g TENSOR ANISOTROPY AND ELECTRON-NUCLEUS DIPOLE-DIPOLE INTERACTION IN THE Cu (II) - $(L\text{-His})_2$ COMPLEX IN SOLUTION

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I. INTRODUCTION

Cu(II) complexes with low molecular weight ligands have been suggested to play relevant roles in the biochemistry of copper. Among them the $Cu(II)(L\text{-His})_2$ species has been recognized as the most abundant in biological fluids. However the binding features of the two L-His molecules have not been yet defined; histamine-like (one amino nitrogen plus one imidazole nitrogen) and/or glycine-like (one amino nitrogen plus one carboxyl oxygen) binding modes have been alternatively suggested. Different rapidly interchanging species can be present as well.

In this report we have combined NMR relaxation rate measurements and ESR lineshape analysis with the aim of delineating the structural and motional features of the title complex in solution.

II. RESULTS AND DISCUSSION

Nuclear relaxation rates measured in the presence of paramagnetic metal ions are usually accounted for by the Solomon Bloembergen-Morgan (SBM) theory which relates structural and motional parameters with the experimental paramagnetic nuclear relaxation rates T_{1p}^{-1} and T_{2p}^{-1} defined as

$$T_{ip}^{-1} = T_{imetal}^{-1} - T_{iblank}^{-1} \qquad (i=1,2)$$

The experimental T_{ip}^{-1} values for the imidazole H_2 proton of L-His are shown in figure 1 as a function of the Cu(II) concentration; since $T_{2p}^{-1} > T_{1p}^{-1}$ the following simplified equation can be used according to the SBM theory

$$T_{1p}^{-1} = \frac{1}{10} qf(\gamma_H^2 g_e^2 \beta_e^2 / r^6)(3\tau_c/1 + \omega_H^2 \tau_c^2)$$

where q is the number of coordinated nuclei, f the fraction of bound nuclei and all the other symbols have the usual meaning.

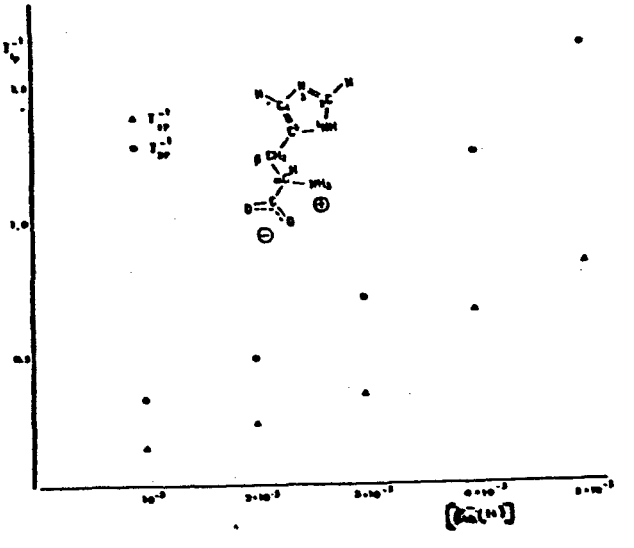

Fig.1 - T_{1p}^{-1} and T_{2p}^{-1} of H_2 of L-His 0.1 M in D_2O vs. the Cu(II) molar concentration; pH=7.0; T=298°K.

With the aim of calculating q for the imidazole moiety in the title complex, r was assumed from X-ray crystallographic data worked out for the Cu(II)(L-His)(D-His) complex[1] (r=3.27 Å)

and τ_c was approximated with that for the water molecules in the same complex (τ_c=5.19x10^{-10} s at 298 K) by measuring the T_{1p}^{-1} values for the water protons and by assuming the crystallographic copper-water distance. The calculated q for H_2 was 0.05 $\pm$ 0.01 which is meaningless since $1 < q < 2$ was expected.

Since using τ_c of water molecules may be thought a rough approximation, computer fitting procedures of the ESR lineshape were utilized. The fit for the spectra at X band (ω= 5.97 x 10^{10} rad/s) S band (ω = 2.14 x 10^{10} rad/s) and L band (ω = 7.54 x 10^9 rad/s) is consistent with the following ESR parameters: g_{iso} = 2.09; $g_{//}$ = 2.23; $g_{\perp}$ = 2.02; A_{iso} = - 65 G; $A_{//}$ = -179 G; $A_{\perp}$ = -8 G; two equivalent nitrogens with a_N' = 13.5 G plus two equivalent nitrogens with a_N'' = 8.5 G; residual linewidth 4 G; τ_c =8x10^{-11} s at 298 K. The number of unknown variables could be suitably reduced in the following way: The values of $g_{//}$ and $A_{//}$ were measured from frozen solution ESR spectra. The distance between the $M_I = -\frac{1}{2}$ and the $M_I=+\frac{1}{2}$ lines gives reasonable estimate of A_{iso} from liquid phase ESR spectra at low frequency. The parameters obtained from the fitting procedure are quite reliable since only one set of values could be found to fit the ESR spectra at all three frequencies.

The correlation time is the reorientational time of the complex modulating the g and A anisotropies and it can be taken as the correlation time responsible for the modulation of the dipole-dipole interaction. It is worth emphasizing that the value of τ_c seems to be quite precise since the fit breaks down for deviations greater than 15%. It has been verified that the ESR lineshape at X band and 345 K is identical with that at S band and 290 K, to make sure that τ_c is a rotational tumbling time.

However even with this correlation time the NMR results are not self consistent since the q value is 0.3 $\pm$ 0.1 which is still about one order of magnitude smaller than expected. The simplified equation derived from the SBM theory breaks down for Cu(II) complexes in solution[2]. As a matter of fact the SBM theory assumes an isotropic electron spin g tensor, while the large g tensor anisotropy of the title complex in solution (Δg = 0.21) gives rise, at high magnetic fields, to an electron g anisotropy Zeeman energy ($|\Delta g|\beta H_0$= 9.15x10^{-17} erg) which cannot be averaged out completely by the rotational tumbling ($\hbar\tau_c^{-1}$ = 1.32x10^{-17}erg). The incomplete averaging out of the electron spin anisotropy's energy brings about a decrease of the electron nucleus dipole-dipole interaction, which reflects in very small paramagnetic contributions. Therefore, the SBM theory results in overestimates of the dipolar interaction energy yielding meaningless values for structural and motional parameters.

It may be concluded that the quantitative analysis of nuclear relaxation rates in solution of Cu(II) ions is not a straightforward matter since ambiguities are arising about the evaluation of the dipole-dipole interaction energy. THe ESR lineshape analysis is, on the other hand, to be preferred provided computer fitting at different frequencies can be carried out. The experimental results were fit using four nitrogen donor atoms including one pair of equivalent nitrogens with a_N'= 13.5 G and one pair of equivalent nitrogens with a_N'' = 8.5 G. These parameters gave the best fit between experimental and computer

simulated spectra at three frequencies. Despite the fact that the nitrogen hyperfine coupling is not resolved in the experimental data, the simulated results are consistent with the previously proposed interpretation. Then in the case of the Cu(II)(L-His)$_2$ complex the structure in which the two L-His ligands are both bound in the histamine-like way appears to be the predominant configuration in solution, although, in principle, minor contributions from other configurations cannot be ruled out, as it has been suggested elsewhere[3].

REFERENCES

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