Inorganica Chimica Acta, 58 (1982) 207–211

Nmr Relaxation Studies in Solution of Transition Metal Complexes. IV. Equilibrium Dynamics in Aqueous Solution of Copper(II)–Glycylglycine System

ISTVÁN NAGYPÁL and FERENC DEBRECZENI

Institute of Inorganic and Analytical Chemistry, L. Kossuth University, H-4010 Debrecen, Hungary

Received June 9, 1981

The dynamics of equilibrium in aqueous solution of copper(II)–glycylglycine system has been studied by NMR relaxation method. The relaxation rate measured in solutions with 1:1 metal–ligand concentration ratios was found to be the linear combination of the concentration of the complexes formed. A very small molar relaxation coefficient was found for the binuclear $Cu_2(LH_{-1})_2OH$ complex. This may be explained by spin-pairing through the bridging OH ligand. The high value for the $Cu(LH_{-1})OH$ complex is interpreted by a fast proton exchange between the bulk water and the coordinated OH^- ligand.

The ligand exchange rate constant for the $CuL(LH_{-1})^- + L^- \rightleftharpoons CuL^*(LH_{-1})^- + L^-$ process was found to be 4.5×10^7 M^{-1} s^{-1}. It is assumed that the incoming ligand replaces the $-COO^-$ group of the ligand coordinated in LH_{-1} form, thus the ligand exchange takes place without Jahn–Teller inversion. It was found that the $-NH_2 - H_2O$ proton exchange processes are also influencing the measured relaxation data. Their rate constants are also given. The paramagnetic relaxation time for the $-NH_2$ protons of the ligand coordinated in L^- form in the $CuL(LH_{-1})$ complex was found to be 2.1×10^{-6} sec.

Introduction

The dynamics of equilibrium in aqueous solution of some copper(II)–diamine and α-aminoacid parent and mixed complexes was reported in the earlier parts of the series [1–3]. The systems studied so far are represented mainly by stepwise complex formation which is disturbed in some cases by the formation of hydrolyzed species. The composition and stability of the species formed in aqueous copper(II)–glycylglycine solution are basically different from that of the simple copper(II)–bidentate ligand systems. It is well known from previous equilibrium studies [4–6], that the copper(II) forms CuL^+, $Cu(LH_{-1})$, $CuL(LH_{-1})^-$, $Cu(LH_{-1})OH^-$ and $Cu_2(LH_{-1})_2(OH)^-$ complexes with glycylglycine, where LH_{-1} stands for that form of the ligand from which the proton of the

$$-\overset{\overset{O}{\parallel}}{C}-NH-$$

group is dissociated.

From a kinetic point of view, Pasternack *et al.* [7] studied the $Cu^{2+} + L^- \rightleftharpoons CuL^+$ formation reaction, Scheinblatt [8] investigated the proton exchange reactions of the peptide group, while Applegate *et al.* [9] measured the proton exchange rate constant of the terminal amino group of the free ligand. The aim of the present work was to get information on the dynamics of equilibrium in aqueous solution, and to see the applicability of the NMR relaxation method to a relatively complicated equilibrium system.

TABLE I. Formation Constants of the Complexes Formed in the Copper(II)–Glycylglycine System in Aqueous Solution (I = 1 *M* KCl, 298 K):

$$\beta_{ijk} = \frac{[Cu_iL_jH_k]}{[Cu]^i[L]^j[H]^k}$$

Composition	logβ
HL	8.139 ± 0.004
H_2L	11.303 ± 0.009
CuL	5.49 ± 0.016
$CuLH_{-1}$	1.13 ± 0.004
$CuLH_{-2}$	−8.38 ± 0.008
CuL_2H_{-1}	4.05 ± 0.018
$Cu_2L_2H_{-3}$	−5.26 ± 0.040

Experimental

The equilibria existing in copper(II)–glycylglycine system are well known. For our purposes however, the equilibrium constants at exactly the same condition which is used for the NMR studies is necessary (1 *M* KCl, 298 K). Therefore the pH-

TABLE II. Total Copper(II) Concentrations and the Concentration Ratios of the Solutions Studied.

No.	T_{Cu}	$T_L:T_{Cu}$	No. of exp. points
1	0.010	1:1	25
2	0.015	1:1	20
3	0.020	1:1	24
4	0.025	1:1	7
5	0.010	2:1	9
6	0.015	2:1	8
7	0.020	2:1	14
8	0.010	4:1	14
9	0.015	4:1	14
10	0.020	4:1	19
11	0.010	8:1	19
12	0.015	8:1	12
13	0.020	8:1	20

metric analysis of the system was carried out at 2.5 × 10^{-3}–10^{-2} *M* total copper(II) concentrations and at variable (1:1–1:4) total copper(II)–total ligand concentration ratios. The stability constants are summarized in Table I.

A Newport N-20 type instrument working at 2.5 MHz frequency was used to measure the T_2 relaxation time by single echo [10] technique. The relaxation studies were carried out as titrations, described previously [1]. The initial concentrations of the solutions to be titrated are summarized in Table II, together with the pH-ranges and the number of experimental points. The evaluation of the results was based on the least squares treatment of the measured log T_2 data according to the models described in the following section.

Results and Discussion

NMR Studies at 1:1 Metal–Ligand Concentration Ratio

The result of titration No. 2 in Table II is illustrated in Fig. 1, together with the concentration distribution of the complexes.

The shape of the curve suggests that the $T_{2p}^{-1} = T_{2M}^{-1} - T_{2o}^{-1}$ data may be represented as a linear combination of the concentration of the individual complexes. The mathematical analysis – including titrations No. 1–4 – showed that this description was correct, the average deviation of the data being 4.4%. The molar relaxation coefficients given for the different complexes formed at 1:1 concentration ratio are in Table III.

The molar relaxation coefficient for the binuclear $Cu_2(LH_{-1})_2OH$ complex was found to be 210 ± 160.

TABLE III. Molar Relaxation Coefficients of the Complexes Formed in the Copper(II)–Glycylglycine System at 1:1 Total Concentration Ratios.

Species	r
Cu^{2+}	2020*
CuL^+	1070 ± 70
$CuLH_{-1}$	726 ± 15
$CuLH_{-2}^-$	3590 ± 40

*Measured in absence of glycylglycine.

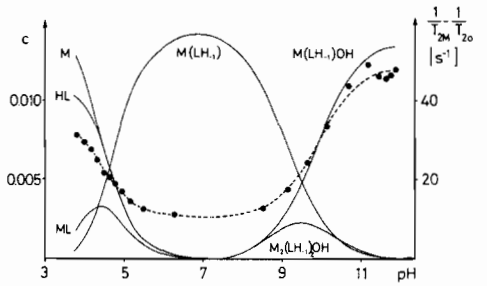
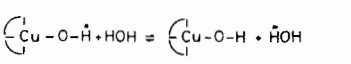


Fig. 1. Concentration distribution of the complexes formed and the change of the paramagnetic contribution to the relaxation rate as a function of pH in aqueous solution for the copper(II)–glycylglycine system at $T_L = T_{Cu} = 0.015$ *M*.

This small value and its high standard deviation indicated that the contribution of the effect of this complex to the measured data was negligible, thus it was omitted. The omission of the effect of $Cu_2(LH_{-1})_2$-OH increased the average deviation by only 0.1%. This finding suggests that the $Cu_2(LH_{-1})_2OH$ complex is a diamagnetic one, probably because of spin-pairing through the bridging OH ligand.

The decrease of the molar relaxation coefficients in the Cu–CuL–Cu(LH_{-1}) order is in accordance with the decreasing number of water molecules remaining in the first coordination sphere. The molar relaxation coefficient for Cu(LH_{-1})OH is surprisingly high.

According to our preliminary experiments on the tetrahydroxo copper(II) complex, the paramagnetic relaxation time (T_{2B}) is much shorter for the protons of the coordinated OH group than for the coordinated H_2O. In the light of this finding, the high value for the molar relaxation coefficient of Cu(LH_{-1})OH may be explained by assuming a fast proton exchange between the bulk water and the coordinated OH group:



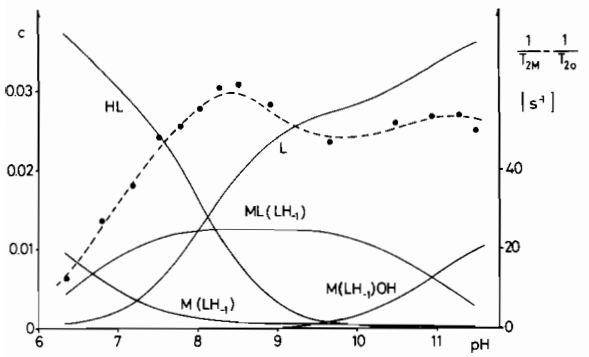


Fig. 2. Concentration distribution of the complexes formed and the change of the paramagnetic contribution to the relaxation rate as a function of pH in aqueous solution for the copper(II)–glycylglycine system at T_L = 0.06 and T_{Cu} = 0.015 *M*.

Relaxation Studies in Ligand Excess

The measured and the back-calculated relaxation rates in case of titration No. 9 are seen in Fig. 2. The change of the measured data as a function of pH follows the same pattern in all titrations, but the maximum of the relaxation rate at pH ~ 8.5 is more pronounced as the ligand concentration is increased. For the interpretation of the data, the following possibilities were considered:

i) The increase of the relaxation rate compared to that of the relaxation rate at 1:1 ratio is a linear function of $[CuL(LH_{-1})]$ which is formed only in ligand excess. The calculations based on this assumption did not lead to any acceptable fit of the experimental data.

ii) Beside *i*, the ligand exchange

$$CuL(LH_{-1})^- + \overset{*}{L}^- \underset{}{\overset{k_2}{\rightleftharpoons}} Cu\overset{*}{L}(LH_{-1})^- + L^-$$

takes place. In this case the measured data would be the linear combination of the concentration of the complexes formed and of the $[CuL(LH_{-1})]$ [L] concentration product. This model did not lead to an acceptable fit either.

iii) The effect of the above ligand exchange is assumed, but at higher ligand concentration the paramagnetic relaxation of the $-NH_2$ protons controls the measured data. The average fit in this case was much better than in cases *i* and *ii*, but considerably higher (14.3%) than acceptable.

iv) Beside *iii*, it was assumed that the $-NH_2 \rightleftharpoons H_2O$ proton exchange also influences the measured data. It is known from the ultrasonic result of Applegate *et al.* [9] that at pH ~ 11–12 the proton exchange takes place mainly through the

$$R{-}NH_2 + H_2O \underset{}{\overset{k_1}{\rightleftharpoons}} R{-}NH_3^+ + OH^-$$

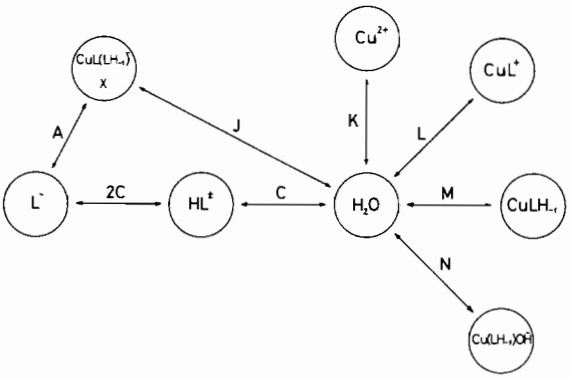
process, with a rate constant of 3.1×10^4 sec^{-1}. The assumption of this proton exchange only resulted in an average deviation of 11.5%, which is also higher than acceptable. Taking into account that the pH-range where the proton exchange influences the measured relaxation time is much lower than in Applegate's ultrasonic experiment, and that the

$$R{-}NH_2 + \overset{*}{H}OH + R{-}NH_3^+ \underset{}{\overset{k_3}{\rightleftharpoons}}$$

$$R{-}NH_2\overset{*}{H}^+ + HOH + R{-}NH_2$$

proton exchange was found to be significant in case of glycine [1, 12], this process has also been assumed. The average deviation of the measured data was 5.9% in this case.

According to the above the following model can be used to describe the $T_{2M}^{-1} - T_{2o}^{-1} = T_{2p}^{-1}$ data in case of the copper(II)–glycylglycine system, including the measurements at 1:1 concentration ratio and at ligand excess:



where

$$A = 2k_2[CuL(LH_{-1})^-][L^-]$$
$$X = 2[CuL(LH_{-1})]/T_{2B}$$
$$C = k_1[L] + k_3[L][HL]$$
$$K = 2020\ [Cu^{2+}]$$
$$L = 1070\ [CuL^+]$$
$$M = 726\ [Cu(LH_{-1})]$$
$$N = 3590\ [Cu(LH_{-1})OH]$$
$$J = r_{CuL(LH_{-1})}[CuL(LH_{-1})]$$

The stoichiometric number in equation for X means that only the exchange of that ligand is assum-

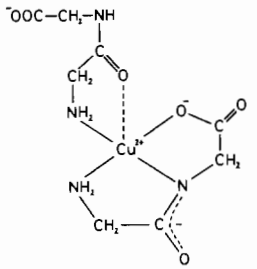


TABLE IV. The Different Kinetic Parameters given by the Least Squares Fit of the Experimental Data.

$r_{CuL(LH_{-1})}$ M^{-1} s^{-1}	k_2 M^{-1} s^{-1}	T_{2B} s	k_1 s^{-1}	k_3 M^{-1} s^{-1}
1940	4.5×10^7	2.1×10^{-6}	1.6×10^5	4.7×10^7

ed which is bound to the equatorial position through the $-NH_2$ group and to an axial position through the carbonyl group, in accordance with the structure suggested for the $CuL(LH_{-1})^-$ complex [4, 6].

The exchange of that ligand which is coordinated in the three equatorial positions in LH_{-1} form is assumed to be negligible compared to the other. This assumption is supported by the following:

– The exchange of the LH_{-1} ligand may take place in the $Cu(LH_{-1})OH$ complex also, and such type of exchange could not be detected.

– High resolution spectra were detected in a solution containing 0.3 *M* glycylglycine and 0.001 *M* $CuCl_2$ as a function of pH. It was found that the signal of the $-CH_2-$ at the carboxylate end of the ligand is detectable in the whole pH-range, while that of the other $-CH_2-$ is broadened so much, that it can be detected only in the pH > 11.5 range, where $Cu(LH_{-1})OH$ dominates over $CuL(LH_{-1})$.

The arrow directly connecting the $CuL(LH_{-1})$ and H_2O environments expresses that proton exchange which takes place from $CuL(LH_{-1})$ without the exchange of the whole ligand, thus the constant of process J is in fact a molar relaxation coefficient, similar to those denoted by K. L, M, N. According to the above model, the T_{2p}^{-1} data can be represented by the following equation:

$$T_{2p}^{-1} = K + L + M + N + J + \frac{1}{2[H_2O]} \frac{\frac{AX}{A+X} \cdot \frac{2}{3} C}{\frac{AX}{A+X} + \frac{2}{3} C}$$

Because the molar relaxation coefficients for Cu^{2+}, CuL, $CuLH_{-1}$ and $Cu(LH_{-1})OH$ are known from the experiments at 1:1 concentration ratio, only five parameters, the molar relaxation coefficient for $CuL(LH_{-1})$, the k_2 ligand exchange, the k_1, k_3 proton exchange rate constants and the T_{2B} for the coordinated $-NH_2$ were calculated by a direct search method. The average fit was acceptable (5.9%) and the appropriate constants are included in Table IV.

The molar relaxation coefficient for $CuL(LH_{-1})$ is surprisingly high. If only the water molecule remaining in one of the axial positions were responsible for it, its value would be expected at about 200 M^{-1} sec^{-1}. The high value may be explained on a similar way as was done earlier in the case of some copper(II) diaminomonocarboxylate complexes [11]. Namely, there is a continuous intramolecular rearrangement of the ligands in $CuL(LH_{-1})$ and during this process one of the $-NH_2$ groups may become free for a short time, which is long enough for the proton exchange with water to take place.

The T_{2B} for the $-NH_2$ of the coordinated ligand in $CuL(LH_{-1})$ is higher than in the case of the aminoacids and ethylenediamine. This may probably be explained by the fact that the electron density on the $-NH_2$ group of glycylglycine is smaller than in the other ligands, which is reflected in its lower pK value also.

The agreement between the k_1 proton exchange rate constant determined by Applegate *et al.* (3.1×10^4 sec^{-1}) and by us is acceptable taking into account the basically different experimental conditions and methods. No comparable data for the k_3 proton exchange rate constant is available in the literature.

The k_2 ligand exchange rate constant is surprisingly high, as one may expect that the two nitrogen donors in the adjacent positions of the equatorial plane prevent the $CuL(LH_{-1})$ complex from the rapid Jahn–Teller inversion, which is in general responsible for the kinetic lability of the copper(II) complexes. In spite of this, the ligand exchange rate constant is only slightly less than for the copper(II)–glycine and much higher than for the copper(II)–ethylenediamine complex. A possible explanation is that the incoming ligand replaces the coordinated $-COO^-$ of the LH_{-1} ligand, thus it is bound directly to the equatorial plane, without Jahn–Teller inversion.

References

1 I. Nagypál, F. Debreczeni and R. E. Connick, *Inorg. Chim. Acta, 48,* 225 (1981).
2 I. Nagypál, F. Debreczeni and F. Erdödi, *Inorg. Chim. Acta, 57,* 125 (1981).
3 F. Debreczeni and I. Nagypál, *Inorg. Chim. Acta, 57,* 135 (1981).
4 A. Kaneda and A. E. Martell, *J. Coord. Chem., 4,* 137 (1975).
5 G. Brookes and L. D. Pettit, *J. Chem. Soc. Dalton,* 2106 (1975).

6 A. Gergely and I. Nagypál, *J. Chem. Soc. Dalton*, 1104 (1977).
7 R. F. Pasternack, M. Angwin and E. Gibes, *J. Am. Chem. Soc.*, *92*, 5878 (1970).
8 M. Scheinblatt, *J. Am. Chem. Soc.*, *92*, 2505 (1970).
9 K. Applegate, L. J. Slutsky and K. C. Parker, *J. Am. Chem. Soc.*, *90*, 6909 (1968).
10 T. C. Farrar and E. D. Becker, 'Fulse and Fourier Transform NMR', Academic Press, New York and London, 1971.
11 A. Gergely, E. Farkas, I. Nagypál and E. Kas, *J. Inorg. Nucl. Chem.*, *40*, 1709 (1978).
12 K. C. Chang and E. Grunwald, *J. Phys. Chem.*, *80*, 1422 (1976).