

Metal complexes of some peptide derivatives. Part-XIV. Complex formation of copper(II) with *N*-benzenesulfonamides of some dipeptides

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Combined potentiometric and spectrophotometric investigation on the complex formation equilibria of Cu^{II} with *N*-benzenesulfonyl derivatives of some dipeptides, viz. glycylglycine, glycyl-*dl*- α -alanine, glycyl-*dl*-methionine, glycyl- β -alanine, β -alanylglycine (AH₂) in aqueous solution provides evidence of complexes of the types : Cu(AH)⁺, Cu(H₋₁AH), Cu(H₋₁A)⁻, Cu(H₋₁A)(OH)²⁻, Cu(AH)₂, Cu(H₋₁AH)(AH)⁻, Cu(H₋₁AH)₂²⁻, Cu(H₋₁A)(H₋₁AH)³ and Cu(H₋₁A)₂⁴⁻. Deprotonation constants (pK^HCOOH and pK^HSO₂NH) of the ligands and formation constants of the complexes at 25 ± 1° in aqueous solution, I = 0.2 M (NaNO₃), are correlated with the modes of coordination of the amide and sulfonamide groups, size of the chelate rings, and metal-ligand and ligand-ligand π -interactions. Deprotonation constants of coordinated H₂O molecules in the square-planar, or distorted octahedral Cu(H₋₁A)(H₂O)⁻ complexes indicate their equatorial disposition. The tendency of the ternary hydroxo complexes, Cu(H₋₁A)(OH)²⁻ to transform into to Cu(H₋₁A)₂⁴⁻ with precipitation of Cu(OH)₂ at pH >9 is found to be in the inverse order of stability constants of these complexes.

Complex formation of metal ions of biological importance with amino acids, small peptides and their derivatives are of great significance, as many of these systems offer simple models of otherwise complex metal-protein equilibria occurring in enzymic processes. At low pH, the peptide group undergoes both protonation and metallation at the carbonyl oxygen atom. Metal ion coordination with the amide nitrogen atom takes place only upon substitution of the amide proton, for which a primary ligating site at a chelating position is, however, essential^{1,2}. With a view to study the effect of a sulfonamide group at a chelating position on the modes of metal ion coordination by the amide group in dipeptides, the present paper describes the results of a systematic equilibrium study on the complex formation of Cu^{II} with a series of *N*-benzenesulfonyl derivatives (1),



1

of the following dipeptides, viz. glycylglycine, SGG ($x = 1$, $y = 1$, R = H), glycyl-*dl*- α -alanine, SGA ($x = 1$, $y = 1$, R = CH₃), glycyl-*dl*-methionine, SGM ($x = 1$, $y = 1$, R = CH₂CH₂SCH₃), glycyl- β -alanine, SGB ($x = 1$, $y = 2$, R = H) and β -alanylglycine, SBG ($x = 2$, $y = 1$, R = H) in aqueous solution, I = 0.2 M (NaNO₃) at 25 ± 1° by combined potentiometric and spectrophotometric methods, coupled with computerized evaluation of the equilibrium constants³. Formation constants of the complexes are cor-

related with the modes of metal ion coordination by the amide and the sulfonamide moieties, size of the chelate rings and metal-ligand and ligand-ligand- π -interactions.

Results and Discussion

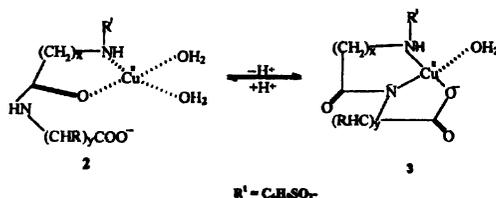
Proton-ligand equilibria : All the five sulfonamidodipeptide ligands, viz. SGG, SGA, SGM, SGB and SBG titrate as diprotic acids (AH₂) giving two well-separated buffer regions, pH 2.5~4.4 and pH 8~11, corresponding to the deprotonation of the COOH and the SO₂NH groups in successive steps. In the absence of Cu^{II} the amide (CONH) group remains neutral in the entire pH range^{4,5}. The analogous ligand acetylglycine, CH₃CONHCH₂COOH titrates as a monoprotic acid (AH) in the pH range 2.5~12.0. This supports the proposition of deprotonation of the SO₂NH group of the free ligands in the second step⁶.

1 : 1 Cu^{II} : AH₂ equilibria : The initial buffer region (pH 2.5~5.5) in the pH-metric titrations of 1 : 1 Cu^{II} : AH₂ mixtures (AH₂ = SGG, SGA, SGM, SGB and SBG) coincides with that due to deprotonation of the COOH group of the corresponding ligands (AH₂) in the absence of Cu^{II}. Thus, deprotonation of the COOH group of the ligands is not influenced by the presence of Cu^{II}. This is followed by two well-separated buffer regions, pH 5~7 and pH 8~11. Two moles of base ($a = 2$) per mole of Cu^{II} are consumed in the lower pH buffer region (pH 5~7) giving a sharp inflection

point, beyond which a third mole of base ($a = 3$) per Cu^{II} is consumed in the higher pH buffer region (pH 8–11). All the five ligands remain mainly in their COOH deprotonated monoanionic (AH^-) forms in the first buffer region (pH 5–7) of complex formation. Therefore, formation of 1 : 1 $\text{Cu}^{\text{II}} : \text{AH}^-$ complexes with release of two protons per Cu^{II} obviously involves deprotonation of both SO_2NH as well as the CONH groups, according to equilibrium (1),

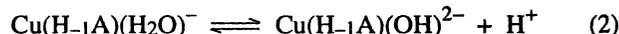


The λ_{max} ($\log \epsilon$) values of 1 : 1 $\text{Cu}^{\text{II}} : \text{AH}^-$ mixtures at pH values corresponding to $a = 0, 1$ and 2 show a large blue-shift from $\sim 740 \text{ nm}$ (1.5) at $a = 0$ to $\sim 645 \text{ nm}$ (2.05) at $a = 1$ and a small blue-shift $\sim 5 \text{ nm}$ from $a = 1$ to $a = 2$. The observed λ_{max} values at $a = 0$ and $a = 1$ are close to the calculated values for square-planar Cu^{II} -dipeptide complexes with $[\text{Cu}(\text{N},\text{O}), 2(\text{H}_2\text{O})]$ and $[\text{Cu}(\text{N},\text{N},\text{O}), (\text{H}_2\text{O})]$ coordination¹. This indicates the existence at $a = 0$, of a complex, $\text{Cu}(\text{AH})(\text{H}_2\text{O})^+$, in which the ligand AH^- ion coordinates Cu^{II} as a (N,O)bidentate ligand using the carbonyl O-atom of the amide group and neutral N-atom of the sulfonamide group, the remaining two positions around square-planar Cu^{II} are coordinated by two H_2O ligands (2). The carboxylate O-atom of AH^- ions fails to coordinate Cu^{II} in these complexes due to angle strain in 7/8-membered ring. The initial large blue-shift of λ_{max} with rise of pH may be attributed to substitution of the amide carbonyl O-atom in 2 by deprotonated amide N-atom, thereby transforming the ligand ion AH^- into $\text{H}_{-1}\text{AH}^{2-}$ ion, which coordinates Cu^{II} using the neutral N-atom of the sulfonamide group, deprotonated amide N-atom of the peptide group. The latter provides a stronger ligand field than the amide carbonyl O-atom and is obviously responsible for the blue-shift of the absorption maxima of Cu^{II} by $\sim 90\text{--}100 \text{ nm}$. This structural change also brings the carboxylate O-atom of the ligand to a chelating position, making the $\text{H}_{-1}\text{AH}^{2-}$ ligand ions a (N,N',O⁻)terdentate ligand in the resulting $\text{Cu}(\text{H}_{-1}\text{AH})(\text{H}_2\text{O})$ complexes (3).



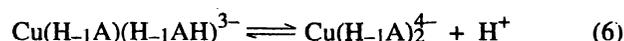
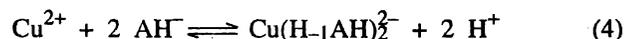
A similar blue-shift of λ_{max} of Cu^{II} with increase of $\log \epsilon$ has also been observed in case of conversion of $\text{Cu}(\text{AlaH})^{2+}$ into $\text{Cu}(\text{H}_{-1}\text{AlaH})^+$, where $\text{AlaH} = \text{alaninamide}$ ⁷. On further increase of pH (i.e. in going from $a = 1$ to $a = 2$), the coordinated $-\text{SO}_2\text{NH}-$ group in the $\text{Cu}(\text{H}_{-1}\text{AH})(\text{H}_2\text{O})$ complexes undergoes deprotonation to produce the complexes, $\text{Cu}(\text{H}_{-1}\text{A})(\text{H}_2\text{O})^-$ without any significant change of λ_{max} of Cu^{II} , as the strengths of the ligand fields provided by a neutral and a deprotonated sul-

fonamide N-atom are not very much different. The observed λ_{max} values of $\sim 640 \text{ nm}$ of 1 : 1 $\text{Cu}^{\text{II}} : \text{AH}^-$ mixtures at $a = 2$ (pH ~ 7.25) are fairly close to the calculated value ($\sim 632 \text{ nm}$) for a square-planar Cu^{II} complex, $\text{Cu}(\text{H}_{-1}\text{A})(\text{H}_2\text{O})^-$, in which the ligand $\text{H}_{-1}\text{A}^{3-}$ ions coordinate Cu^{II} with deprotonated amide N-atom, deprotonated sulfonamide N-atom, carboxylate O-atom and a H_2O molecule. The higher pH-buffer region (pH 8–11) of 1 : 1 $\text{Cu}^{\text{II}} : \text{AH}^-$ mixture obviously corresponds to deprotonation of the coordinated H_2O ligand in these $\text{Cu}(\text{H}_{-1}\text{A})(\text{H}_2\text{O})^-$ complexes according to equilibrium (2), since there are no other dissociable proton in these complexes,



The λ_{max} values of Cu^{II} remain practically unchanged in going from $a = 2$ to $a = 3$, as H_2O and OH^- are very closely placed in the spectrochemical series⁸.

1 : 2 $\text{Cu}^{\text{II}} : \text{AH}_2$ equilibria : The initial buffer regions (pH 2.5–4.0) in the pH-metric titrations of 1 : 2, 1 : 5 and 1 : 10 $\text{Cu}^{\text{II}} : \text{AH}_2$ mixtures ($\text{AH}_2 = \text{SGG}, \text{SGA}, \text{SGM}$ and SGB) coincide with those corresponding to the deprotonation of the COOH groups of the corresponding free ligands in the absence of Cu^{II} , similar to the 1 : 1 $\text{Cu}^{\text{II}} : \text{AH}_2$ systems. This is followed by two well-defined buffer regions, pH 4.5–6.5 and 7.5–11. In each of these regions, two moles of base ($a = 2, a = 4$) per mole of Cu^{II} are consumed. Mole ratio plots⁹ of the $\text{Cu}^{\text{II}} : \text{AH}_2$ mixtures at pH values corresponding to $a = 0, 2$ and 4 by spectrophotometric method at the appropriate λ_{max} values indicates the existence of both 1 : 1 and 1 : 2 $\text{Cu}^{\text{II}} : \text{AH}_2$ complexes, as well as the absence of complexes higher than 1 : 2. As all these ligands in their lower pH-buffer region (pH 4.5–6.5) of complex formation remain in the forms of their COOH deprotonated monoanions (AH^-), therefore, the formation of 1 : 1 and 1 : 2 $\text{Cu}^{\text{II}} : \text{AH}^-$ complexes involving the release of two to four protons per Cu^{II} in stepwise manner may be represented according to equilibria (3)–(6),



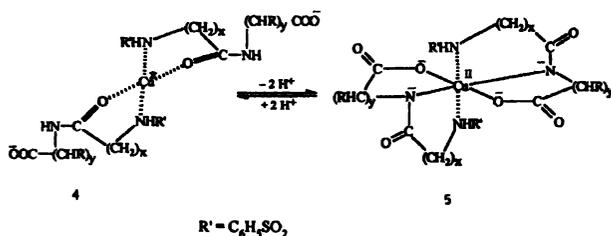
in addition to equilibrium (1) described earlier. The λ_{max} ($\log \epsilon$) values of 1 : 5 $\text{Cu}^{\text{II}} : \text{AH}_2$ mixtures at pH values corresponding to $a = 0, 1, 2, 3$ and 4 show a large blue-shift by $\sim 60\text{--}65 \text{ nm}$ in going from $a = 0$ to $a = 2$ and a small blue-shift of $\sim 5 \text{ nm}$ in going from $a = 2$ to $a = 4$. The first blue-shift indicates a significant increase of ligand field strength around Cu^{II} in going from $a = 0$ to $a = 2$, which may be attributed to a change from $[\text{Cu}(\text{N},\text{O})_2]$ to $[\text{Cu}(\text{N},\text{N},\text{O})_2]$ coordination^{1,6}. Thus, at $a = 0$, the 1 : 2, $\text{Cu}^{\text{II}} : \text{AH}^-$ complexes may be $\text{Cu}(\text{AH}_2)$ in which Cu^{II} is (N,O)biden-

Table 1. Formation constants of proton-ligand and Cu^{II}-ligand complexes with SGG, SGA, SGM, SGB and SBG (AH₂), and Cu^{II}-promoted deprotonation constants of coordinated CONH, SO₂NH and H₂O ligands*Temp. = 25 ± 1°, I = 0.2 M (NaNO₃), in aqueous solution

Cu _p A _q (OH) _r	p q r	Constant	SGG	SGA	SGM	SGB	SBG
AH ₂	0 1-2	-log K ^H _{COOH}	3.55	3.44	3.24	4.32	3.45
AH	0 1-1	-log K ^H _{SO₂NH}	9.65	9.74	9.70	9.73	10.66
Cu(AH)	1 1-2	log K ^{Cu} _{Cu(AH)}	2.75	2.47	3.05	2.92	3.48
Cu(H ₋₁ AH)	1 1-2	-log K ^H _(Cu+AH)	2.60	2.93	1.94	2.29	2.97
Cu(H ₋₁ A)	1 1 0	-log K ^{2H} _(Cu+AH)	8.50	8.44	7.99	7.93	10.30
Cu(H ₋₁ A)(OH)	1 1 1	-log K ^{3H} _(Cu+AH+H₂O)	17.75	17.79	16.99	17.13	19.80
		-log K _d	-1.55	-2.15	-2.32	-5.08	-
Cu(AH) ₂	1 2-4	log K ^{Cu} _{Cu(AH)₂}	4.80	4.34	5.50	5.24	6.36
Cu(H ₋₁ AH)(AH)	1 2-3	log K ^H _(Cu+2AH)	-0.40	-1.06	1.00	0.76	-
Cu(H ₋₁ AH) ₂	1 2-2	-log K ^{2H} _(Cu+2AH)	6.40	6.60	5.49	7.13	-
Cu(H ₋₁ A)(H ₋₁ AH)	1 2-1	-log K ^{3H} _(Cu+2AH)	15.20	15.93	14.82	16.93	-
Cu(H ₋₁ A) ₂	1 2 0	-log K ^{4H} _(Cu+2AH)	25.05	25.73	24.30	27.34	-
Cu ^{II} : AH ₂	Equilibria						
1: 1	(7)	pK ^H _[Cu(CONH)]	5.35	5.40	4.99	5.21	6.45
1: 1	(8)	pK ^H _[Cu(SO₂NH)]	5.90	5.51	6.05	5.64	7.33
1: 2	(7)	pK ^H _[Cu(CONH)₂]	5.20	5.40	4.50	6.00	-
1: 2	(7)	pK ^{2H} _[Cu(CONH)₂]	11.22	10.94	10.99	12.37	-
1: 2	(8)	pK ^H _[Cu(SO₂NH)₂]	8.80	9.33	9.33	9.80	-
1: 2	(8)	pK ^{2H} _[Cu(SO₂NH)₂]	18.65	19.15	18.81	20.01	-
1: 1	(2)	pK ^H _[Cu(H₋₁A)(H₂O)]	9.25	9.35	9.00	9.10	9.50

*Limits of error = ± 0.02 ~ 0.05 in log unit. Changes are not shown for clarity.

tate coordinated by the neutral N-atom of the neutral SO₂NH group and O-atom of the neutral CONH group (4), the O-atom of the COO⁻ group of AH⁻ fails to coordinate because of angle strain in 7/8-membered ring. In going from *a* = 0 to *a* = 2, these Cu(AH)₂ complexes certainly undergo a structural change involving substitution of the amide carbonyl O-atom by the deprotonated amide N-atom. This simultaneously brings the COO⁻ group at a chelating position making the H₋₁AH²⁻ ion a (N,N⁻,O⁻)terdentate ligand. Cu^{II} in the resulting amide deprotonated Cu(H₋₁AH)₂²⁻ complexes (5) is terdentate (N,N⁻,O⁻) chelated by the N-atom of neutral SO₂NH group, deprotonated amide N-atom and the carboxylate O-atom.



The large blue shift of λ_{max} in going from *a* = 0 to *a* = 2 is the result of substitution of the amide carbonyl O-atom by the deprotonated amide N-atom within the Cu^{II} coordination sphere. A similar blue-shift in the absorption maxima

of Cu^{II} has also been observed in the case of conversion of Cu(AlaH)₂²⁻ into (Cu(H₋₁AlaH)₂), where AlaH = alaminamid⁷. Smaller shift in the present case may be due to axial coordination of Cu^{II}, possibly by the N-atoms of the SO₂NH groups in the Cu(H₋₁AH)₂²⁻ complexes (5). The observed absorption maxima ~640 nm (log ε = 2) of Cu^{II} at *a* = 2 are in good agreement with tetragonally distorted octahedral Cu(N,N⁻,O⁻)₂ geometry¹. The calculated λ_{max} for a square-planar Cu(N,N⁻)₂ geometry with two neutral and two deprotonated amide N-atoms as donors, making allowance for acidity of the SO₂NH group, should be around 580 nm, which is about 60 nm lower than the observed values (~640 nm) of the amide deprotonated Cu(H₋₁AH)₂²⁻ complexes (5). Such a difference strongly suggests axial coordination of Cu^{II} in the Cu(H₋₁AH)₂²⁻ complexes¹⁰.

The higher pH-buffer region (pH-7.5-11), *a* = 2 to *a* = 4, obviously involves deprotonation of the two coordinated SO₂NH groups of the Cu(H₋₁AH)₂²⁻ complexes (5) according to eqm. (5) and (6) to form the fully deprotonated Cu(H₋₁A)₂⁴⁻ complexes, in which Cu^{II} is (N,N⁻,O⁻)terdentate chelated by the N-atoms of deprotonated sulfonamide and amide groups and the O-atom of the carboxylate group of the ligand H₋₁A³⁻ ions. As the strengths of the ligand fields exerted by the N-atom of the neutral and deprotonated SO₂NH groups are not expected to be very

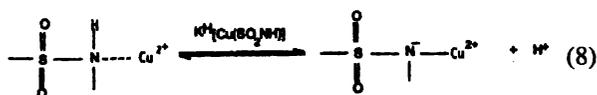
much different, the λ_{\max} ($\log \epsilon$) values of 1 : 2 Cu^{II} : AH^- mixtures remain practically unchanged in going from $a = 2$ to $a = 4$.

The first step of complex formation (eqm. 1 or 3 as the case may be) is found to be complete at pH values much lower than the buffer region corresponding to the hydrolytic equilibria of $\text{Cu}^{2+}(\text{aq})$ ions, so the binary hydroxo complexes, $\text{Cu}(\text{OH})^+$, $\text{Cu}(\text{OH})_2$ etc. have been excluded in calculating the formation constants³ of $\text{Cu}^{\text{II}}\text{-AH}_2$ complexes. Formation constants of some of the 1 : 2 $\text{Cu}^{\text{II}}\text{-SBG}$ complexes could not be determined due to the commencement of precipitation.

The overall formation constants of the complexes have been obtained as computer out-put, from which the Cu^{II} -promoted deprotonation constants of coordinated amide (CONH), sulfonamide (SO_2NH) and H_2O ligands have been calculated (Tablet 1) using appropriate relations. Although the amide group in the free ligands remains neutral in the entire pH-range, metallation with amide N-atom takes place upon amide deprotonation¹¹ (eqm. 7) in the presence of Cu^{II} in the pH range 4.5–6.5 (eqm. (2) \rightleftharpoons (3) and eqm. (4) \rightleftharpoons (5)) :



Acidity of coordinated SO_2NH group in the $\text{Cu}(\text{H}_{-1}\text{AH})$ complexes is enhanced by 3–4 log units over the acidity of uncoordinated SO_2NH group in the free ligands. This strongly suggests an equatorial disposition of the sulfonamide N-atom with the deprotonated amide-N and carboxylate O-atoms in the square-planar coordination geometry of $\text{Cu}(\text{H}_{-1}\text{AH})$ complexes (3). However, such increase of acidity of SO_2NH group in the 1 : 2 complexes $\text{Cu}(\text{H}_{-1}\text{AH})_2^{2-}$, (5) is quite small, ~0.1–0.5 log unit, suggesting a weak and possibly an axial coordination of the sulfonamide N-atom in these distorted octahedral Cu^{II} complexes. Further, it is observed that Cu^{II} promoted amide deprotonation (eqm. 7) takes place at pH values much lower than the buffer region corresponding to deprotonation of coordinated sulfonamide group (eqm. 8),



obviously due to favorable entropy effect arising out of a change from bidentate (N,O) mode of coordination by the ligand AH^- ions in $\text{Cu}(\text{AH})(\text{H}_2\text{O})_2^{\pm}$ (2) and $\text{Cu}(\text{AH})_2$ (4), to the terdentate (N,N⁻,O⁻) mode of coordination by the ligands $\text{H}_{-1}\text{AH}^{2-}$ ions in $\text{Cu}(\text{H}_{-1}\text{AH})(\text{H}_2\text{O})$ (3) and $\text{Cu}(\text{H}_{-1}\text{AH})_2^{2-}$ (5) complexes.

Stability constants of the (N,O)bidentate chelated

$\text{Cu}(\text{AH})(\text{H}_2\text{O})_2^{\pm}$ and $\text{Cu}(\text{AH})_2$ complexes fall in the ligand order : $\text{SBG} > \text{SGM} > \text{SGB} > \text{SGG} > \text{SGA}$. Higher stability of $\text{Cu}(\text{AH})(\text{H}_2\text{O})_2^{\pm}$ and $\text{Cu}(\text{AH})_2$ complexes derived from SBG may be due to lower angle strain in the six-membered chelate ring with a (C=O) double bond as compared to that in the corresponding complexes derived from the other ligands having five-membered chelate rings with (C=O) double bond. Comparatively higher stability of the complexes derived from SGM may be due to additional coordination by the methionine sulfur atom possibly in an intermolecular mode. Such intermolecular coordination of methionine sulfur in the $\text{Cu}(\text{AH})(\text{H}_2\text{O})_2^{\pm}$ and $\text{Cu}(\text{AH})_2$ complexes possibly takes place at a position *trans* to the coordinated amide group, as is evident from the comparatively higher acidity of the amide proton (eqm. 7) in the complexes derived from SGM, suggesting some metal ($d\pi$) \rightarrow methionine $S(d\pi)$ back-bonding, which may enhance the acidity of amide proton. The resulting amide deprotonated complexes (3, 5) derived from SGM may be further stabilized through hydrophobic stacking interaction^{12,13} between the vacant ($d\pi$) orbitals of methionine sulfur and the delocalized π -mo of the deprotonated amide (CON) moiety.

Deprotonation constants of coordinated H_2O molecule in $\text{Cu}(\text{H}_{-1}\text{A})(\text{H}_2\text{O})^-$ complexes (eqm. 2) are found to be fairly close to those of equatorially coordinated H_2O molecules in square-planar Cu^{II} complexes¹⁴. Formation of $\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}$ complexes starts at $\text{pH} \geq 7$ and the solutions turn turbid around $\text{pH} \sim 10$, where the concentration of the $\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}$ complexes rise to $\geq 80\%$. Absorption maxima (~635 nm) of the clear filtrates are almost the same as the absorption maxima of 1 : 2 Cu^{II} : AH^- mixtures are $a = 4$ ($\text{pH} \approx 11$). Calculation of the concentration of copper in the clear filtrates using the $\log \epsilon$ values (~2.05) of the corresponding 1 : 2 Cu^{II} : AH^- mixtures at $a = 4$ provides evidence of formation of the fully deprotonated 1 : 2 Cu^{II} -ligand complexes, $\text{Cu}(\text{H}_{-1}\text{A})_2^{4-}$ possibly through dissociation of the ternary hydroxo complexes, $\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}$, according to eqm. (9),



of which the dissociation K_d may be calculated using the relation (10),

$$\log K_d = \log K_{\text{Cu}(\text{H}_{-1}\text{A})_2^{4-}}^{\text{H}} + K_{\text{Cu}}^{2\text{H}} - 2 \log K_{\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}}^{3\text{H}} \quad (10)$$

where, $K_{\text{Cu}}^{2\text{H}}$ is the hydrolysis constant of Cu^{2+} (aq.) ion producing $\text{Cu}(\text{OH})_2$. The $\log K_d$ values (Table 1) fall approximately in the reverse order of the formation constants of $\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}$ complexes. Comparatively higher stability of the $\text{Cu}(\text{H}_{-1}\text{A})(\text{OH})^{2-}$ complexes derived from SGB is possibly due to greater configurational flexibility of a combination of five- and six-membered chelate ring system in this complex over five-membered ring systems in

the complexes derived from the other ligands. Due non-availability of $K_{(Cu+2AH)}^{4H}$ value for the 1 : 2 Cu^{II} : SBG system, the corresponding K_d value could not be calculated.

Experimental

The ligands SGG, SGA, SGM and SGB were prepared by condensing *N*-benzenesulfonylglycyl chloride (0.02 mol) with the sodium salt (0.02 mol) of the corresponding amino acids (*viz.* glycine, α -alanine, *dl*-methionine and β -alanine) at room temperature in aqueous solution at pH \approx 9 maintained by adding 5% NaOH solution with constant stirring following the procedure as described earlier⁶. After stirring the reaction mixture for 1h, it was cooled in an ice-water bath and acidified (pH \approx 2) with 2 M HCl. The resulting white crystalline needles were further purified by crystallization from hot water and air-dried. The ligand SBG was prepared by condensing *N*-benzenesulfonyl β -alanil chloride with sodium glycinate following an analogous procedure. All the ligands were characterized by elemental analysis, equivalent weight determination and IR and UV spectral data. ν_{max}^{15} for the COOH, amide (CONH) and sulfonamide (SO₂NH) groups were identified in the usual regions : 1740 ~ 1710 (COOH), 1640–1590 (amide I), 1565–1535 (amide II), 1285–1240 (amide III), 1350–1320 (sulfonamide I) and 1175–1155 cm⁻¹ (sulfonamide II). All the other reagents were of A.R. grade and their solutions were prepared in double-distilled CO₂-free water. Cu(NO₃)₂ solution was standardized by combined ion exchange, acid-base and complexometric EDTA titrations¹⁶.

pH was measured with a Systronics 335 pH meter (accuracy \pm 0.01 pH) using a special glass electrode in conjunction with a SCE. Electronic spectra were measured on a Hitachi U-3501 spectrophotometer and IR (KBr) on a Parkin-Elmer 681 spectrometer.

Experimental determination of the proton-ligand and Cu^{II}-ligand complex formation constants involved pH-metric titration¹⁷ of a series of aqueous solutions of known amounts (0.001 ~ 0.01 M) of the ligands (AH₂ = SGG, SGA, SGM, SGB and SBG as the case may be) containing known amount of (0.01 M) free HNO₃ in each case, in the absence and in the presence of known amounts (0.001 ~ 0.002 M) Cu(NO₃)₂ with a carbonate-free standard (0.125 M) NaOH solution¹⁸ maintaining a constant ionic strength, $I = 0.2$ M (NaNO₃) at 25 \pm 1°.

Analytical concentrations of hydrogen ion, correspond-

ing to the pH-meter reading were calculated by following the usual procedure¹⁹. Ionic product of water at the experimental temperature and activity coefficients of H⁺ ion at the experimental ionic strength were obtained from literature^{20,21}. Formation constants were calculated with the aid of SCOGS computer programme³ using the pH vs volume of NaOH data as were the averages of three titrations, each time repeating the cycle of operation up to the minimum value of standard deviation.

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