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Coordination equilibria in the complex formation of guanylurea with Cu^{II}: Formation and stability of binary Cu^{II}-guanylurea and ternary Cu^{II}-guanylurea–glycinate complexes

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Abstract. Combined pH-metric and spectrophotometric investigations on the complex formation equilibria of Cu^{II} with guanylurea ($H_2{}^1NC(=O)\ {}^2NH.C(={}^3NH)\ {}^4NH_2$), hereafter, GuH, in the absence and in the presence of glycine (GlyH), in aqueous solution indicates variety of binary and mixed-ligand complexes: $Cu(Gu)^+$, Cu(Gu)(OH); $Cu(Gu)_2$, $Cu(Gu\text{-}H)(Gu)^-$, $Cu(Gu\text{-}H)_2^{2-}$, $Cu(Gu\text{-}H)(Gu\text{-}2H)^{3-}$; $Cu(Gly)^+$, Cu(Gly)(OH); Cu(Gly)(Gu); $Cu(Gly)(Gu\text{-}H)^-$, $Cu(Gly)(Gu\text{-}2H)^{2-}$; $(Gly)Cu(Gu)Cu(Gly)^+$, (Gly)Cu(Gu-H)Cu(Gly) and $(Gly)Cu(Gu\text{-}2H)Cu(Gly)^-$. At pH < 6, guanylurea anion (Gu^-) acts as a [(C=O), ${}^3N^-$] or [$={}^1NH$, ${}^3N^-$] bidentate ligand and above pH 7 it is transformed through a coordination equilibrium into a ($={}^1N^-$, $={}^3N^-$) bidentate ligand, similar to biguanide dianion. Occurrence of dinuclear complex species, (Gly)Cu(Gu)Cu(Gly)$^+$, in the complexation equilibria, indicates bridging double bidentate [(${}^1NH_2$, ${}^3N^-$), (C=O, ${}^4NH_2$)] and/or [(${}^1NH_2$, ${}^4NH_2$), (C=O, ${}^3N^-$)] chelation by Gu^- ion in an isomeric equilibrium. Above pH 6·5, the dinuclear complex decomposes mostly to the mononuclear species, Cu(Gly)(OH) and Cu(Gu)(OH) and only partly deprotonates to (Gly)Cu(Gu-H)Cu(Gly) and $(Gly)Cu(Gu\text{-}2H)Cu(Gly)^-$. Electronic spectral shifts, with change of pH have been correlated with the possible modes of coordination of guanylurea species.

Keywords. Cu^{II}; guanylurea; glycinate; mixed-ligand complex; formation constants.

1. Introduction

Transition metal complexes with guanylurea and its ${}^1N$-alkyl/${}^1N$-aryl derivatives had been studied by many workers.[1–4] Majority of these studies were aimed at isolation and characterization of metal complexes and elucidation of their structures by various physicochemical methods. Studies on the metal–ligand complex formation equilibria of this group of ligands were, however, scanty. Protonation–deprotonation equilibria of guanylurea and its ${}^1N$-methyl and ${}^1N$-ethyl derivatives and complex formation of these ligands with Cu^{II} and Ni^{II} were studied by spectrophotometric and pH-metric methods and instability constants of these complexes were compared to the corresponding complexes with the biguanide analogue.[5] A strong blue shift of the absorption maximum of Cu^{II}-guanylurea mixture from 650–660 nm at pH ~ 6 to 530–540 nm at pH 7·5 was observed and assigned to 1 : 1 and 1 : 2 Cu^{II}-guanylurea complexes respectively. This opened the scope for further work in this area, to investigate as to whether any structural change involving alteration in the modes of coordination of the guanylurea ligand species is also responsible for such a strong blue shift of the absorption maximum of Cu^{II} with rise of pH of the solution. Moreover, literature survey revealed the absence of any report of systematic study on the mixed-ligand complex formation equilibria with guanylurea and its derivatives as ligands.

In view of these, it was considered worthwhile to undertake a systematic pH-metric and spectrophotometric investigation on the binary and mixed-ligand complex formation equilibria of metal ions with guanylurea in presence of typical (N, O) donors, such as aminoacids, small peptides as auxiliary ligands, for elucidating the exact nature of the complexation equilibria and the modes of coordination of guanylurea in the resulting complexes occurring at different pH.

In this paper, we describe the results of a combined spectrophotometric and computer-based pH-

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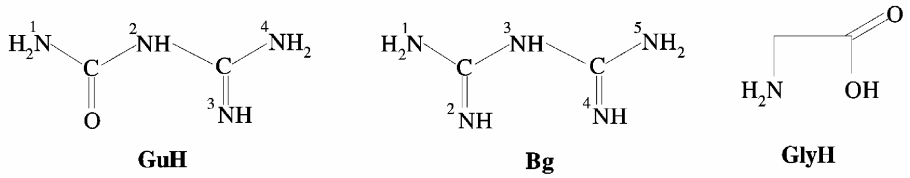


Scheme 1.

metric equilibrium study on the complex formation of Cu^{II} with guanylurea (GuH) (scheme 1) in the absence and in the presence of the simplest amino acid, glycine (GlyH) as the auxiliary ligand in aqueous solution at 25 ± 1°C at a fixed ionic strength, $I = 0{\cdot}1$ mol.dm^{-3} ($NaNO_3$).

Varied modes of metal ion coordination by guanylurea species in binary and mixed ligand complexes with Cu^{II}, as indicated from this study, have been compared with the modes of coordination of isostructural biguanide (Bg) ligand species in analogous complexes described earlier.[6]

2. Experimental

2.1 *Materials and methods*

Guanylurea sulphate dihydrate, $(GuH_2^+)_2(SO_4^{2-})\cdot 2H_2O$, was prepared and purified following the literature procedure.[1] Purity of the compound was checked from elemental analysis and its equivalent weight was determined by pH-metric acid-base titration method.[7] All the other reagents were of AR grade and their solutions were prepared in double distilled CO_2 free water. Cu^{II} nitrate solution was prepared by dissolving freshly precipitated alkali free $Cu(OH)_2$ in AR nitric acid and was standardized by combined ion-exchange, acid-base and complexometric EDTA titration methods.[7] Equilibrium study for the determination of proton–ligand and metal–ligand complex formation constants involved pH-metric titrations of a series of solutions, each of initial volume 0·025 dm^3, containing known amounts (0·001–0·002 mol.dm^{-3}) of the ligands, guanylurea and/or glycine in their protonated forms (GuH_2^+ and/or $GlyH_2^+$ respectively) in the absence and in the presence of known amounts (0·0002–0·001 mol.dm^{-3}) of Cu^{II} nitrate and known amount (0·005 mol.dm^{-3}) of free HNO_3 with a carbonate free standard 0·1 mol.dm^{-3} NaOH solution,[8] maintaining a constant ionic strength, $I = 0{\cdot}1$ mol.dm^{-3} ($NaNO_3$) at 25 ± 1°C (thermostated).

pH measurements were carried out with a *Systronics* digital pH meter (type 335) using a special glass electrode (pH 1–14, accuracy ± 0·01 pH) in conjunction with a saturated calomel electrode. Some representative pH-titration curves are presented in figure 1. pH-volume (of standard 0·1 mol.dm^{-3} NaOH) data, as the averages of three titrations, were accepted for calculating the equilibrium constants using the computer program SCOGS,[9] run on a Pentium-4 computer. Refined values of the constants (table 1) corresponding to the minimum standard deviations were accepted for calculating the speciation curves (figures 2, 3), required for elucidation of the complexation equilibria. Some related constants are presented in table 2. Preliminary estimates of some of the constants supplied to the computer as input data, were either obtained from literature[10] or calculated according to the method of Irving and Rossotti.[11] Ionic product of water at the experimental temperature and the activity coefficient of hydrogen ion at

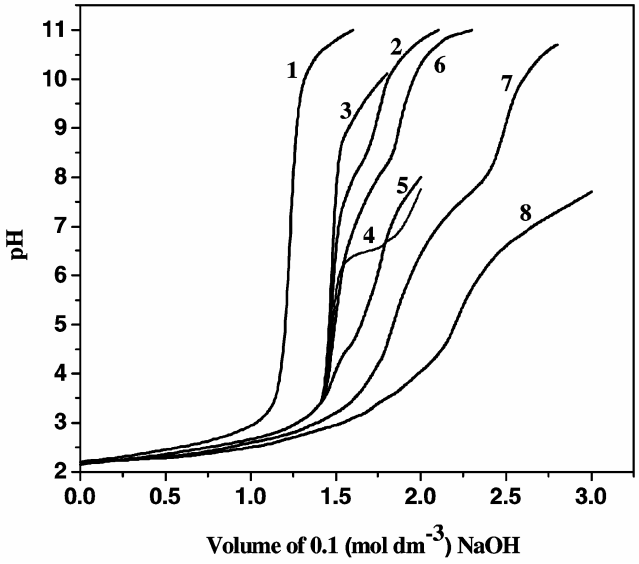


Figure 1. Representative pH titration curves (M = mol.dm^{-3}): 1, 0·005 (M) HNO_3; 2, (1) + 0·001 (M) H_2Gu^+; 3, (1) + 0·001 (M) H_2Gly^+; 4, (2) + 0·001 (M) Cu^{II}; 5, (3) + 0·001 (M) Cu^{II}; 6, (2) + 0·0002 (M) Cu^{II}; 7, (5) + 0·001 (M) H_2Gu^+; 8, (2) + 0·002 (M) H_2Gly^+ + 0·002 (M) Cu^{II}; initial volume = 0·025 dm^3, titrant = 0·1 (M) NaOH, ionic strength, $I = 0{\cdot}1$ mol.dm^{-3} ($NaNO_3$).

Table 1. Formation constants (β_{pqrs}) of binary and mixed ligand Cu^{II} complexes with guanylurea (Gu^-) and glycinates (Gly^-) in aqueous solution, Ionic strength, [I = 0·1 mol. dm^{-3} ($NaNO_3$)] at 25 ± 1°C.

Sl. no.	Complex species	p	q	r	s	$\log\beta_{pqrs}$
1.	H_2Gu	0	1	0	–2	10·20
2.	HGu	0	1	0	–1	08·20
3.	HGlyH	0	0	1	–2	11·87
4.	GlyH	0	0	1	–1	09·61
5.	$Cu(OH)^+$	1	0	0	1	–6·29
6.	$Cu(OH)_2$	1	0	0	2	–13·05
7.	$Cu(Gly)^+$	1	0	1	0	08·23
8.	Cu(Gly)(OH)	1	0	1	1	01·11
9.	$Cu(Gly)_2$	1	0	2	0	15·19
10.	$Cu(Gu)^+$	1	1	0	0	05·61
11.	Cu(Gu)(OH)	1	1	0	1	–0·24
12.	$Cu(Gu)_2$	1	2	0	0	10·25
13.	Cu(Gu)(Gu-H)	1	2	0	1	03·15
14.	$Cu(Gu\text{-}H)_2$	1	2	0	2	–04·36
15.	Cu(Gu-H)(Gu-2H)	1	2	0	3	–12·21
16.	Cu(Gly)(Gu)	1	1	1	0	12·97
17.	Cu(Gly)(Gu-H)	1	1	1	1	05·11
18.	Cu(Gly)(Gu-2H)	1	1	1	2	–05·48
19.	(Gly)Cu(Gu)Cu(Gly)	2	1	2	0	26·00
20.	(Gly)Cu(Gu-H)Cu(Gly)	2	1	2	1	18·10
21.	(Gly)Cu(Gu-2H)Cu(Gly)	2	1	2	2	10·50

Limits of error: ± 0·02 in log scale

Table 2. Deprotonation constants and decomposition constants of some binary Cu^{II}–Gu^- and ternary Cu^{II}–Gu^-–Gly^- complexes.

$\log K^{H}_{Cu(Gu)(H2O)}$	$\log K^{H}_{Cu(Gu)2}$	$\log K^{2H}_{Cu(Gu)2}$	$\log K^{3H}_{Cu(Gu)2}$
–14·05	–7·10	–14·61	–22·46
$\log K_{d(1101)}$	$\log K_{d(1020)}$	$\log K_{d(2120)}$	
–4·61	–14·08	–25·13	

Limits of error: ± 0·02 in log scale

the experimental ionic strength were obtained from literature.[12,13] Analytical concentrations of hydrogen ion, [H^+], at different pH meter readings were calculated by following the usual procedure.[14] To elucidate the modes of coordination by the ligands, electronic spectra (figure 4) of the metal–ligand mixtures at different pH values, particularly at pH values corresponding to the concentration maxima of some specific complexes, were run on a Hitachi UV-3501 spectrophotometer against water as blank.

2.2 *Calculation of formation constants*

The overall formation constant (β_{pqrs}) of a homometallic ternary complex of generalised stochiometry, $Cu_p(Gu)_q(Gly)_r(OH)_s$, (table 1), may be defined (omitting the charges) according to,

$$p\mathrm{Cu} + q\mathrm{Gu} + r\mathrm{Gly} + s(\mathrm{OH}) \rightleftharpoons \mathrm{Cu}_p(\mathrm{Gu})_q(\mathrm{Gly})_r(\mathrm{OH})_s \quad (1)$$

$$\beta_{pqrs} = \frac{[\mathrm{Cu}_p(\mathrm{Gu})_q(\mathrm{Gly})_r(\mathrm{OH})_s]}{[\mathrm{Cu}]^p[\mathrm{Gu}]^q[\mathrm{Gly}]^r[\mathrm{OH}]^s}, \quad (1a)$$

where the stochiometric integers, p, q and r may be positive or zero. s is a positive integer for a deprotonated or a hydroxo species like Cu(OH), Cu(Gly)(OH), Cu(Gu-H), a negative integer for a protonated species like GlyH, $GlyH_2^+$, GuH, GuH_2^+ and zero for a neutral species like $Cu(Gly)^+(aq)$, $Cu(Gu)^+(aq)$, Cu(Gly)(Gu), etc. For binary 1 : 1 and 1 : 5 metal : ligand mixtures, p = 1 and the values of q or r depend on the molar ratio of the ligand:metal in the complexes supposed to be formed in the solution. For the 1 : 1 : 1 Cu^{II} : GuH : GlyH ternary mixture, $p = q = r = 1$, and for the 2 : 1 : 2 Cu^{II} : GuH : GlyH mixture, p = 2, q = 1, and r = 2. Since the pH range of some of the complex formation equilibria are overlapping with the hydrolytic equilibria of the

$Cu^{2+}(aq)$ ions, formation of hydroxo species, $Cu(OH)^{+}$ and $Cu(OH)_2$, Cu(Gu)(OH) and Cu(Gly)(OH) have also been taken into consideration in calculating the formation constants (β_{pqrs}). However, pH-titration data, prior to the appearance of any turbidity, have only been subjected to calculation for the constants.

(N, O^{-}) bidentate chelating mode of coordination by glycinate (Gly^{-}) ligand in its metal complexes are well known.[15] Complexes involving other modes of coordination of glycine/glycinate, viz. N-monodentate, $(HOOCCH_2H_2N)Cu$, O-monodentate ($H_2N CH_2COO^{-}$)Cu and (N,O) bridging bidentate Cu($H_2N CH_2COO^{-}$)Cu, have also been considered along with the complexes involving the expected (N,O^{-}) bidentate chelating glycinate, in calculating the formation constants of the complexes, using the literature values[10] of the stability constants of Cu^{II} complexes with ethylamine and acetate ion as ligands, as tentative estimates. The values of standard deviations in all such calculations are found to be large and the concentrations of the corresponding complexes are negligibly so small that they are not even identifiable on the speciation curves (figures 2, 3). Therefore, such complexes have been excluded in the final calculation of the formation constants.

3. Results and discussion

3.1 *Proton–ligand equilibria*

Protonated guanylurea cation, GuH_2^{+}, provides two well separated buffer regions, (pH < 4 and 7 < pH < 9), due to successive deprotonation[5] of either $-^{1}NH_3^{+}$ (or $-^{4}NH_3^{+}$) and the $=^{3}NH$ moieties to form ultimately the monoanion, Gu^{-}. Similarly glycinium cation ($GlyH_2^{+}$), also provides two well separated buffer regions (2 < pH < 4 and 8 < pH < 10) due to successive deprotonation of COOH and the NH_3^{+} groups.[10,15]

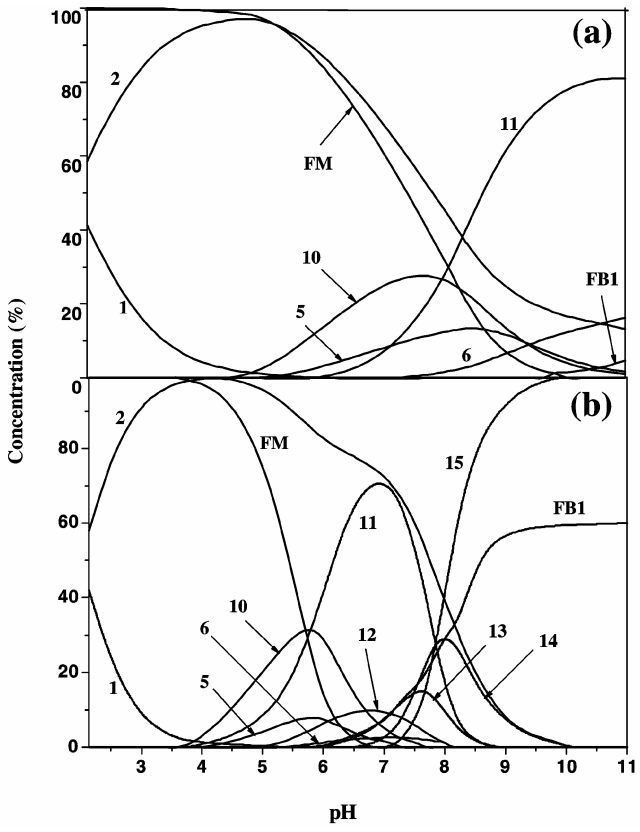


Figure 2. Speciation curves of (**a**) 1 : 1 and (**b**) 1 : 5 Cu^{II} : GuH systems: 1, H_2Gu^{+}; 2, HGu; 5, $Cu(OH)^{+}$; 6, $Cu(OH)_2$; 10, $Cu(Gu)^{+}$; 11, Cu(Gu)(OH); 12, $Cu(Gu)_2$; 13, Cu(Gu)(Gu-H)$^{-}$; 14, Cu(Gu-H)$_2^{2-}$; 15, Cu(Gu-H)(Gu-2H)$^{3-}$; FM = Free Cu^{II}, FB1 = Free Gu^{-}.

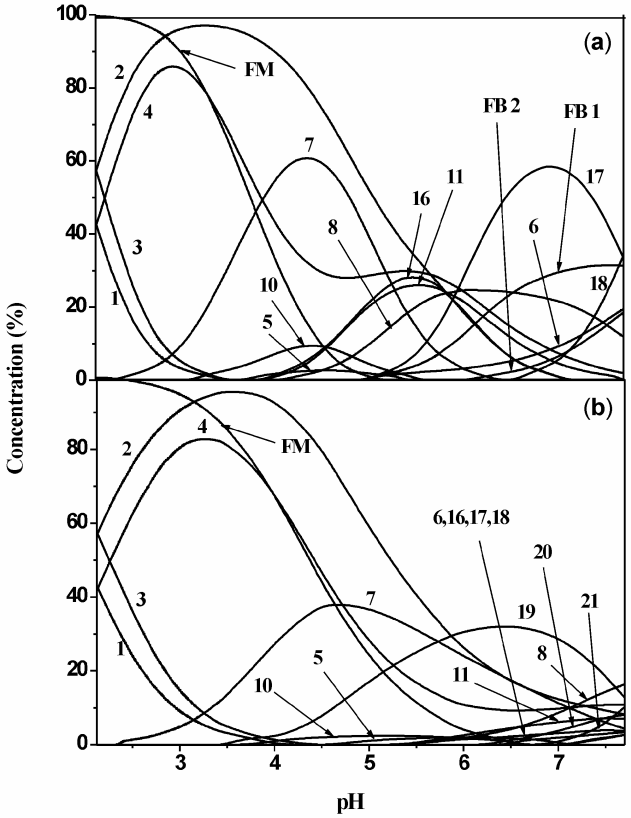


Figure 3. Speciation curves of (**a**) 1 : 1 : 1 and (**b**) 2 : 1 : 2 Cu^{II} : GuH : GlyH systems: 1, H_2Gu^{+}; 2, HGu; 3, H_2Gly^{+}; 4, HGly; 5, $Cu(OH)^{+}$; 6, $Cu(OH)_2$; 7, $Cu(Gly)^{+}$; 8, Cu(Gly)(OH); 10, $Cu(Gu)^{+}$; 11, Cu(Gu)(OH); 16, Cu(Gly)(Gu); 17, Cu(Gly)(Gu-H)$^{-}$; 18, Cu(Gly)(Gu-2H)$^{2-}$; 19, (Gly)Cu(Gu)Cu(Gly)$^{+}$; 20, (Gly)Cu(Gu-H)Cu(Gly); 21, (Gly)Cu(Gu-2H)Cu(Gly)$^{-}$; FM = Free Cu^{II}; FB1 = Free Gu^{-}; FB2 = Free Gly^{-}.

3.2 *Binary Cu^{II} : GuH and Cu^{II} : GlyH equilibria*

Complex formation in both (1 : 1) and (1 : 5) Cu^{II} : GuH mixtures starts around pH ≥ 4, where $Cu(Gu)^+$ (*aq*) and Cu(Gu)(OH) complexes appear simultaneously (figures 2a, b) according to following equilibria:

$$Cu^{2+}(aq) + HGu \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} Cu(Gu)^+(aq) \quad (2)$$

$$(2a)\ +H^+ \underset{-H^+}{\overset{}{\rightleftharpoons}} \quad +H^+ \underset{-H^+}{\overset{}{\rightleftharpoons}} \quad (4)$$

$$Cu(OH)^+ + HGu \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} Cu(Gu)(OH)\cdot \quad (3)$$

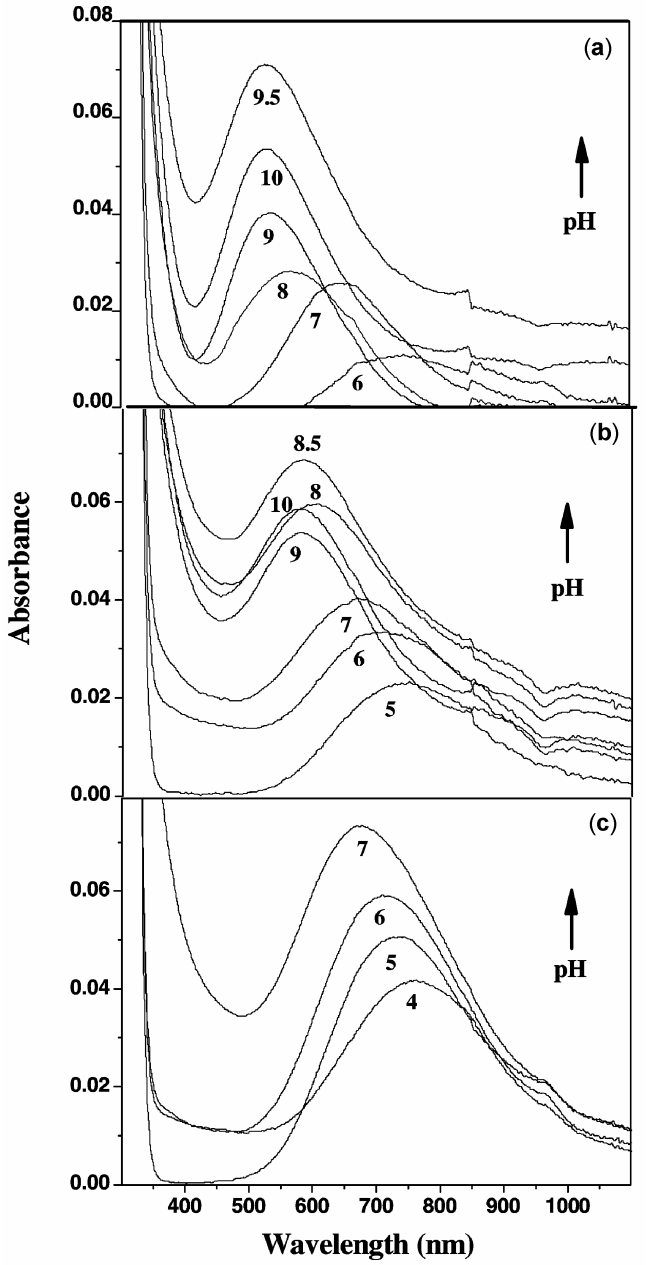


Figure 4. Electronic spectral curves of (**a**) 1 : 5 Cu^{II} : GuH; (**b**) 1 : 1 : 1 Cu^{II} : GuH : GlyH; (**c**) 2 : 1 : 2 Cu^{II} : GuH : GlyH mixtures at different pH. Ionic strength, I = 0·1 mol dm^{-3} ($NaNO_3$).

After passing through a concentration maximum (~ 25%) around pH 5·5, $Cu(Gu)^+(aq)$ is transformed to Cu(Gu)(OH), possibly due to deprotonation (4) of a coordinated H_2O molecule. The corresponding deprotonation constant,

$$K^{H}_{Cu(Gu)+(aq)} = \frac{[Cu(Gu)(OH)][H^+]}{[Cu(Gu)^+]}, \quad (4a)$$

may be calculated using the relation,

$$\log K^{H}_{Cu(Gu)+(aq)} = \log\beta_{1101} - \log\beta_{1100} - \log\beta_{010\text{-}1} \quad (4b)$$

since the constants $\log\beta_{1101}$, $\log\beta_{1100}$, and $\log\beta_{010\text{-}1}$ are obtained as computer output. Unlike the 1 : 1 Cu^{II} : biguanide (Bg) system,[6] in which biguanide ^2N or ^4N deprotonated Cu(Bg–H)(OH) complex occurs as the dominant species above pH 9, no such guanylurea deprotonated hydroxo complex, like Cu(Gu–H)(OH), is indicated. Small amounts of $Cu(OH)^+$ (2a) and $Cu(OH)_2$ are also indicated at this pH. Appearance of turbidity, possibly due to precipitation of either $Cu(OH)_2$ and/or Cu(Gu)(OH) prevents further titration of the 1 : 1 mixture above pH 7·5. Speciation curves (figure 2a) indicate decomposition of Cu(Gu)(OH) to $Cu(OH)_2$, setting free Gu^- ion above this pH, according to,

$$Cu(Gu)(OH) + H_2O \rightleftharpoons Cu(OH)_2 + Gu^- + H^+. \quad (5)$$

Although pH titration data prior to appearance of any turbidity are accepted for calculation, but the pure equilibrium constant for the reaction (5) can not be calculated, since, precipated $Cu(OH)_2$ may occur in more than one solid (*s*) phase according to,

$$CuO\cdot H_2O(s) \rightleftharpoons Cu(OH)_2(s) \rightleftharpoons Cu(OH)^+ + OH^- \rightleftharpoons Cu^{2+} + 2OH^-. \quad (5a)$$

In the 1 : 5 Cu^{II} : GuH system, the $Cu(Gu)^+(aq)$ and Cu(Gu)(OH) complexes occur to the same extent

around pH 5·5, but the solution remains clear even above pH 10. Cu(Gu)(OH) passes through a concentration maximum (~ 70%) around pH 7, at which the 1 : 2 binary complex, $Cu(Gu)_2$, appears according to,

$$Cu(Gu)^+(aq) + HGu \rightleftharpoons Cu(Gu)_2 + H^+, \quad (6)$$

and shows a concentration maximum (~ 10%). Above pH 7, the solution shows another buffer region corresponding to ~ 3 moles of H^+ per Cu^{2+}, suggesting successive deprotonation of coordinated guanylurea (Gu^-) according to,

$$Cu(Gu)_2 \rightleftharpoons Cu(Gu\text{-}H)(Gu)^- + H^+ \quad (7)$$

$$Cu(Gu)(OH) + HGu \rightleftharpoons Cu(Gu\text{-}H)(Gu)^- + H_2O + H^+ \quad (8)$$

$$Cu(Gu\text{-}H)(Gu)^- \rightleftharpoons Cu(Gu\text{-}H)_2^{2-} + H^+ \quad (9)$$

$$Cu(Gu\text{-}H)_2^{2-} \rightleftharpoons Cu(Gu\text{-}2H)(Gu\text{-}H)^{3-} + H^+ \quad (10)$$

as the speciation curves (figure 2b) imply. Here, $(Gu\text{-}H)^{2-}$ and $(Gu\text{-}2H)^{3-}$ anions result from deprotonation of either $^1NH_2$ or $^4NH_2$ group and both $^1NH_2$ and $^4NH_2$ groups respectively of coordinated guanylurea. Successive deprotonation constants of coordinated Gu^- in $Cu(Gu)_2$ may be calculated using the relations,

$$\log K^{H}_{Cu(Gu)2} = \log\beta_{1201} - \log\beta_{1200} \quad (7a)$$

$$\log K^{H}_{Cu(Gu\text{-}H)(Gu)} = \log K^{2H}_{Cu(Gu)2} - \log K^{H}_{Cu(Gu)2} = \log\beta_{1202} - \log\beta_{1201} \quad (9a)$$

$$\log K^{H}_{Cu(Gu\text{-}H)2} = \log K^{3H}_{Cu(Gu)2} - \log K^{2H}_{Cu(Gu)2} = \log\beta_{1203} - \log\beta_{1202} \quad (10a)$$

and the overall deprotonation constants may be calculated using the relations,

$$\log K^{2H}_{Cu(Gu)2} = \log\beta_{1202} - \log\beta_{1200} \quad (9b)$$

$$\log K^{3H}_{Cu(Gu)2} = \log\beta_{1203} - \log\beta_{1200}. \quad (10b)$$

Above pH 9, almost the entire amount of copper is transformed into the complex, Cu(Gu-H)(Gu-2H)$^{3-}$ ion, when the solution assumes a pinkish-violet colour.

The major complex in the 1 : 1 Cu^{II} : GlyH system in the pH range (3·5 < pH < 7) is $Cu(Gly)^+(aq)$. The binary hydroxo species, $Cu(OH)^+$ and $Cu(OH)_2$ are practically non-existent below pH 7. Above pH 7, the $Cu(Gly)^+(aq)$ complex is transformed to Cu(Gly)(OH) due to deprotonation of a coordinated H_2O molecule.[6] The 1 : 5 Cu^{II} : GlyH system is dominated by the binary $Cu(Gly)^+(aq)$ and $Cu(Gly)_2$ complexes. Binary hydroxo species $Cu(OH)^+$ and $Cu(OH)_2$ are non-existent. The ternary hydroxo complex, Cu(Gly)(OH), however, starts appearing in minute amounts above pH ~ 5, but its concentration increases abruptly above pH 9 with decline in the concentration of $Cu(Gly)_2$, suggesting decomposition of $Cu(Gly)_2$ according to,

$$Cu(Gly)_2 + H_2O \rightleftharpoons Cu(Gly)(OH) + Gly^- + H^+. \quad (11)$$

The decomposition constant ($K_{d(1020)}$) of $Cu(Gly)_2$ complex may be calculated from the difference in *log* scale of the stability constants of this complex from that of Cu(Gly)(OH) complex according to,

$$\log K_{d(1020)} = \log\beta_{1011} - \log\beta_{1020}. \quad (11a)$$

3.3 *Ternary Cu^{II} : GuH : GlyH systems*

The lower pH buffer region (pH 3–6) of, the ternary 1 : 1 : 1 Cu^{II} : GuH : GlyH mixture is dominated by the binary complex, $Cu(Gly)^+(aq)$, which passes through a concentration maximum (~ 60%) at pH ~ 6. The remaining Cu^{II} is made up of almost equal amounts (<10%) of $Cu^{2+}(aq)$, $Cu(Gu)^+(aq)$, Cu(Gu)(OH) and Cu(Gly)(Gu), and very small amounts (< 5%) of $Cu(OH)^+$ and Cu(Gly)(OH). With rise of pH, the $Cu(Gly)^+(aq)$ and $Cu(Gu)^+(aq)$ complexes gradually disappear with concomitant appearance of three ternary complexes, Cu(Gly)(Gu), Cu(Gu)(OH) and Cu(Gly)(OH) according to equilibria (12)–(14) and (3):

$$Cu(Gly)^+(aq) + HGu \rightleftharpoons Cu(Gly)(Gu) + H_3O^+ \quad (12)$$

$$Cu(Gly)^+(aq) + H_2O \rightleftharpoons Cu(Gly)(OH) + H_3O^+ \quad (13)$$

$$Cu(Gu)^+(aq) + H_2O \rightleftharpoons Cu(Gu)(OH) + H_3O^+ \quad (14)$$

and dominate the region of biological pH, (7–7·5), as the speciation curves (figure 3a) imply. Both Cu(Gly)(Gu) and Cu(Gu)(OH) are, however, transformed to $Cu(Gly)(Gu\text{-}H)^-$ at pH above 7·5, through deprotonation of the coordinated Gu^- ligand ion,

$$Cu(Gly)(Gu) \rightleftharpoons Cu(Gly)(Gu\text{-}H)^- + H^+ \quad (15)$$

$$Cu(Gu)(OH) + GlyH \rightleftharpoons Cu(Gly)(Gu\text{-}H)^- + H^+ + H_2O. \quad (16)$$

On further rise of pH above 9, the $Cu(Gly)(Gu\text{-}H)^-$ complex ion looses another proton from the coordinated $(Gu\text{-}H)^-$ ligand ion producing $Cu(Gly)(Gu\text{-}2H)^{2-}$ (17) and eventually decomposes along with Cu(Gu)(OH) (5) to set free Gu^- and Gly^- ligands, rendering the solution turbid, possibly due to precipitation of $Cu(OH)_2$:

$$Cu(Gly)(Gu\text{-}H)^- \rightleftharpoons Cu(Gly)(Gu\text{-}2H)^{2-} + H^+ \quad (17)$$

$$Cu(Gly)(Gu\text{-}H)^- + 2H_2O \rightleftharpoons Cu(OH)_2\downarrow + Gly^- + Gu^- + H^+ \quad (18)$$

$$Cu(Gly)(OH) + H_2O \rightleftharpoons Cu(OH)_2\downarrow + Gly^- + H^+. \quad (19)$$

Since precipitated $Cu(OH)_2$ may exist in more than one solid form (5a), it is not convenient to calculate the decomposition constants corresponding to equilibria (18) and (19).

In the $2:1:2$ $Cu^{II}:GuH:GlyH$ system an additional ~ 1 mol of H^+ per mole of Cu^{II} is released over that released in the $1:1:1$ system (figure 1). The dominant copper containing species in the lower pH buffer region (pH 2·5–5·5) is $Cu(Gly)^+(aq)$ as in the $1:1:1$ system. But interestingly, the binary $Cu(Gu)^+(aq)$, and the ternary Gu(Gly)(Gu), $Cu(Gly)(Gu\text{-}H)^-$, $Cu(Gly)(Gu\text{-}2H)^{2-}$, Cu(Gly)(OH), Cu(Gu)(OH) complexes, which occur in the ternary $1:1:1$ system (figure 3a), are practically non-existent in this system below pH 6·5. Only minute amounts (≤ 5% each) of these complexes are formed above pH ~ 7. Speciation curves (figure 3b) shows the appearance of a dinuclear complex, $Cu_2(Gu)(Gly)_2^+$ around pH ~ 4 according to,

$$pH > 3{\cdot}5,\ 2Cu^{2+}(aq) + 2GlyH + GuH \rightleftharpoons Cu_2(Gu)(Gly)_2^+ + 3H^+ \quad (20)$$

$$pH > 5,\ 2Cu(Gly)^+(aq) + GuH \rightleftharpoons Cu_2(Gu)(Gly)_2^+ + H^+ \quad (21)$$

$Cu_2(Gu)(Gly)_2^+$ passes through a concentration maximum (~ 30%) at ~ pH 6·5 and then disappears with rise of pH. Above pH ≥ 6·5, it decomposes to the mononuclear species, Cu(Gly)(OH) and Cu(Gu)(OH) with release of the GlyH ligand according to,

$$Cu_2(Gu)(Gly)_2^+ + 2H_2O \rightleftharpoons Cu(Gu)(OH) + Cu(Gly)(OH) + GlyH + H^+ \quad (22)$$

and only partly deprotonates to form the guanylurea deprotonated dinuclear species, (Gly)Cu(Gu-H)Cu(Gly) and $(Gly)Cu(Gu\text{-}2H)Cu(Gly)^-$, as are evident from the speciation curves (figure 3b). Above pH 7, the solution gradually becomes turbid, possibly due to precipitation of Cu(Gu)(OH) and/or Cu(Gly)(OH) or, due to precipitation of $Cu(OH)_2$, resulting from decomposition of these ternary hydroxo complexes (5 and 19).

The decomposition constant of the dinuclear complex, $Cu_2(Gu)(Gly)_2^+$, (22), may be defined according to,

$$K_{d(2120)} = \frac{[Cu(Gly)(OH)][Cu(Gu)(OH)][GlyH][H^+]}{[Cu_2(Gu)(Gly_2)^+]}, \quad (22a)$$

and calculated from the difference in log scale of the stability constant of $[Cu_2(Gu)(Gly)_2^+]$ from the sum of the stability constants of Cu(Gu)(OH) and Cu(Gly)(OH), using the relation,

$$\log K_{d(2120)} = \log\beta_{1011} + \log\beta_{1101} - \log\beta_{2120}. \quad (22b)$$

Formation of the dinuclear $Cu_2(Gu)(Gly)_2^+$ complex requires guanylurea anion, (Gu^-), to act as a bridging double bidentate ligand, in a puckered boat like conformation, providing two pairs of chelating donor sites, viz. $[(^1NH_2,\ ^3N^-=),\ (^4NH_2,\ O{=}C)]$ or $[(^1NH_2,\ ^4NH_2),\ (=\ ^3N^-,\ O{=}C)]$, for bridging two $Cu(Gly)^+(aq)$ species, producing two isomeric dinuclear structures (scheme 8), in each of which both the Cu^{II} ions acquire square planar geometry, similar

to the corresponding complexes with the biguanide (Bg) ligand described earlier.[6] But unlike the dinuclear biguanide complex, $Cu_2(Bg)(Gly)_2^{2+}$, which with rise of pH, exclusively undergoes stepwise deprotonation of the coordinated Bg ligand, the $Cu_2(Gu)(Gly)_2^+$ complex mostly decomposes to mononuclear species above pH 6·5 (22) and only partly deprotonates from the coordinated Gu^- ligand ion.

3.4 *Electronic spectral study*

The modes of metal ion coordination in square planar Cu^{II} complexes with amino acids and small peptide ligands can be tentatively assigned from the shift of the absorption maxima of Cu^{II} in such complexes with change of pH of the solution.[16] Expected λ_{max}(nm) values of such Cu^{II} complexes with glycyl peptides may be estimated using equations of the type (23):

$$\lambda_{max}(\text{nm}) = 10^3/[0{\cdot}301(\text{C=O/H}_2\text{O/OH}^-) + 0{\cdot}342\ (\text{COO}^-) + 0{\cdot}453\ (\text{NH}_2) + 0{\cdot}485\ (\text{N}^-=)], \quad (23)$$

where the groups in the parentheses represent the number of such coordinating groups (total not exceeding 4) and the numerical coefficients are the ligand field contributions in μm^{-1} of the corresponding coordinating groups in the parentheses. >C=O group, H_2O and OH^- ion are considered to exert almost the same ligand field. This concept may be applied to elucidate the most probable modes of coordination of guanylurea ligand species [Gu^-, $(Gu\text{-}H)^{2-}$, $(Gu\text{-}2H)^{3-}$] in binary Cu^{II}–GuH and ternary Cu^{II}–GuH–GlyH complexes, since the nature of the coordinating groups in these ligand species are similar to those in the peptide ligands and the absorption maxima of Cu^{II} in these complexes show blue shifts with rise of pH, like the Cu^{II}-peptide complexes. Since a >C=NH group is isoelectronic with a >C=O group, ligand field strength due to these two coordinating groups may be considered to be the same. Similarly O^--coordinated carboxylate ($-COO^-$) group and O^--coordinated enolate group derived from the amide ($-CONH^-$) moiety may be considered to exert similar ligand fields. From these considerations an amide ($-CONH_2$) group in its neutral and ionized forms should be isoelectronic and isostructural with the corresponding forms of an amidine [$-C(=NH)-NH_2$] group: (scheme 2).

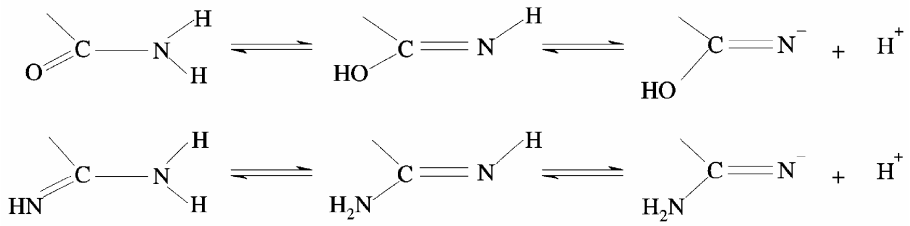
So the strength of the ligand field due to these two types of coordinating groups in their respective forms may also be taken as almost the same. From these considerations the expected λ_{max} (nm) values of square planar Cu^{II} complexes resulting from different modes of coordination of guanylurea ligand species may be estimated using the equation (23) and compared with the experimental λ_{max} (nm) values, particularly with those, at pH values corresponding to the concentration maxima of the dominant complex species (figures 2 and 3) at equilibrium.

In the binary 1 : 5 Cu^{II} : GuH system, the $Cu(Gu)^+$ (*aq*) complex (**10**) (table 1) passes through a concentration maximum around pH 6, at which the λ_{max} of the mixture is 745 nm.With rise of pH to 7, at which the ternary hydroxo complex, Cu(Gu)(OH), (**11**) passes through its concentration maximum (~ 70%), λ_{max} of the solution is blue shifted to 639 nm. As $Cu^{II}(d^9)$ prefers a square planar geometry and Gu^- ligand ion may coordinate Cu^{II} in three different bidentate chelating modes (**10a**), (**10b**) and (**10c**) (scheme 3), the $Cu(Gu)^+(aq)$ complex (**10**) should exist in solution as $Cu(Gu)(H_2O)_2^+$.

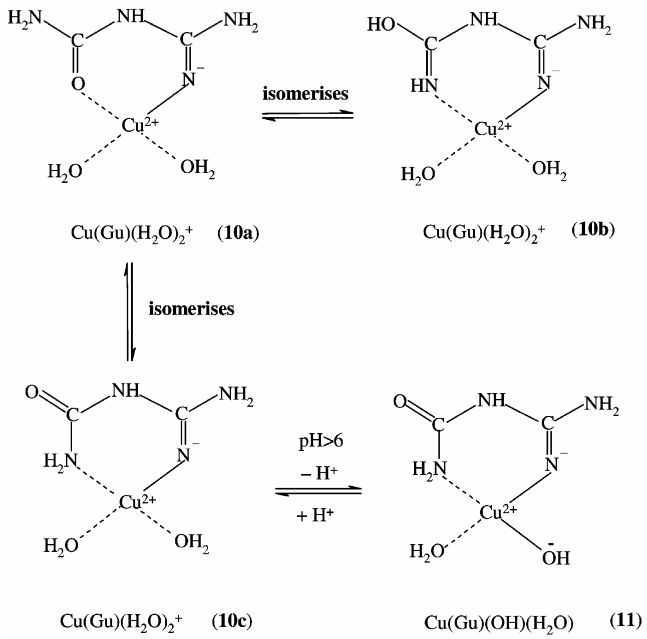
Calculated λ_{max} values (23) of the structures (**10a**), (**10b**) and (**10c**) are 722, 722 and 650 nm respectively, of which the higher value (722 nm) appears to be close to the experimental λ_{max} value (745 nm) at pH ~ 6, whereas, the lower value (650 nm) is close to the experimental λ_{max} value (639 nm) of the solution at pH ~ 7. It may, therefore, be tentatively concluded that, at pH ≤ 6 the complex $Cu(Gu)(H_2O)_2^+$ preferably exists in structures (**10a**) and/or (**10b**), but with rise of pH it changes to structure (**10c**), through which it can deprotonate to form the complex, $Cu(Gu)(OH)(H_2O)$ (**11**).

Three modes of coordination (**12a**), (**12b**) and (**12c**) (scheme 4) of the two Gu^- ligand ions are possible for the binary 1 : 2 complex, $Cu(Gu)_2$, (**12**). Calculated λ_{max} values for the structures (**12a**), (**12b**) and (**12c**) are 636, 535 and 636 nm respectively. The experimental λ_{max} value (639 nm) at pH ~ 7, at which the concentration maxima of both the complexes (**11**) and (**12**) occur (figure 2b), is close to the calculated λ_{max} value (636 nm) of (**12a**) and (**12c**). Thus, (**12a**) and (**12c**) appear to be the more likely structures of the complex (**12**).

On further rise of pH (≥ 7·5), the absorption maximum of 1 : 5 Cu^{II} : GuH mixture shows a strong blue shift from 639 nm at pH 7 through 568 nm at pH ~ 8, 548 nm at pH 8·5 to 525–530 nm at pH ≥ 9,

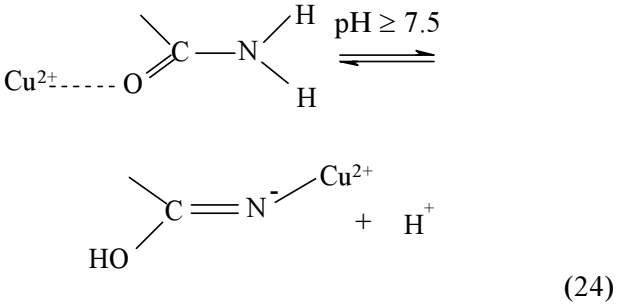


Scheme 2.



Scheme 3.

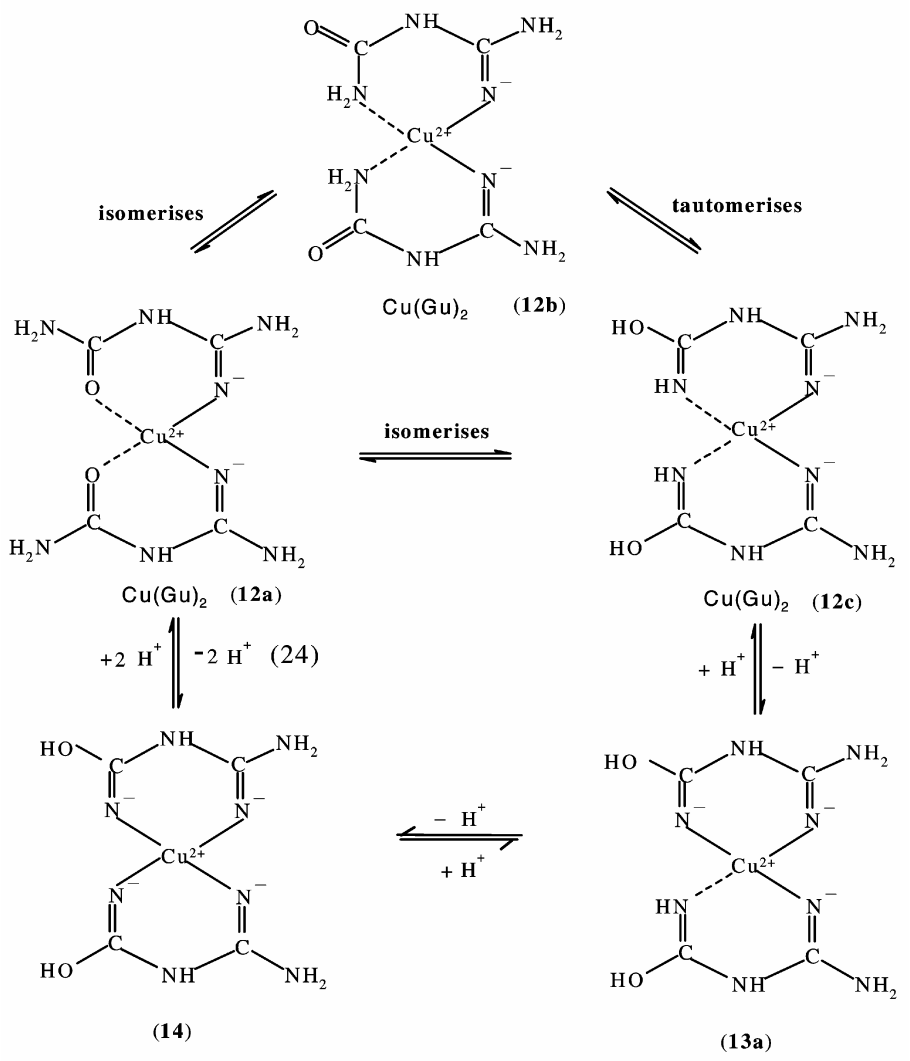
as the 1 : 2 complex $Cu(Gu)_2$, (**12**) deprotonates to $Cu(Gu\text{-}H)(Gu)^-$, (**13**) and $Cu(Gu\text{-}H)_2^{2-}$, (**14**) in stepwise manner (7–10). Starting with the structure (**12a**) for the complex (**12**), its two-step deprotonation to form (**14**) may involve coordination equilibria of the type (24):



(24)

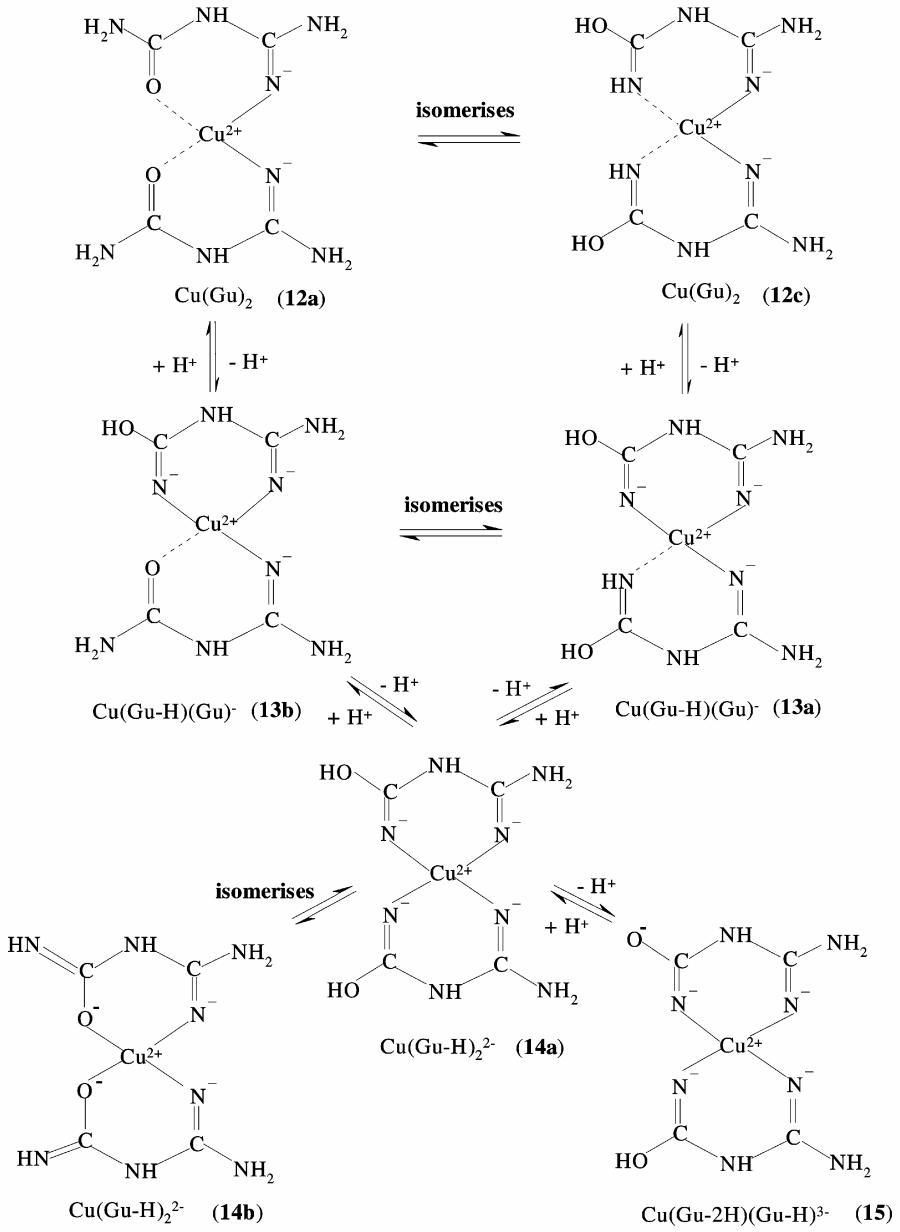
in which a carbonyl O-atom in the copper coordination sphere is replaced by a deprotonated amide N-atom, resulting in a significant increase of the strength of the ligand field around Cu^{II} ion, as observed in Cu^{II}-peptide complexes.[16,17] On the other hand, starting with structure (**12c**) of complex (**12**), its two-step deprotonation may involve release of two protons from the two coordinated ^{1}NH moieties, as described by the equilibria: (**12c**) ⇄ (**13b**) and (**13b**) ⇄ (**14a**) (scheme 5). Calculated λ_{max} values of 636, 570 and 517 nm respectively of the complexes $Cu(Gu)_2$, (**12**), $Cu(Gu\text{-}H)(Gu)^-$, (**13**), and $Cu(Gu\text{-}H)_2^{2-}$, (**14**) as described by structures (**12a**) and (**12c**), (**13a**) and (**13b**) and (**14a**) involving $Cu[(>C=O)_2(=N^-)_2]$ and $Cu[(=NH)_2,(=N^-)_2]$, $Cu[(=NH),(=N^-)_3]$ and $Cu[(>C=O)(=N^-)_3]$ and $Cu[(=N^-)_4]$ geometries (scheme 5) are in close agreement with the experimental λ_{max} values of 639, 568 and 525–530 nm of the 1 : 5 Cu^{II} : GuH mixture at pH ~ 7, ~8 and ≥9. The alternative structure (**14b**) of the complex (**14**) involving enolate O-atom coordinated $Cu[(-C(=NH)-O^-)_2(=N^-)_2]$ geometry, for which the calculated λ_{max} values comes around 606 nm, is unlikely to contribute. At pH values above 8·5, both the complexes (**13**) and (**14**) disappear completely through deprotonation (7, 9, 10) with concomitant building up concentration of the complex, $Cu(Gu\text{-}H)(Gu\text{-}2H)^{3-}$, (**15**), but no change in λ_{max} value from 525–530 nm is observed, suggesting ionization of one of the two uncoordinated enolic (OH) groups of the complex (**14**) as described by structure (**14a**) (scheme 5) at this last step, for which there is practically no alternation in the ligand field strength around the metal ion.

λ_{max} value of 1 : 1 : 1 Cu^{II} : GuH : GlyH mixture is blue shifted from 710–717 nm at pH 5·5 ~ 6, through (630–600) nm at pH ~ 7–7·5 to 580–585 nm at pH > 9. Dominant copper containing species in the pH range 5·5–6, are $Cu(Gly)(H_2O)_2^+$, (**7**), and $Cu(Gu)(H_2O)_2^+$, (**10**) (figure 3a). λ_{max} value of 710–717 nm is in close agreement with the calculated values of 716 nm and 722 nm respectively for $Cu(Gly)(H_2O)_2^+$ (**7**) (scheme 6) and $Cu(Gu)(H_2O)_2^+$,



Scheme 4.

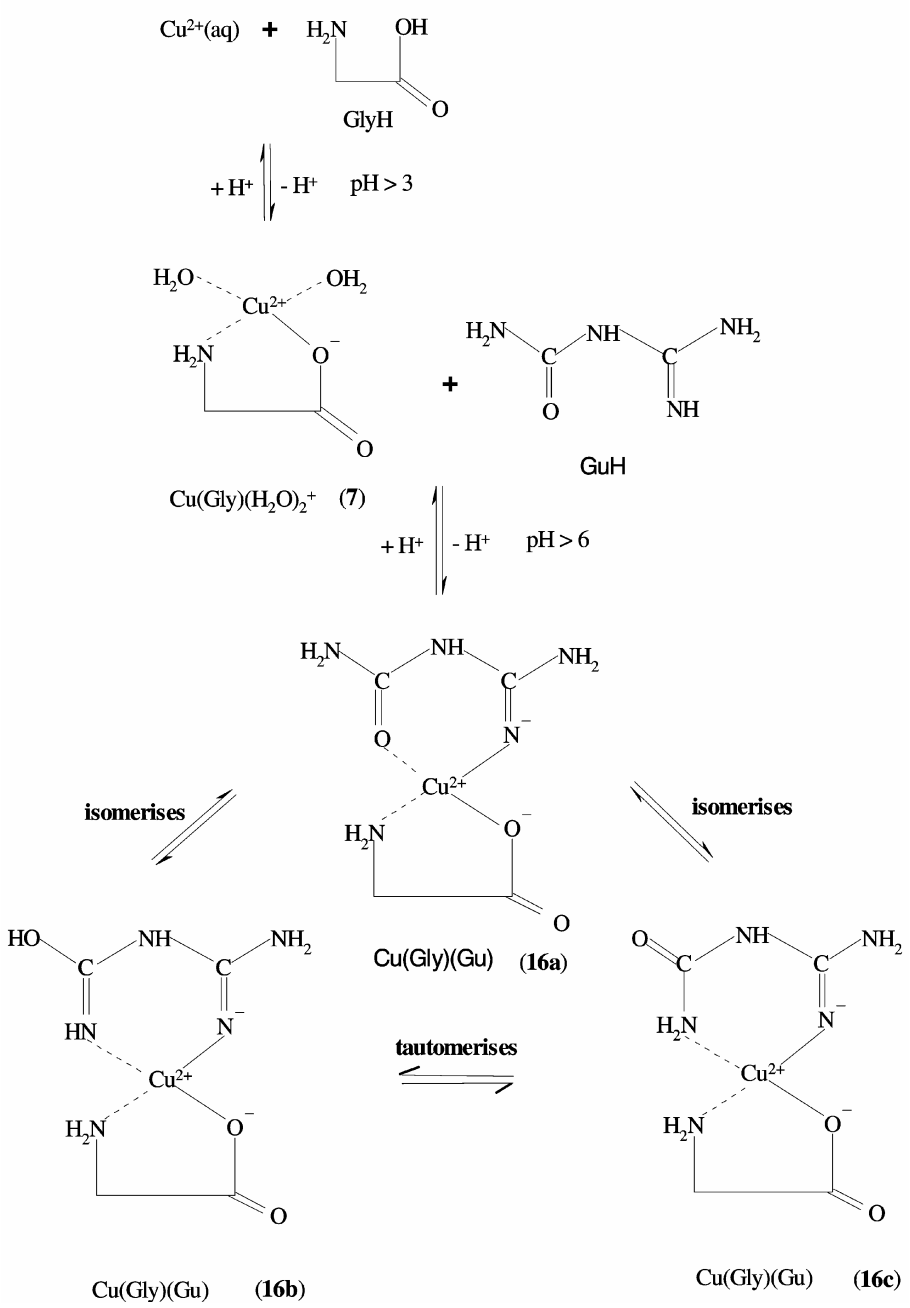
(**10**), (**10a, b**) (scheme 3). The dominant complex species at pH 7–7·5 are Cu(Gly)(Gu), (**16**), Cu(Gly)(OH)(H_2O), (**8**) and Cu(Gu)(OH)(H_2O), (**11**). Of the three possible modes of coordination of Gu^- ligand ion, (**16a**), (**16b**) and (**16c**), for the 1 : 1 : 1 Cu^{II} : Gu^- : Gly^- complex (**16**) (scheme 6), (**16c**) is less probable, as its calculated λ_{max} (577 nm) is much lower than the experimental value (630–600 nm) at this pH. Close agreement of this experimental λ_{max} with the calculated value (632 nm) for (**16a**) and (**16b**) indicates these are the probable modes of coordination of Gu^- in the Cu(Gly)(Gu) complex (**16**). Deprotonation of complex (**16**), as described by structure (**16a**), at pH ≥ 8·5–9, to Cu(Gu-H)$(Gly)^-$ (**17**) (15), accompanied by a strong blue shift from (630–600 nm) to (585–580 nm), suggests the involvment of the coordination equilibrium (24). On the other hand, deprotonation with structure (**16b**), involves loss of the proton from the coordinated ^{1}NH moiety. The complex (**17**) may involve two isomeric modes of coordination by the $(Gu\text{-}H)^{2-}$ ligand ion, viz. $[Cu(=N^-)_2(H_2N)(COO^-)]$, (**17a**) and $[Cu(=N^-)(=C\text{–}O^-)(H_2N)(COO^-)]$, (**17b**), for which the calculated λ_{max} values are 566 and 616 nm respectively. Close agreement of the former value with the experimental λ_{max} value at this pH, suggests (**17a**) as the most probable structure of (**17**). It is interesting to note that this λ_{max} value (585–580 nm) of the 1 : 1 : 1 Cu^{II} : GuH : GlyH mixture at pH ≥ 8·5–9 is quite close to the λ_{max} value (583 nm) of 1 : 1 : 1 Cu^{II} : biguanide (Bg) : GlyH mixture at this pH range, where, Cu(Bg-H)(Gly) is the dominant complex species.[6] It may, therefore, be concluded that, although at pH values lower than 7, guanylyrea an-



Scheme 5.

ion (Gu^-) may provide bidentate chelation in more than one ways involving any two of its four binding sites, viz. carbonyl O-atom, amino N-atom (^1N or ^4N) and deprotonated imino $^3N^-$ atom, but at higher pH values (pH > 8·5), it provides (=N^-, =N^-) bidentate chelation using the two deprotonated imino N-atoms ($^1N^-$ and $^3N^-$) in the same manner as the biguanide $(Bg\text{-}H)^-$ anion. On further rise of pH (pH > 9·5), although the complex $Cu(Gly)(Gu\text{-}H)^-$, (**17**), gradually disappears due to deprotonation, with concomitant building up of concentration of the complex, $Cu(Gly)(Gu\text{-}2H)^{2-}$ ion, (**18**), (figure 3a), but no change of λ_{max} is observed, suggesting deprotonation of one of the uncoordinated enolic (OH) group in (**17a**), (scheme 7) for which there is no change in the ligand field strength around Cu^{II}.

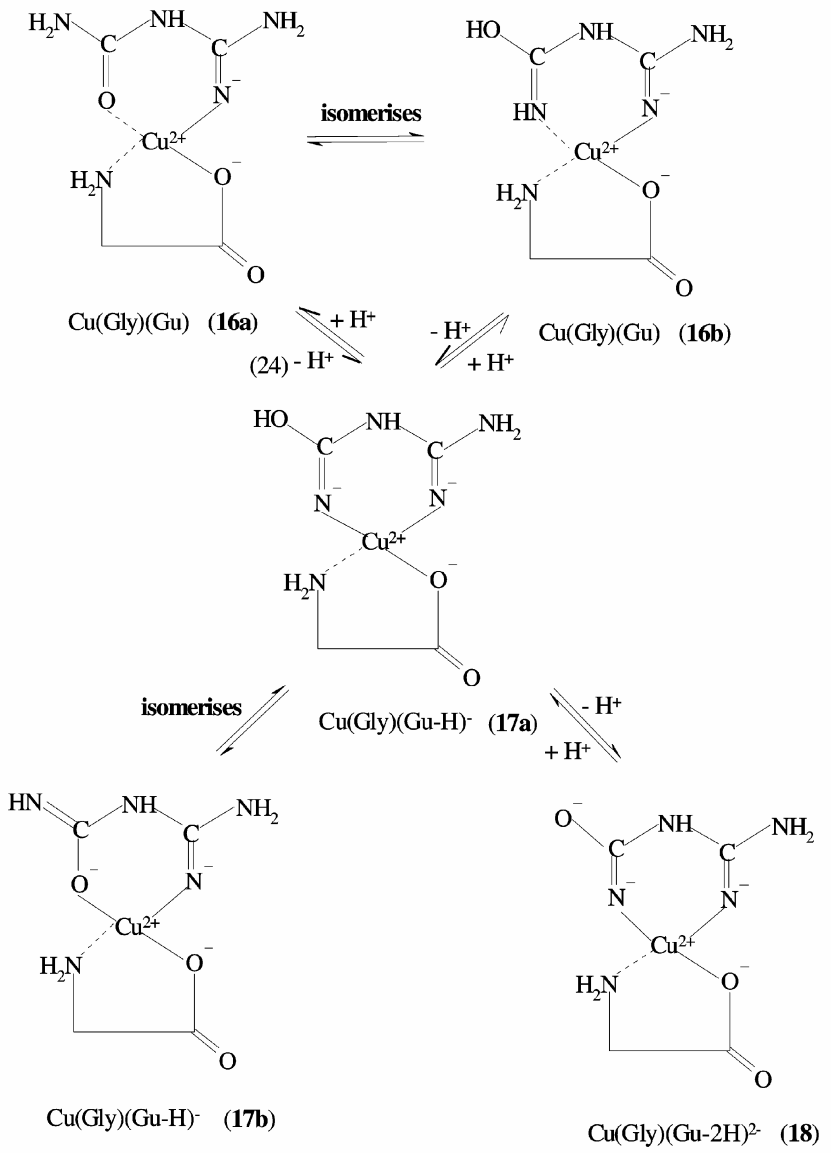
Absorption maximum (736 nm) of 2 : 1 : 2 Cu^{II} : GuH : GlyH mixture at pH ~ 5 is close to that of the 1 : 1 complex, $Cu(Gly)(H_2O)_2^+$, (**7**), that dominates at this pH (figure 3b). A small blue shift to ~ 706–695 nm occurs at pH ~ 6·5, at which the dinuclear complex, $Cu_2(Gly)_2Gu^+$, (**19**) is the dominant species. Above pH 6·5, major part of this dinuclear



Scheme 6.

complex (**19**) decomposes (22) to the mononuclear complexes Cu(Gly)(OH)(H_2O), (**8**) and Cu(Gu)(OH)(H_2O), (**11**), which absorb at higher wave lengths, 716 and 722 nm respectively and a minor part of it deprotonates to Cu_2(Gu-H)$(Gly)_2$ Cu_2(Gu-2H)$(Gly)_2^-$ complexes. Consequently, no significant blue shift is observed, like the 2 : 1 : 2 Cu^{II} : Bg : GlyH complex, $(Gly)Cu(Bg)Cu(Gly)^{2+}$, which exclusively undergoes deprotonation from the coordinated biguanide with rise of pH.[6] Bridging double bidentate chelation by the Gu^- ligand ion may give rise to two isomeric structures, (**19a**) and (**19b**) (scheme 8) for the dinuclear complex (**19**).

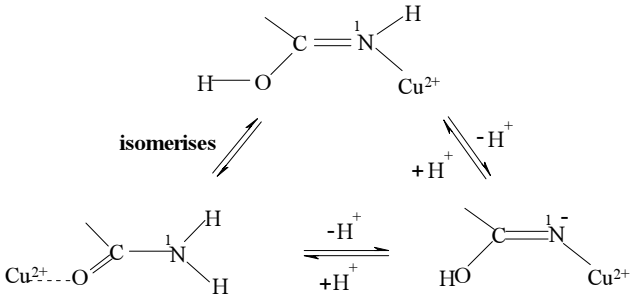
Estimated λ_{max} values of the mononuclear fragments of these structures, and their mean values are lower than the experimental λ_{max} values of these mixtures at this pH. This further supports the proposition of the decomposition equilibrium (22).

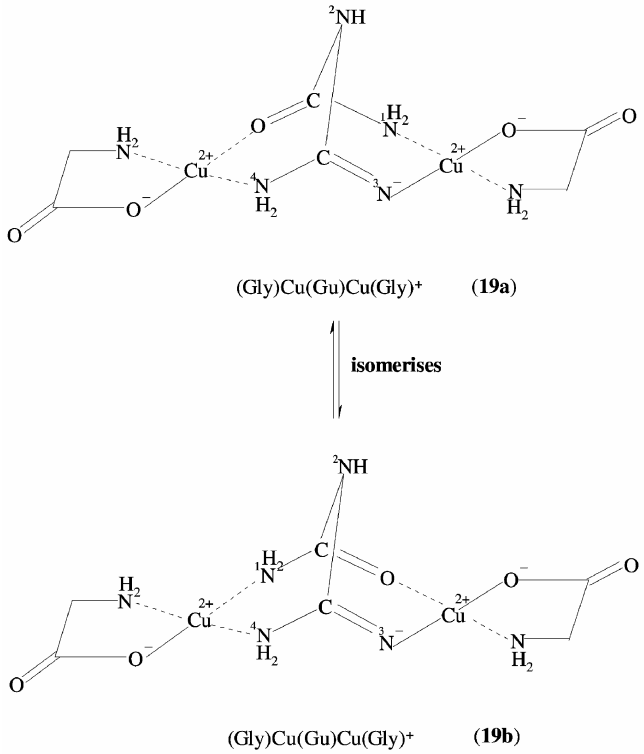


Scheme 7.

4. Conclusions

Equilibrium study on the complex formation of guanylurea (GuH) with Cu^{II} in the absence and in the presence of glycine (GlyH) in different molar proportions of the reactants provided evidence of variety of binary and mixed-ligand complexes and revealed varied modes of coordination of guanylurea species Gu^-, $(Gu\text{-}H)^{2-}$ and $(Gu\text{-}2H)^{3-}$. At pH < 7 guanylurea species provide bidentate (O=C<, $=^3N^-$) and/or ($=^1NH$, $=^3N^-$) chelation using the carbonyl O-atom or ($=^1NH$) of tautomerised $[-C(=O)^1NH_2]$ function and the deprotonated imino $^3N^-$-atom, both in binary Cu^{II}-GuH and ternary Cu^{II}-GuH-GlyH complexes. At pH ≥ 7·5, the carbonyl O-atom of coordinated Gu^- ligand ion is replaced by the deprotonated imino ^1N-atom through a coordination equilibrium, like the Cu^{II}-peptide complexes.





Scheme 8.

These changes are accompanied by blue shift of the electronic spectral absorption maximum of Cu^{II}, since, at pH ≥ 7·5, guanylurea species $(Gu\text{-}H)^{2-}$ provides stronger ligand field due to bidentate (=N^-, =N^-) chelation to Cu^{II}, like the biguanide anion $(Big\text{-}H)^-$. In the dinuclear $(Gly)Cu(Gu)Cu(Gly)^+$ complex, the Gu^- ion functions as a bridging double bidentate [($^1NH_2$, $^3N^-$), (C=O, $^4NH_2$)] and/or [($^1NH_2$, $^4NH_2$), (C=O, $^3N^-$)] ligand to coordinate Cu^{II} in the two $Cu(Gly)^+$ complex species in an isomeric equilibrium. Unlike the analogous biguanide bridged dinuclear Cu^{II} ternary complex, $(Gly)Cu(Bg)Cu(Gly)^{2+}$, which exclusively undergoes deprotonation from the bridging Bg ligand with rise of pH above pH 5, this guanylurea bridged dinuclear Cu^{II} ternary complex mostly decomposes to mononuclear species, Cu(Gly)(OH) and Cu(Gu)(OH) and only partly deprotonates to (Gly)Cu(Gu-H)Cu(Gly) and (Gly)Cu(Gu-2H)Cu $(Gly)^-$ complexes. Above pH 9·5, the ternary hydroxo complexes Cu(Gu)(OH) and Cu(Gly)(OH), decompose to precipitate $Cu(OH)_2$. Comparatively higher acidity of coordinated H_2O molecule in the $Cu(Gu)^+$ (aq) complex ($pK^H_{Cu(Gu)(H_2O)}$, 5·85), relative to that in the $Cu(Gly)^+(aq)$ complex ($pK^H_{Cu(Gly)(H_2O)}$, 7·12), is possibly the result of metal to ligand π-bonding in the (Cu^{2+}–N^-=) moiety.

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