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# Polynuclear Complex Formation. I. Copper(II) and 2,7-Diaminosuberic Acid

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2,7-Diaminosuberic acid (DAS) forms mono- and polynuclear complexes with copper(II) ion in aqueous solution. The latter comprise straight chain polymers and ring-type complexes such as di-$\mu$-(2,7-diaminosuberato)-dicopper(II) as major species. Stability constants of log $K_1$ = 8.03 and log $\beta_2$ = 14.20 (at 20° and an ionic strength of 0.15) for the mononuclear species indicate simple mono-(amino acid)-type bonding. Constants for the polynuclear complexes are statistically related to $K_1$ and $K_2$. Di-$\mu$-(2,7-diaminosuberato)-dicopper(II) has been isolated from solution and its magnetic moment has been measured.

Ligands of the general type, $LRL^{2-}$, where R is a group that prevents simultaneous complex formation by both ends of the ion with a single metal ion, would be expected to give polynuclear species with metal ions in solution. Thus Schwarzenbach[2] observed a tendency for ligands related to ethylenediaminetetraacetic acid to form polynuclear complexes with various metals as the length of the methylene chain increased. Although numerous polynuclear complexes have been isolated from solution,[3] no extensive quantitative investigation has previously been made of the types of species present in solutions of metal ions and polydentate ligands to which the above restriction applies. 2,7-Diaminosuberate anion is such a ligand and, in the present paper, the equilibria between hydrated copper(II) ion and 2,7-diaminosuberic acid, $HOOCCHNH_2CH_2CH_2CH_2CHNH_2COOH$ (DAS), are studied potentiometrically and the stability constants of the mono- and polynuclear species present, and hence their concentrations under various conditions, are obtained.

## Experimental

**Apparatus and Reagents.**—A stock copper perchlorate solution (0.0277 *M*) was prepared as described by Perrin[4] and standardized both by cation exchange (IR-120, $H^+$ resin), the liberated acid being titrated with standard alkali, and by EDTA-murexide titration.[5] A stock solution of 0.1 *N* carbonate-free sodium hydroxide was prepared by ion exchange. Sodium perchlorate (British Drug Houses Ltd.), purified by recrystallization from aqueous ethanol, was dried at room temperature *in vacuo*. 2,7-Diaminosuberic acid, prepared according to the method of Simmonds,[6] was recrystallized from water to give colorless crystals, m.p. >360°.

*Anal.* Calcd. for $C_8H_{16}O_4N_2$: C, 47.05; H, 7.90; N, 13.72. Found: C, 46.94; H, 7.97; N, 13.79.

The titration cell was a cylindrical glass vessel of about 200 ml. capacity, closed by a rubber stopper through which passed a glass electrode, a gas-bubbler, a thermometer, and a fine-bore polythene tube connected to an "Agla" micrometer syringe. The cell was joined by an ammonium nitrate–sodium nitrate–agar salt bridge to an external saturated calomel electrode. An inert atmosphere was maintained in the vessel by continuously passing scrubbed nitrogen through the solutions which were stirred by a magnetic stirrer. All pH measurements were made at 20 ± 0.1° on a Cambridge bench model pH meter, taking as standard 0.05 *M* potassium hydrogen phthalate, pH 4.00 at 20°. The titrations were performed by adding 0.1 *N* sodium hydroxide in small portions from a micrometer syringe to the solutions which had been adjusted to an ionic strength of 0.15 by the addition of sodium perchlorate. Hydrogen ion concentrations corresponding to measured pH values were obtained from a blank titration of the sodium perchlorate solution with standard hydrochloric acid.

**Acid Dissociation Constants.**—DAS has four acid dissociation constants, given by

$$K_{a_1} = [HLRLH_2^+][H^+]/[H_2LRLH_2^{2+}]$$
$$K_{a_2} = [HLRLH][H^+]/[HLRLH_2^+]$$
$$K_{a_3} = [HLRL^-][H^+]/[HLRLH]$$
$$K_{a_4} = [LRL^{2-}][H^+]/[HLRL^-]$$

Because $K_{a_1}$ and $K_{a_2}$ and $K_{a_3}$ and $K_{a_4}$ "overlap," a graphical method similar to that of Speakman[7] had to be used to obtain the $pK_a$ values from potentiometric titrations. These were found to be $pK_{a_1}$ = 1.84, $pK_{a_2}$ = 2.62, $pK_{a_3}$ = 9.23, and $pK_{a_4}$ = 9.89.

**Preparation of Crystalline Copper(II)–DAS Complex.**—A crystalline complex was prepared by mixing equimolar amounts of 2,7-diaminosuberic acid and copper(II) sulfate pentahydrate in 1 *N* hydrochloric acid, heating the solution to near boiling, and adding a dilute ammonia solution dropwise until the solution was neutral. The blue, finely crystalline precipitate was extremely insoluble: no solvent was found that would dissolve it in the cold or on boiling. Analysis indicated a 1:1 copper:DAS ratio in the complex.

*Anal.* Calcd. for $Cu(C_8H_{14}N_2O_4)\cdot H_2O$: Cu, 22.39; C, 33.86; H, 5.68; N, 9.87. Found: Cu, 22.43; C, 34.02; H, 5.55; N, 9.90.

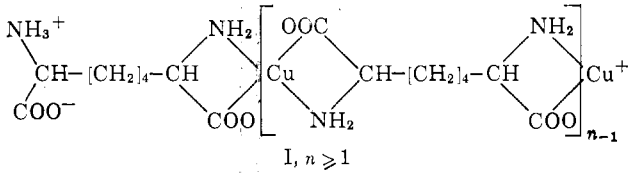
## Discussion

**Equilibria in Solution.**—The difference of 0.66 between $pK_{a_3}$ and $pK_{a_4}$ for DAS agrees, within experimental error, with the factor, 0.60 (= log 4), predicted on statistical grounds for consecutive $pK$ values of identical, non-interacting groups attached to the same molecule. (Compare $pK_{a_3}$ = 8.02 ± 0.03, $pK_{a_4}$ = 8.71 ± 0.03, difference 0.69 ± 0.06, for cystine.[8]) This agreement implies that the electrostatic interaction between the two ends of the DAS molecule is negligible. Hence the amino acid groups in DAS should act independently of each other in metal complex formation, with the restriction, as shown by Leybold

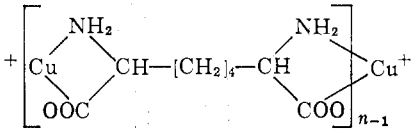
(1) Australian National University Scholar.
(2) G. Schwarzenbach, *Helv. Chim. Acta*, **35**, 2344 (1952).
(3) J. C. Bailar, Jr., "The Chemistry of the Co-ordination Compounds," Reinhold Publishing Corp., New York, N. Y., 1956, pp. 253–260, 321–323.
(4) D. D. Perrin, *J. Chem. Soc.*, 3189 (1960).
(5) G. Schwarzenbach, "Complexometric Titrations," Methuen and Co. Ltd., London, 1957, p. 82.
(6) D. H. Simmonds, *Biochem. J.*, **58**, 520 (1954).
(7) J. C. Speakman, *J. Chem. Soc.*, 855 (1940).
(8) J. P. Greenstein, F. W. Klemperer, and J. Wyman, *J. Biol. Chem.*, **129**, 681 (1939).

atomic models, that it is sterically impossible for all four donor atoms of any given DAS molecule to be coördinated to the *same* metal ion. (So long as metal complex formation can occur in which the two amino acid groups from any DAS molecule are able to complex with different metal ions, the energetically less-favored binding through one amino acid grouping and the other amino or carboxyl group of a DAS molecule, although possible, is unlikely to be significant.)

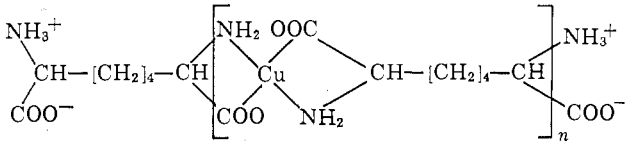
The logarithms of the stepwise formation constants of complexes formed by copper(II) ion with the bidentate ligand, aminoacetic acid, are log $K_1$ = 8.22, log $K_2$ = 6.97, log $K_3 < 1$, at 20° in 0.5 $M$ potassium nitrate solution.[9] Thus, in its amino acid complexes, under conditions of low ligand concentration, copper(II) can be expected to show a maximum coördination number of four. This restriction limits the kinds of complexes copper(II) ion can form with DAS to members of only the four polynuclear series, I–IV.



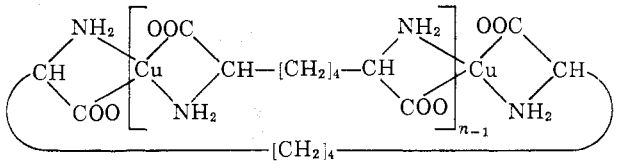
I, $n \geq 1$



II, $n \geq 2$



III, $n \geq 1$



IV, $n \geq 2$

For convenience, these series may be written as HLRL-(CuLRL)$_{n-1}$Cu$^+$ (I), $^+$(CuLRL)$_{n-1}$Cu$^+$ (II), HLRL-(CuLRL)$_n$H (III), and $\overline{\text{LRL[CuLRL]}_{n-1}\text{Cu}}$ (IV), where HLRLH represents neutral (including zwitterionic) DAS. In each member of the linear series, I, II, III, the end groups are, respectively, a free amino acid and a copper ion, two copper ions, and two free amino acids. When at least two DAS molecules and two copper ions are present in a complex, ring formation also can occur, to give the cyclic complexes which comprise series IV. The extent of formation of any complex in any of the above series will be governed by stepwise equilibrium constants.

These considerations indicate, and the experimental results confirm, that the simple Bjerrum-type treatment of the system as one containing only 1:1 and 1:2 metal:ligand complexes is not applicable. Instead, they imply that the extent of complex formation between copper(II) ion and one specified end of a DAS molecule should be essentially independent of whether the other end is uncharged, ionized, or complexed to another copper(II) ion. A similar comment applies to further complex formation by a copper ion which already is complexed to one end of a DAS molecule.

**Calculation of Stability Constants.**—Thus, in the copper–DAS system, one or the other of the usual stepwise formation constants

$$K_1 = [\text{HLRLCu}^+]/[\text{Cu}^{2+}][\text{HLRL}^-]$$
$$K_2 = [\text{Cu(LRLH)}_2]/[\text{HLRLCu}^+][\text{HLRL}^-]$$

refers to each step in the general equilibria

$$\text{X–LRL}^- + \text{Cu}^{2+} \rightleftharpoons \text{X–LRL–Cu}^+ \qquad (K_1)$$

$$\left.\begin{matrix}\text{X–LRL}^- + {}^+\text{Cu–LRL–Y} \\ \text{Y–LRL}^- + {}^+\text{Cu–LRL–X}\end{matrix}\right\} \rightleftharpoons \text{X–LRL–Cu–LRL–Y} \qquad (K_2)$$

independently of the nature of X and Y.

The stability constants and concentrations of all complexes in series I to IV can be expressed as functions of $K_1$, $K_2$, $K_{a_3}$, [H$^+$], [Cu$^{2+}$], and [HLRL$^-$]. These are, in order

$$[\text{HLRL(CuLRL)}_{n-1}\text{Cu}^+] = K_1^n K_2^{n-1} K_{a_3}^{n-1}[\text{Cu}^{2+}]^n[\text{HLRL}^-]^n/[\text{H}^+]^{n-1} \quad (1)$$

$$[{}^+\text{(CuLRL)}_{n-1}\text{Cu}^+] = K_1^n K_2^{n-2} K_{a_3}^{n-1}[\text{Cu}^{2+}]^n[\text{HLRL}^-]^{n-1}/4[\text{H}^+]^{n-1} \quad (2)$$

$$[\text{HLRL(CuLRL)}_n\text{H}] = K_1^n K_2^n K_{a_3}^{n-1}[\text{Cu}^{2+}]^n[\text{HLRL}^-]^{n+1}/[\text{H}^+]^{n-1} \quad (3)$$

$$[\overline{\text{LRL(CuLRL)}_{n-1}\text{Cu}}] = K_1^n K_2^n K_{a_3}^n[\text{Cu}^{2+}]^n[\text{HLRL}^-]^n/2n[\text{H}^+]^n \quad (4)$$

The numerical factors are statistical in origin, as discussed below.

The following examples of stepwise equilibria illustrate the principles involved in deriving these constants.

$$\text{HLRL}^- + \text{Cu}^{2+} \rightleftharpoons \text{HLRLCu}^+$$
$${}^+\text{CuLRLH} \rightleftharpoons {}^+\text{CuLRL}^- + \text{H}^+$$
$${}^+\text{CuLRL}^- + \text{Cu}^{2+} \rightleftharpoons {}^+\text{CuLRLCu}^+$$
$$\text{HLRL}^- + {}^+\text{CuLRLCu}^+ \rightleftharpoons \text{HLRLCuLRLCu}^+$$

Thus by definition

$$[\text{HLRLCu}^+] = K_1[\text{Cu}^{2+}][\text{HLRL}^-]$$
$$[{}^+\text{CuLRL}^-] = K_{a_3}[\text{HLRLCu}^+]/2[\text{H}^+] = K_1K_{a_3}[\text{Cu}^{2+}][\text{HLRL}^-]/2[\text{H}^+]$$

the presence of the copper ion having no effect on the ionic equilibria at the other end of the molecule, and the factor of $^1/_2$ being due to HLRLCu$^+$ having only one site from which a proton can dissociate whereas in HLRLH there are two. In the same way

$$[{}^+\text{CuLRLCu}^+] = K_1[\text{Cu}^{2+}][{}^+\text{CuLRL}^-]/2 = K_1^2K_{a_3}[\text{Cu}^{2+}]^2[\text{HLRL}^-]/4[\text{H}^+]$$

Here the new factor of $^1/_2$ arises because there is only one way in which the complex can form from Cu$^{2+}$ and $^+$CuLRL$^-$ whereas there are two ways in which it can dissociate to give these species. Similarly

(9) H. V. Flood and V. Lorås, *Tidsskr. Kjemi Bergvesen* Met., **5**, 83 (1945).

$$[HLRLCuLRLCu^+] = 4K_2[{}^+CuLRLCu^+][HLRL^-] = K_1^2K_2K_{a_3}[Cu^{2+}]^2[HLRL^-]^2/[H^+]$$

the factor of 4 entering because the complex can be formed in either of two ways from its components but, once formed, it can only dissociate in one way to give the species from which it is derived, whereas in the mononuclear 1:2 complex the second ligand can be added in only one way but, once the complex is formed, dissociation can occur from either end.

Thus, in spite of the complexity of the system, quantitative interpretation of the potentiometric titration data depends on values assigned to only two adjustable parameters, namely, $K_1$ and $K_2$.

In the system where a copper(II) salt is added to a neutral DAS solution and titrated with standard alkali, the three independent equations for total concentrations of metal species, total concentrations of ligand species, and total charges become, respectively

$$[Cu]_T = [Cu^{2+}] + \sum_{n=1}^{n=\infty} (nK_1^nK_2^{n-1}K_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^n/[H^+]^{n-1}) + \sum_{n=2}^{n=\infty} (nK_1^nK_2^{n-2}K_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^{n-1}/4[H^+]^{n-1}) + \sum_{n=1}^{n=\infty} (nK_1^nK_2^nK_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^{n+1}/[H^+]^{n-1}) + \sum_{n=2}^{n=\infty} (K_1^nK_2^nK_{a_3}^n[Cu^{2+}]^n[HLRL^-]^n/2[H^+]^n) \quad (5)$$

$$[HLRLH]_T = [H_2LRLH_2^{2+}] + [HLRLH_2^+] + [HLRLH] + [HLRL^-] + [LRL^{2-}] + \sum_{n=1}^{n=\infty} (nK_1^nK_2^{n-1}K_{a_3}^{n-1}[Cu^{2+}]^n \times [HLRL^-]^n/[H^+]^{n-1}) + \sum_{n=2}^{n=\infty} ((n-1)K_1^nK_2^{n-2}K_{a_3}^{n-1} \times [Cu^{2+}]^n[HLRL^-]^{n-1}/4[H^+]^{n-1}) + \sum_{n=1}^{n=\infty} ((n+1) \times K_1^nK_2^nK_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^{n+1}/[H^+]^{n-1}) + \sum_{n=2}^{n=\infty} (K_1^nK_2^nK_{a_3}^n[Cu^{2+}]^n[HLRL^-]^n/2[H^+]^n) \quad (6)$$

$$2[Cu]_T + [OH^-] + [HLRL^-] + 2[LRL^{2-}] = [H^+] + [Na^+] + 2[H_2LRLH_2^{2+}] + [HLRLH_2^+] + 2[Cu^{2+}] + \sum_{n=1}^{n=\infty} (K_1^nK_2^{n-1}K_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^n/[H^+]^{n-1}) + \sum_{n=2}^{n=\infty} (K_1^nK_2^{n-2}K_{a_3}^{n-1}[Cu^{2+}]^n[HLRL^-]^{n-1}/2[H^+]^{n-1}) \quad (7)$$

Each of the summations is of a binomial series, the sums of which lead to the equations

$$[Cu]_T = [Cu^{2+}] + \frac{x}{(1-x)^2} \times \left\{ \frac{[H^+]}{K_2K_{a_3}} + [HLRLH] + \frac{(2-x)K_1[Cu^{2+}]}{4K_2} \right\} + \frac{x^2}{2(1-x)} \quad (8)$$

$$[HLRLH]_T = g[HLRL^-] + \frac{x}{(1-x)^2} \times \left\{ \frac{[H^+]}{K_2K_{a_3}} + (2-x)[HLRLH] + \frac{K_1[Cu^{2+}]}{4K_2} \right\} + \frac{x^2}{2(1-x)} \quad (9)$$

$$2[Cu]_T = [H^+] + [Na^+] + 2[Cu^{2+}] + \frac{x}{(1-x)} \times \left\{ \frac{[H^+]}{K_2K_{a_3}} + \frac{K_1[Cu^{2+}]}{2K_2} \right\} + 2[H_2LRLH_2^{2+}] + [HLRLH_2^+] - [HLRL^-] - 2[LRL^{2-}] - [OH^-] \quad (10)$$

where

$$x = K_1K_2K_{a_3}[Cu^{2+}][HLRL^-]/[H^+]$$

and

$$g = (1 + [H^+]/K_{a_3} + [H^+]^2/K_{a_2}K_{a_3} + [H^+]^3/K_{a_1}K_{a_2}K_{a_3})$$

Using an iterative procedure, values of $K_1 = 1.08 \times 10^8\ M^{-1}$ and $K_2 = 1.47 \times 10^6\ M^{-1}$ were obtained by simultaneous solution of eq. 8, 9, and 10 at two arbitrarily selected points—one at the beginning and the other at the end of the titration curve for the metal: DAS molar ratio of 1:5.

Knowing $K_1$ and $K_2$, it then was possible to test the quantitative correctness of the above discussion by solving eq. 8 and 9 at each point in the series of potentiometric titrations of copper(II) + DAS shown in Table I. $[Cu^{2+}]$ and $[HLRL^-]$ obtained in this way

TABLE I

TITRATIONS OF COPPER PERCHLORATE AND DAS WITH 0.1 $M$ SODIUM HYDROXIDE[a]

| pH | [NaOH] × 10⁵, M | [Cu²⁺] × 10⁵, M | [HLRL⁻] × 10⁸, M | pH | [NaOH] × 10⁵, M | [Cu²⁺] × 10⁵, M | [HLRL⁻] × 10⁸, M |
|---|---|---|---|---|---|---|---|
| (i) $1 \times 10^{-4}$ $M$ $Cu(ClO_4)_2$ and $4.984 \times 10^{-4}$ $M$ DAS | | | | | | | |
| 4.48 | 0.000 | 5.568 | 0.693 | 4.96 | 7.079 | 2.763 | 1.957 |
| 4.52 | 0.506 | 5.358 | .749 | 5.04 | 8.090 | 2.340 | 2.321 |
| 4.54 | 1.012 | 5.207 | .791 | 5.11 | 9.100 | 1.951 | 2.747 |
| 4.57 | 1.518 | 5.031 | .845 | 5.18 | 10.110 | 1.629 | 3.194 |
| 4.60 | 2.023 | 4.854 | .903 | 5.25 | 11.120 | 1.344 | 3.726 |
| 4.64 | 2.529 | 4.580 | .977 | 5.33 | 12.129 | 1.074 | 4.387 |
| 4.67 | 3.035 | 4.428 | 1.056 | 5.41 | 13.139 | 0.822 | 5.232 |
| 4.74 | 4.046 | 4.006 | 1.232 | 5.49 | 14.148 | 0.604 | 6.311 |
| 4.81 | 5.057 | 3.584 | 1.441 | 5.59 | 15.157 | 0.421 | 7.858 |
| 4.88 | 6.068 | 3.190 | 1.664 | | | | |
| (ii) $2 \times 10^{-4}$ $M$ $Cu(ClO_4)_2$ and $5.029 \times 10^{-4}$ $M$ DAS | | | | | | | |
| 4.29 | 0.000 | 13.400 | 0.427 | 5.04 | 18.183 | 4.743 | 1.957 |
| 4.36 | 2.024 | 12.606 | .496 | 5.12 | 20.200 | 3.906 | 2.296 |
| 4.45 | 4.046 | 11.660 | .594 | 5.19 | 22.215 | 3.193 | 2.666 |
| 4.53 | 6.068 | 10.700 | .708 | 5.26 | 24.229 | 2.602 | 3.071 |
| 4.62 | 8.090 | 9.671 | .843 | 5.34 | 26.243 | 2.052 | 3.582 |
| 4.70 | 10.110 | 8.677 | 1.002 | 5.42 | 28.257 | 1.536 | 4.269 |
| 4.79 | 12.129 | 7.545 | 1.205 | 5.51 | 30.269 | 1.108 | 5.160 |
| 4.88 | 14.148 | 6.563 | 1.426 | 5.61 | 32.281 | 0.754 | 6.398 |
| 4.96 | 16.166 | 5.644 | 1.667 | 5.72 | 34.291 | 0.486 | 8.143 |
| (iii) $5 \times 10^{-4}$ $M$ $Cu(ClO_4)_2$ and $5.034 \times 10^{-4}$ $M$ DAS | | | | | | | |
| 4.06 | 0.000 | 3.922 | 0.226 | 4.89 | 36.301 | 1.869 | 0.885 |
| 4.11 | 2.024 | 3.822 | .250 | 4.93 | 38.310 | 1.763 | .929 |
| 4.16 | 4.046 | 3.731 | .272 | 4.97 | 40.319 | 1.674 | .968 |
| 4.20 | 6.068 | 3.636 | .296 | 5.04 | 44.333 | 1.488 | 1.049 |
| 4.25 | 8.090 | 3.535 | .323 | 5.12 | 48.344 | 1.312 | 1.127 |
| 4.30 | 10.110 | 3.423 | .353 | 5.19 | 52.352 | 1.158 | 1.195 |
| 4.34 | 12.129 | 3.317 | .382 | 5.25 | 56.356 | 1.027 | 1.257 |
| 4.39 | 14.148 | 3.197 | .417 | 5.32 | 60.358 | 0.897 | 1.319 |
| 4.44 | 16.166 | 3.073 | .454 | 5.39 | 64.356 | .780 | 1.375 |
| 4.49 | 18.183 | 2.946 | .494 | 5.47 | 68.351 | .663 | 1.434 |
| 4.54 | 20.200 | 2.814 | .536 | 5.54 | 72.343 | .572 | 1.481 |
| 4.58 | 22.215 | 2.656 | .589 | 5.63 | 76.332 | .476 | 1.532 |
| 4.63 | 24.229 | 2.584 | .612 | 5.71 | 80.317 | .395 | 1.578 |
| 4.68 | 26.243 | 2.453 | .660 | 5.81 | 84.300 | .316 | 1.628 |
| 4.72 | 28.257 | 2.330 | .706 | 5.92 | 88.279 | .248 | 1.676 |
| 4.77 | 30.269 | 2.206 | .752 | 6.04 | 92.255 | .188 | 1.730 |
| 4.81 | 32.281 | 2.084 | .799 | 6.20 | 96.228 | .126 | 1.806 |
| 4.85 | 34.291 | 1.975 | .841 | 6.43 | 100.20 | .071 | 1.936 |

[a] Concentrations of $[Cu^{2+}]$ and $[HLRL^-]$ computed from the titration data using eq. 8 and 9 (see text).

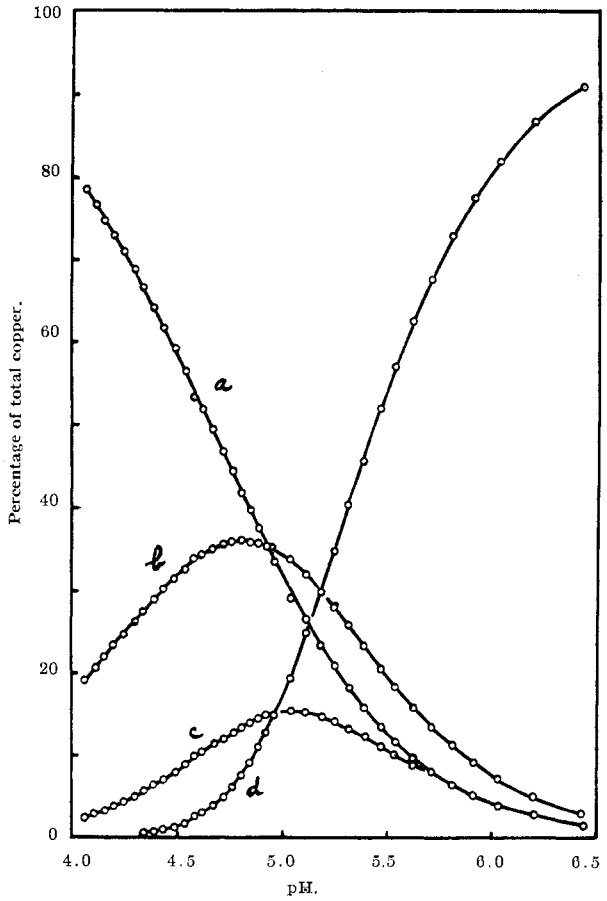



Fig. 1.—Distribution of copper species (as % total copper) for system in which $[Cu]_T = 5 \times 10^{-4}$ *M*, [DAS] = $5.034 \times 10^{-4}$ *M*: a, $Cu^{2+}$; b, $HLRLCu^+$; c, $^+CuLRLCu^+$; d, $(CuLRL)_2$*.

then could be used to evaluate the right hand side of eq. 10 to provide a comparison with the already known value of $2[Cu]_T$. Because of the inherent mathematical complexity, solution of eq. 8 and 9 at each point was carried out on an IBM 1620 digital computer using Fortran, the machine being required to find, by an incremental method, unique values of $[Cu^{2+}]$ and $[HLRL^-]$, at any point, *i*, in the titrations, lying within the limits

$$[Cu]_T \geq [Cu^{2+}]_{i-1} \geq [Cu^{2+}]_i \geq 0$$

$$[HLRLH]_T \geq [HLRL^-]_i \geq [HLRL^-]_{i-1} \geq 0$$

and satisfying eq. 8 and 9. These values are listed in Table I for the $[Cu]_T$:DAS molar ratios of 1:5, 2:5, and 1:1, the corresponding total copper concentrations being 1, 2, and $5 \times 10^{-4}$ *M*.

The average deviation of the computed values of $2[Cu]_T$ from the experimental values, using eq. 10, was less than ±0.9%; in no case did it exceed 1.8%. This agreement strongly suggests that equilibria in the $Cu^{2+}$–DAS systems are correctly represented by statistical distributions of complexes of the types postulated. The mathematical analysis is very sensitive to the values assigned to log $K_1$ and log $K_2$, changes of 0.04 in either (or both) values producing, in the computed $2[Cu]_T$ values, systematic deviations exceeding 1%.

Knowing $K_1$ and $K_2$, the over-all stability constants of the various species can be obtained by substitution in eq. 1 to 4. Constants for the more important species are given in Table II.

TABLE II

OVER-ALL STABILITY CONSTANTS AT 20° AND $\mu$ = 0.15

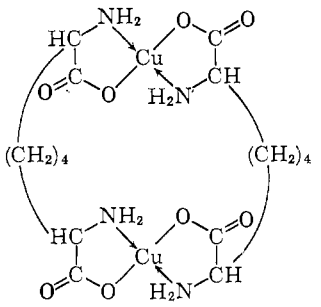
| Species | Products | Constant |
|---|---|---|
| $HLRLCu^+$ | $Cu^2 + HLRL^-$ | $\log \beta_{1:1} = 8.03$ |
| $HLRLCuLRLCu^+$ | $2Cu^{2+} + LRL^{2-} + HLRL^-$ | $\log \beta_{2:2} = 22.83$ |
| $HLRLCuLRLH$ | $Cu^{2+} + 2HLRL^-$ | $\log \beta_{1:2} = 14.20$ |
| $HLRLCuLRLCuLRLH$ | $2Cu^{2+} + LRL^{2-} + 2HLRL^-$ | $\log \beta_{2:3} = 29.00$ |
| $^+CuLRLCu^+$ | $2Cu^{2+} + LRL^{2-}$ | $\log \beta_{2:1} = 16.06$ |
| $(CuLRL)_2$*[a] | $2Cu^{2+} + 2LRL^{2-}$ | $\log \beta^*_{2:2} = 29.00$ |

[a] Cyclic complex, $n = 2$ in series IV.

Comparison of the stability constants for the mononuclear complexes of copper(II) and DAS with those of the simple amino acid copper(II) complexes shows that in the former the ligand from DAS acts as a simple amino acid bidentate chelate (log $K_1$ = 8.03, log $\beta_2$ = 14.20, $pK_a$ = 9.23; *cf.* $Cu^{2+}$ + glycine,[10] log $K_1$ = 8.12, log $\beta_2$ = 15.03, $pK_a$ = 9.85).

**Distribution of Species in Copper(II)–DAS Systems.**—From Table I and $K_1$, $K_2$, and $K_{a_3}$, the concentration of each of the complexes represented by the general equations 1 to 4 can be calculated throughout a titration, and hence their individual significance in any system can be assessed. Results for copper:DAS molar ratios of 1:1 and 1:5 are shown in Fig. 1 and 2; results for the 2:5 ratio lie between them. It is probable that, over the later stages of the titrations and in spite of the low concentrations used, the solutions were supersaturated with respect to di-$\mu$-(2,7-diaminosuberato)-dicopper(II); precipitation slowly occurred when the final solutions were allowed to stand. The species $HLRLCu^+$, $Cu(LRLH)_2$, $^+CuLRLCu^+$, and (CuLRL)* (where the asterisk denotes a ring-type complex belonging to series IV) account for more than 97% of all copper present in the complexes.

Although polynuclear complex formation was expected, the major importance of the binuclear species, $(CuLRL)_2$*, especially over the second half of each titration, was surprising. This complex is postulated to be di-$\mu$-(2,7-diaminosuberato)dicopper-(II) and to have the structure shown below.




The *trans–trans* structure is shown, but there is no evidence to discriminate between this and the *cis–cis* configuration: both are sterically possible. In this structure each copper forms part of two five-membered rings which, in turn, are linked in pairs by two tetra-

(10) At 20° in 0.1 *M* KCl; H. Irving, R. J. P. Williams, D. J. Ferrett, and A. E. Williams, *J. Chem. Soc.*, 3498 (1954).

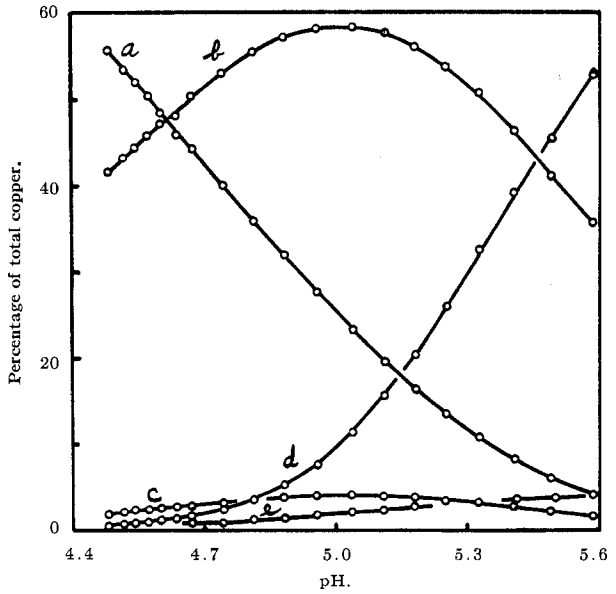



Fig. 2.—Distribution of copper species (as % total copper) for system in which $[Cu]_T = 1 \times 10^{-4}$ *M*, [DAS] = $4.984 \times 10^{-4}$ *M*: a, $Cu^{2+}$; b, HLRLCu$^+$; c, $^+$CuLRLCu$^+$; d, $(CuLRL)_2$*; e, $Cu(LRLH)_2$.

methylene bridges. Dimers with structures analogous to this have been demonstrated cryoscopically for the copper(II) complexes of substituted disalicylidenebenzidine, disalicylidene-*p*-phenylenediamine, and disalicylidene-*m*-phenylenediamine.[11] The complex precipitated from neutral solutions of DAS containing copper(II) ion is believed to be di-$\mu$-(2,7-diaminosuberato)-dicopper(II), which is the main species present in solution under the experimental conditions and which would be expected to be only sparingly soluble because of its non-ionic character. Chemical analysis is consistent with this structure, but its molecular weight could not be determined because of insolubility. The magnetic moment of 1.91, determined by the Gouy method, is typical of simple copper(II) complexes[12] and indicates the absence of Cu–Cu $\delta$-bonding in this compound.

**Acknowledgments.**—The authors thank Miss Elizabeth Reid for the computer program and operation and Dr. N. Gill for use of the magnetic balance.

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(12) *E.g.*, $\mu$ = 1.93 for bis-(glycinato)-copper(II) monohydrate; P. Rây and D. N. Sen, *J. Indian Chem. Soc.*, **25**, 473 (1948).

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# Polynuclear Complex Formation. II. Copper(II) with Cystine and Related Ligands

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In aqueous solution, cystine and copper(II) form mono- and polynuclear complexes. Stability constants for the polynuclear complexes are statistically related to the stepwise formation constants, $K_1$ and $K_2$, of the 1:1 and the 1:2 mononuclear complexes. At 20° and an ionic strength of 0.15, log $K_1$ is 7.00 and log $K_2$ is 6.72. These values are consistent with mono-(amino acid)-type bonding with a contribution from the disulfide group. A compound, believed to be the polynuclear complex, di-$\mu$-cystinatodicopper(II), which is a major species over a wide range of conditions, has been isolated from solution and its magnetic moment has been measured. Complex formation between copper(II) ion and a number of ligands closely related to cystine also has been investigated. Stability constants of their copper(II) complexes at 20° and an ionic strength of 0.15 have been determined for bis-(2-aminoethyl) disulfide (BAED), 2,2′-dicarboxydiethyl disulfide (DDD), 3-(2-aminoethyldithio)-L-alanine (AEDA), and L-methionine. In all cases the sulfur atoms contribute to the coördination with copper(II), but polynuclear complex formation was not important under the experimental conditions examined.

Although it would be of some biochemical interest, no extensive and quantitative study of equilibria in the aqueous copper(II)–cystine system appears to have been made. This probably is due, in part, to the sparing solubilities of the ligand and the copper(II)–cystine complex and, in part, to the complicated nature of the problem. Kolthoff and Stricks[2] concluded from polarographic evidence that complex formation between copper(II) and cystine was not significant in ammoniacal solution. On the other hand, Hamaguchi and Kamemoto[3] explained polarographic observations by the slow formation of a mononuclear complex, in which (as previously postulated by Rây and Bhaduri[4] and Scaife[5]) the two amino acid groupings are coördinated to the same metal ion. However, Leybold atomic models show that simultaneous attachment of both ends of the cystine anion to the same copper(II) ion is sterically impossible. This restriction also applies to the structurally related bis-(amino acid), 2,7-diaminosuberic acid, where it leads to both mono- and polynuclear copper(II) complex formation.[6]

In the present paper, equilibrium studies in aqueous solution between hydrated copper(II) ion and L-cystine are described, and the stability constants of the mono-

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