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Magnetic Studies of Two New Copper Hippurate Dimers

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The EPR spectra and temperature-dependent magnetic susceptibility of two copper(II)–amino acid complexes have been determined. Results suggest a dimer structure for both the dimethyl sulfoxide and the dimethylformamide adducts of bis(*N*-benzoylglycinato)copper(II). The temperature variation of the magnetic susceptibility of these compounds shows a broad maximum near 265 K, indicating a strong antiferromagnetic interaction between the Cu^{2+} ions within the pairs. A superexchange mechanism via the bridging carboxylate groups is compatible with our results and suggests that N-substituted amino acids, or small peptides, can act as simple carboxylate ligands for copper(II), providing model complexes for the EPR-nondetectable copper in enzymes.

Introduction

One of the characteristic reactions of amino acids is the formation of blue copper chelates.[1] Peptides also bind copper in a chelatelike fashion, deprotonated peptides linkages forming stable Cu–N bonds.[2] *N*-Benzoylglycine, hippuric acid, is unusual in that its substituted nitrogen does not seem to coordinate to copper, while its acidic function acts as a bridging bidentate group.

A considerable amount of research has been reported on the magnetic properties of polynuclear copper(II) complexes.[3-5] Two different types of binuclear complexes have been found with a variety of carboxylate ligands. A first type of compounds, of which copper acetate monohydrate is the simplest example, is characterized by strong exchange interaction between copper ions of spin $^1/_2$ forming isolated pairs. The antiferromagnetic exchange interaction results in a $S = 0$ singlet ground state and $S = 1$ triplet state. The separation between these states is $2J = -285$ cm^{-1} in copper acetate monohydrate,[6] and qualitative evidence points to a superexchange mechanism of interaction occurring via the bridging carboxylate groups and not via a direct metal–metal bond.[7]

On the other hand, monoatomic oxygen bridges, such as found in the copper hippurate tetrahydrate complex,[8] are present in another class of compounds characterized by smaller $2J$ values ranging from -18 to -40 cm^{-1}.[9,10] Recently, several groups of workers have studied the copper–hippuric acid system,[11-14] and very low temperatures were needed to detect the weak antiferromagnetic interaction in the tetrahydrate, for which $-2J = 4.3$ cm^{-1} (or 6.2 K). The ammine adducts seem to be monomeric.

We report EPR and magnetic susceptibility results for the first adducts of a copper–amino acid complex found to exhibit strong antiferromagnetic interactions.

Experimental Section

Synthesis. *N*-Benzoylglycine (hippuric acid, Hip) was purchased from British Drug House Biochemicals, and the anhydrous copper complex was prepared by standard methods.[15] The adducts $Cu(Hip)_2{\cdot}Me_2SO$ and $Cu(Hip)_2{\cdot}DMF$ were isolated by dissolving anhydrous copper hippurate in pure Me_2SO or DMF and by evaporating the excess solvent under vacuum. Quantitative analysis by Chemalytics Inc., Tempe, Ariz., gave satisfactory results for the Me_2SO adduct. Anal. Calcd for $Cu(C_6H_5CONHCH_2COO)_2{\cdot}(CH_3)_2SO$: C, 48.23; H, 4.45; N, 5.62. Found: C, 48.11; H, 4.45; N, 5.63. However, only approximate results for the less air-stable DMF adduct were obtained. Anal. Calcd for $Cu(C_6H_5CONHCH_2COO)_2{\cdot}(CH_3)_2NCHO$: C, 51.14; H, 4.70; N, 8.53. Found: C, 50.17; H, 4.44; N, 8.29.

EPR Spectra. EPR spectra were recorded at X-band frequencies on a Varian E-9 spectrometer at liquid nitrogen and room temperatures. The magnetic field was swept from 0 to over 8 kG and calibrated every 1 kG with a digital NMR gaussmeter. Room-temperature K-band spectra were obtained with a JESME ESR spectrometer. Several samples of each complex were run and showed identical features.

Table I. Magnetic Parameters for Copper Hippurates at 77 K and X-Band Frequencies

	anhydrous	Me_2SO adduct	DMF adduct
$g_\parallel$	2.363	2.363	2.353
$g_\perp$	2.071	2.075	2.065
$\bar{g}$	2.146	2.149	2.139
D,[a] cm^{-1}	0.37	0.35	0.34_5
D, cm^{-1}	0.352	0.345	0.342
E, cm^{-1}	<0.01	<0.01	<0.01
$2J$, cm^{-1}	327	292 ± 14	313 ± 17

[a] Approximate values derived from the difference between the perpendicular components of room-temperature 24.8-GHz and 35.0-GHz spectra.

Static Magnetic Susceptibility. The magnetic susceptibility of finely powdered samples has been measured in a Faraday apparatus[16] over the temperature range 65–320 K. The apparatus was calibrated with a 99.999% pure platinum sample, using 201.9×10^{-6} emu/mol as the value of its susceptibility at room temperature. Measurements at different field strengths, up to 8 kG, showed no dependence of the susceptibility on the applied field. The overall relative accuracy of the measurements was found to be 1%.

Results

EPR Spectra. Figures 1–3 show the first-derivative X-band EPR spectra of the anhydrous compound and the Me_2SO and the DMF adducts of $Cu(Hip)_2$. In each case, an absorption is observed near 3000 G which arises from mononuclear impurities of spin $S = {}^1/_2$. The intensity of this absorption increases as the temperature is lowered. Calculation of the corresponding anisotropic g factors gives $g_\parallel = 2.36$ and $g_\perp = 2.07$ in the three cases examined.[17] The amount of impurities appears to be especially important in the less stable DMF adduct.

The other absorption lives are due to transitions in the triplet state.[18] Both $Cu(Hip)_2{\cdot}Me_2SO$ and $Cu(Hip)_2{\cdot}DMF$ show well-defined hyperfine structure, in their low-temperature spectra, whereas the anhydrous compound does not. These transitions may be represented by a $S = 1$ spin Hamiltonian of the form in eq 1, where β is the Bohr magneton, $\vec{H}$ is an external magnetic field, $\mathbf{g}$ is an anisotropic Landé splitting tensor, $\vec{S}$ is the total spin vector, and S_x, S_y, and S_z are the spin operators of its mutually perpendicular components.

$$H = \beta\vec{H}\mathbf{g}\vec{S} + D(S_z^2 - {}^2/_3) + E(S_x^2 - S_y^2) \qquad (1)$$

The four transitions resolved in the 77 K spectra allowed us to calculate the zero-field splitting parameters D and E and to obtain values for $g_\parallel$ and $g_\perp$ following the procedure described by Chasteen.[19] Results are shown in Table I.

Magnetic Susceptibility. Diamagnetic corrections were determined by the method of Pascal[20] (-221.7×10^{-6} emu/mol

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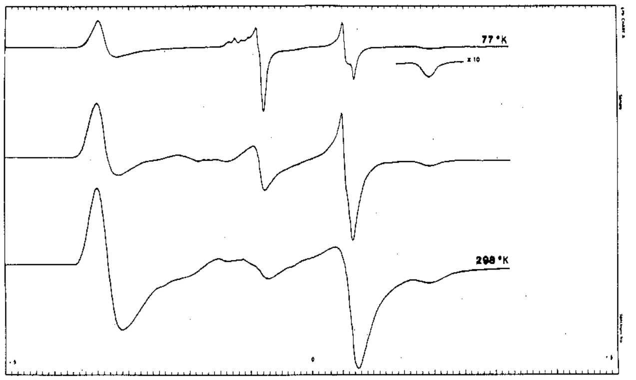

Figure 1. Electron paramagnetic resonance spectrum of $Cu(Hip)_2$. The intermediate spectra were recorded at temperatures between liquid nitrogen and room temperatures; microwave frequency 9.126 GHz. All spectra in the figures are centered at zero = 4000 G, with a scan range of 10 000 G.

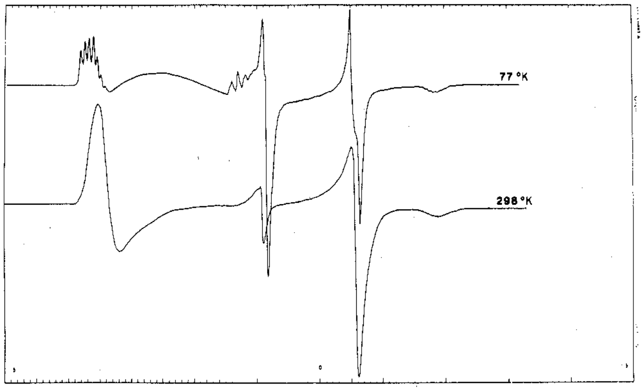

Figure 2. Electron paramagnetic resonance spectrum of $Cu(Hip)_2{\cdot}DMF$; microwave frequency 9.087 GHz.

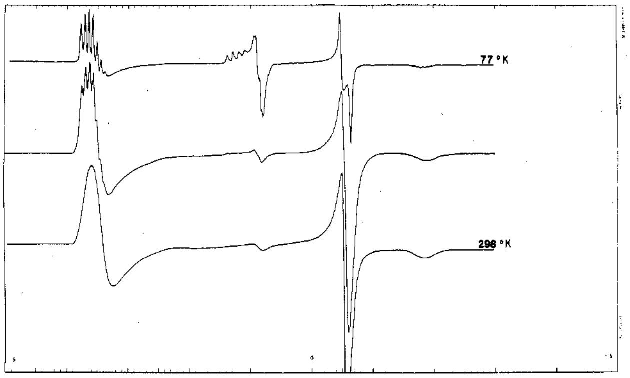

Figure 3. Electron paramagnetic resonance spectrum of $Cu(Hip)_2{\cdot}Me_2SO$; microwave frequency 9.083 GHz.

and -217.8×10^{-6} emu/mol for the Me_2SO and DMF adducts, respectively) and subtracted from the measured values of the total susceptibility. The resulting paramagnetic susceptibilities per mole are shown in Figure 4. The temperature variation of the molar susceptibility of the $Cu(Hip)_2{\cdot}Me_2SO$ complex exhibits a broad maximum near 265 K. The full line in Figure 4 is the best fit to the expression of the paramagnetism for a singlet–triplet system (eq 2), where χ_m is corrected

$$\chi_m = \frac{Ng^2\beta^2}{3kT}\left[1 + \tfrac{1}{3}\exp\left(\frac{-2J}{kT}\right)\right]^{-1} + N\alpha \qquad (2)$$

molar susceptibility, N is Avogadro's number, $g = 2.149$ is the EPR-determined value of the Landé splitting factor (see Table I), $N\alpha = 60 \times 10^{-6}$ emu/mol is the assumed temperature-independent paramagnetism,[21] and T is the absolute

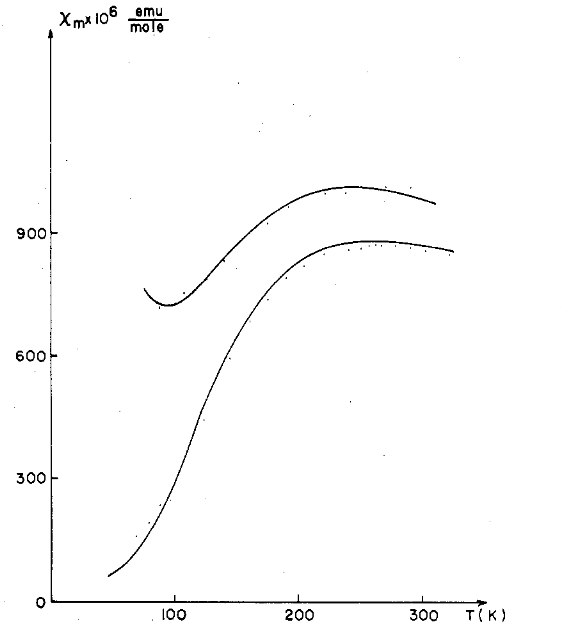

Figure 4. Corrected molar susceptibilities of $Cu(Hip)_2{\cdot}DMF$ (top) and $Cu(Hip)_2{\cdot}Me_2SO$ (bottom); the full line is the best fit to eq 2 for the Me_2SO adduct. In the case of the DMF adduct, an impurity term is added to eq 2 to fit the results (see text).

temperature. The best fit was obtained for a $2J$ value of -292 cm^{-1} which indicates a relatively strong magnetic interaction between the two copper ions.

The results for $Cu(Hip)_2{\cdot}DMF$ could not be fitted to eq 2 alone, as in the previous case. However, we expect from the EPR spectrum that mononuclear impurities, which should exhibit a normal Curie-type temperature variation, eq 3, where

$$\chi(\text{mono}) = C/T \qquad (3)$$

$\chi(\text{mono})$ is the mononuclear impurity susceptibility and C is the corresponding Curie constant, will contribute significantly to the total susceptibility. Indeed, if such a term is added to eq 2, the theoretical curve is found to be in good agreement with the experimental data, using a $2J$ value of -313 cm^{-1} and $C = 4.89 \times 10^{-2}$ emu. In this case, the value of g is 2.129 (see Table I), and a concentration of $S = {}^1/_2$ impurities of 5% produces the best fit to the experimental results.

Discussion

The EPR spectra of the anhydrous compound and the Me_2SO and DMF adducts of copper hippurate all show triplet-state features characteristic of large antiferromagnetic exchange. The crystal field removes the degeneracy of the triplet state. In this case, the crystal field has quasi-axial symmetry, and $M_s = \pm 1$ states are almost degenerate. Two zero-field splitting parameters D and E ($D \gg E$) are thus defined, where D arises from the presence of a unique axis, Z (the metal–metal axis), and E takes account of a small difference between X and Y directions. The calculated values of the four parameters D, E, $g_\parallel$, and $g_\perp$ are within the range of other similar compounds.[22] The seven-line dinuclear hyperfine pattern of the $g_\parallel$ part of the triplet spectrum of the Me_2SO and DMF adducts is typical of copper carboxylates with singlet–triplet separation much larger than that the hyperfine components. However, no such hyperfine interaction was detected for the anhydrous compound, pointing to possible interdimer exchange and consequent broadening. Consequently it seems that the bulky coordinated solvent molecules help isolate the dimeric units along the Z direction. The splitting between the H_{x2} and H_{y2} absorptions indicates a largest rhombic distortion for the Me_2SO adduct (see Figure

3) even though only $g_\perp$ was calculated for the three compounds studied. The g values for the triplet state are found to be very close to the g values of the monomeric impurities, indicating that the environment of the Cu^{2+} ions is very similar in both cases. This reinforces the view that the interaction occurs through a superexchange-type mechanism.

Magnetic susceptibility data support the hypothesis of isolated copper dimers with a negative intradimer exchange. The $2J$ values obtained for both the Me_2SO (-292 cm^{-1}) and the DMF (-313 cm^{-1}) adducts are quite comparable to those reported for similar copper carboxylates.[5] The value of $2J$ for the DMF complex may be less precise, because we had to fit an additional parameter arising from the presence of mononuclear impurities. Our values are slightly smaller than that reported for the anhydrous compound (-327 cm^{-1}) by Hyde et al.,[23] this being due to their overestimation of g.[11] It should be noted that since hyperfine structure is resolved in the adducts, interdimer exchange must be smaller than 0.1 cm^{-1} (the observed $A_\parallel$ for the triplet is 70 G). Since the J values found are of the order of 300 cm^{-1}, it follows that the alternate Heisenberg chain model[24,25] cannot describe properly the magnetic properties for these compounds of unknown structure and that the isolated dimer model is strongly favored.

Conclusion

Our results on the Me_2SO and DMF adducts provide two clear examples of strong antiferromagnetic exchange for the copper hippurate system. This type of magnetic behavior indicates that the adducts are most likely to adopt the typical carboxylate cage structure, even though an example is known of a polymeric copper carboxylate exhibiting dimerlike behavior.[26] In any case, the results establish that N-substituted amino acids, such as hippuric acid[27] can act as "simple" carboxylic acids.

This finding enables us to propose an explanation for the properties of a class of enzyme known to contain the so-called type 3 copper. Hemocyanin, tyrosinase, and laccase contain EPR-nondetectable copper and, recently, binuclear model complexes have been synthesized with macrocyclic ligands.[28-30] However, it seems that copper complexes of biologically important ligands afford more appropriate model compounds for these enzymes. Previous EPR work has revealed dipolar coupling in frozen Me_2SO solutions of copper *N*-(hydroxyethyl)glycinate.[31] We would like to propose exchange coupling through the appropriate carboxylate groups of the peptidic chain as the mechanism which can account for the observed antiferromagnetic behavior[32] of type 3 copper enzymes. The exact identification of the bridging groups in enzymes cannot be made from the magnitude of J alone. Our identification of strongly superexchanged-coupled bridged binuclear units in N-substituted amino acid complexes shows it is feasible to consider copper acetate like interactions under certain conditions, even for such notorious chelating agents as amino acids and peptides. Acetamide, and probably other biologically important molecules, can replace Me_2SO or DMF as the axial ligand in these dimers. Further studies are aimed at relating magnetic properties and structural features for the exchange-coupled species herein reported.

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Registry No. $Cu(Hip)_2{\cdot}Me_2SO$, 68332-10-5; $Cu(Hip)_2{\cdot}DMF$, 68332-11-6; $Cu(Hip)_2$, 59980-63-1.

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