{h}$ and $\beta$ have

$$D_{expt.} = \{0.75[(\boldsymbol{h}\nu)^2 - (2g\beta H_{min})^2]\}^{\frac{1}{2}} \qquad (1)$$

their usual meanings, $\nu$ is the spectrometer frequency, $g$ is the average $g$ value, and $H_{min}$ is the magnetic-field position of the band in the e.s.r. spectrum, employing the usual approximations [equation (1) strictly applies only to nearly isotropic systems].

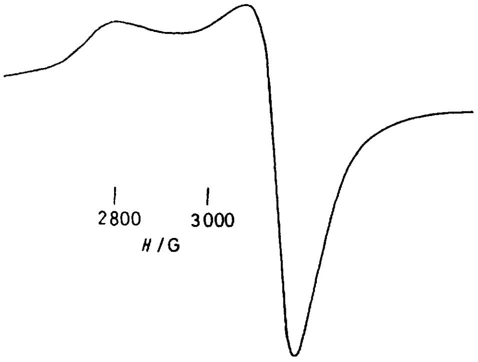

FIGURE 2 E.s.r. spectrum of $[\{Cu_3(guop)_3(OH_2)_8 \cdot 5H_2O\}_n]$; $\nu = 9.324 \times 10^9$ Hz

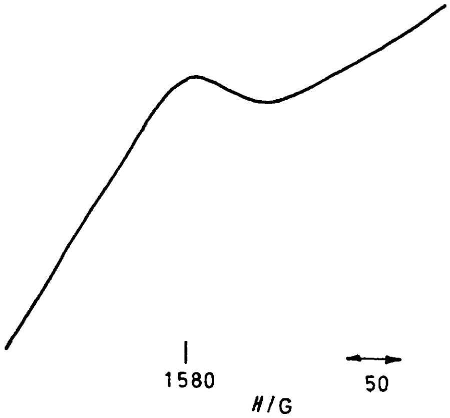

FIGURE 3 E.s.r. spectrum of $[\{Cu_3(guop)_3(OH_2)_8 \cdot 5H_2O\}_n]$ at *ca.* 1 600 G; $\nu = 9.523 \times 10^9$ Hz

The electronic spectrum had one band in the visible–near-i.r. range, at 13 800 $cm^{-1}$, with a tail into the i.r. This band can be attributed [16] to the nearly accidental degenerate transitions from the $B_{1g}$ ground state to the $E_g$ set and $B_{2g}$ excited states in approximate $D_{4h}$ symmetry. The transition to the $A_{1g}$ state is at much higher energies.

It is extremely interesting to note that the electronic transitions, colour, and therefore the energy levels of this complex are almost identical to and certainly in the range of those copper(II)–Schiff base complexes of approximate $D_{4h}$ symmetry previously reported.[17] It is then possible, considering the similarity of geometry surrounding the metal, equal co-ordination number, and similar $g$ values (within 0.01 units) and electronic transition, that the nature of co-ordination in the nucleotide complex does not differ much from those of the Schiff-base complexes and that the co-ordination of the $[PO_4]^{2-}$ groups appears to be as effective as that of the $H_2O$ or N atoms. This is unexpected in the light of previous postulates [2] from *in vitro* reactions involving nucleic acids where significant interactions with $Cu^{II}$ occur at the heterocyclic bases and not at the $[PO_4]^{2-}$ groups, while

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* Throughout this paper: 1 G = $10^{-4}$ T; 1 B.M. ≈ $9.27 \times 10^{-24}$ A $m^2$.

the interactions with $Na^+$ or $Mg^{2+}$ occur *via* the $[PO_4]^{2-}$ groups.

$$\chi = Ng^2\beta^2/2kT\left[\frac{\exp(-2J_1/kT)+\exp(-2J_2/kT)}{1+3\exp(-2J_1/kT)+3\exp(-2J_2/kT)+\exp(-E/kT)}\right]+N\alpha \qquad (2)$$

The inverse magnetic-susceptibility and magnetic moment of this complex in the significant region from 110 to 15 K are shown in Figure 4. Several models were used in order to interpret the magnetic-susceptibility data, including the Van Vleck dimer [18] and Ising [19] chain polymeric models. All these models were inadequate and a new model had to be devised in order to successfully duplicate the experimental points. This model consisted of two concomitant and different dimeric systems, Cu(a)–Cu(a) and Cu(a)–Cu(b) where a and b represent the two types of $Cu^{II}$ present in the polymer, each with an associated $2J$ value. In addition, the energy separation between the ground states of the dimers was also allowed to vary. Equation (2) was obtained summing over a Boltzmann distribution [20] in the energy levels present in the system. Here, $g$, $k$, $\beta$, $N$, $\chi$, and $T$ have their usual meaning, $2J_1$ and $2J_2$ are the corresponding singlet–triplet separations, $E$ is the separation between the ground states of both dimers, and $N\alpha$ is the temperature-independent paramagnetism (t.i.p.) term. The best-fit values obtained were $-130$, $-15$, and 2 $cm^{-1}$ and 2.1 for $2J_1$, $2J_2$, $E$, and $g$, respectively (negative $2J$ values indicate a singlet ground state). The routine used calculated and compared the $g$ values at each experimental point with the average $g$ value. The standard deviation obtained was 0.06, clearly demonstrating the excellence of this model. The good fit is also shown by the graphical display of experimental points and theoretical lines in Figure 4. Even though the energy separation between the ground states of both dimers, $E$, was allowed to vary, the value obtained in the best fit was only 2 $cm^{-1}$, too small to be considered significant because there is an inherent $\pm 10$ $cm^{-1}$ uncertainty in this method. Therefore both ground states are taken as equal in energy.

These results are perfectly concordant with the crystal structure recently published.[5,6] As can be seen from Figure 1, Cu(a1) and Cu(b) are connected by a $PO_2$ group. This may allow for considerable delocalization of an antiferromagnetic nature through overlapping orbitals producing the larger $2J_1$ value. Also, Cu(a1) and Cu(a2) are situated such that there can be some through-space antiferromagnetic coupling of much smaller magnitude, corresponding to $2J_2$. It should be pointed out that the connections between this unit cell and adjacent ones, indicated by arrows in Figure 1, are not conducive to magnetic coupling because the metal ions are well separated in space by nucleotide moieties and there are only multiatom bridges between the ions.

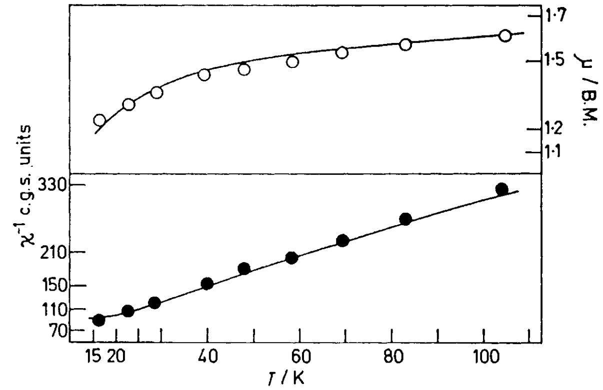

FIGURE 4 Inverse magnetic susceptibility (●), magnetic moments (○), and theoretical best fit lines (—) for $[\{Cu_3(guop)_3(OH_2)_8\cdot 5H_2O\}_n]$

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