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Binary Copper(II) and Uranyl(VI) Complexes of Glycocyamine, Taurine and Pyridoxal and Ternary Complexes Involving 2,2′-Bipyridine, 1,10-Phenanthroline or Nitrilotriacetic Acid

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Chelating tendencies of several biologically important compounds viz. glycocyamine (*GCN*: *N*-amidino-aminoethanoic acid) taurine (*TRN*: 2-aminoethanesulphonic acid) and pyridoxal [*PDL*; 3-hydroxy-5-(hydroxymethyl)--2-methyl-pyridine-4-carbaldehyde] have been examined by pH-metric titration technique in their binary complex formation with copper(II) and uranyl(VI) ions. The work has further been extended to investigating the ternary complex formation involving 2,2′-bipyridine, 1,10-phenanthroline or nitrilotriacetic acid as a primary and *TRN* and *PDL* as secondary ligands. All the experiments were carried out at 25 °C and at an ionic strength of 0.1*M* ($NaClO_4$) in aqueous or 50% (*v*/*v*) aqueous-ethanol medium according to the suitability of the experimental conditions. Stabilities of ternary complexes as compared to those of the corresponding binary complexes of the secondary ligands have also been discussed.

Binäre Kupfer(II)- und Uranyl(VI)-Komplexe von Glycocyamin, Taurin und Pyridoxal: Erweiterung zu ternären Systemen mit 2,2′-Bipyridin, 1,10-Phenanthrolin und Nitrilotriessigsäure

Das Komplexierungsvermögen einiger biologisch wichtiger Verbindungen [Glycocyamin (*GCN*: *N*-Amidino-aminoethansäure), Taurin (*TRN*: 2-Aminoethansulfonsäure und Pyridoxal (*PDL*; 3-Hydroxy-5-(hydroxymethyl)-2-methyl-pyridin-4-carbaldehyd)] gegenüber Kupfer(II)- und Uranyl(VI)-Ionen wurde untersucht. Für *TRN* und *PDL* wurde das System auf ternäre Komplexe erweitert (2,2′-Bipyridin, 1,10-Phenanthrolin und Nitrilotriessigsäure als Primärligand). Die Messungen wurden bei 25 °C und bei Ionenstärken von 0,1*M*($NaClO_4$) in Wasser oder 50% Wasser—Ethanol durchgeführt. Die Stabilität der ternären Komplexe im Vergleich zu den entsprechenden binären wird diskutiert.

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Introduction

The importance of transition metal ions in the biological systems and the phenomenon of chelation is well recognized[1,2]. However, an accurate elucidation of the chelation process, is apparently complicated in metabolic reactions where a variety of equilibria involving a number of metal ions and donor molecules coexist. Yet studies on complexation reactions between biologically important metal ions and donor molecules *in vitro* is desirable, as one of the steps to an understanding of the subject, and work in this direction is already in progress[3,4]. The advantages of investigations involving two or more different ligands are also evident, as complexation equilibria in such systems would be much closer to those existing in metabolic reactions.

Results of studies on the chelating tendencies of copper(II) and uranyl(VI) ions with glycocyamine (*N*-amidino-aminoethanoic acid; *GCN*), taurine (2-aminoethanesulphonic acid; *TRN*) and pyridoxal [3-hydroxy-5-(hydroxymethyl)-2-methyl-pyridine-4-carbaldehyde; *PDL*] are being reported here. The work has further been extended to examining the ternary complexing systems involving 2,2′-bipyridine (*BIPY*), 1,10-phenanthroline (*PHEN*) and nitrilotriacetic acid (*NTA*) as primary (*A*) and *TRN* and *PDL* as secondary (*L*) ligands where a few copper(II) complexes could be studied. It may be mentioned that various ligands viz. *GCN*, *TRN*, *PDL*, *BIPY*, *PHEN*, and *NTA* are all of biological importance[5–11].

Formation constants corresponding to various complexation equilibria in the binary *M*—*L* systems have been investigated by the *Irving* and *Rossotti* pH-titration technique[12], while those occurring in the ternary complexing systems by the same technique as modified by *Chidambaram* and *Bhattacharya*[13]. All the experiments were carried out at 25 °C and at an ionic strength of 0.1*M* maintained by sodium perchlorate in aqueous or 50 % (*v*/*v*) aqueous-ethanol medium according to the suitability of the experimental conditions.

Experimental

Solutions and Materials

All the solutions were prepared in doubly distilled CO_2- free water and the reagents used were of analytical grade.

Stock solutions of cupric perchlorate (0.1*M* in 0.2*M* perchloric acid), uranyl perchlorate (0.1*M* in 0.2*M* perchloric acid) and sodium perchlorate (1.0*M*) were prepared and standardized. Perchloric acid (0.2*M*) and sodium hydroxide (0.1*M*) were prepared and used after standardization. Stock solutions (0.01*M*) of the chelating ligands viz. *GCN*, *TRN*, *PDL*, *BIPY*, *PHEN*, and *NTA* were prepared by direct weighing and dissolving them separately in water.

BCPW sample of absolute alcohol was used whenever necessary, after distilling it.

Procedure

All the measurements were carried out at 25 °C using a Leeds and Northrup pH-meter with a glass-calomel electrode assembly:

For pH-metric titration of binary and ternary complexing systems (involving *BIPY* as a primary ligand) the following mixtures were prepared: (*A*) 5.0 ml perchloric acid (0.02*M*) + 5.0 ml sodium perchlorate (1.0*M*) + 40.0 ml water, (*B*) 5.0 ml perchloric acid (0.02*M*) + 5.0 ml sodium perchlorate (1.0*M*) + 5.0 ml ligand (0.01*M* of *GCN*, *TRN* or *PDL*) + 35.0 ml water, (*C*) 4.0 ml perchloric acid (0.02*M*) + 1.0 ml metal perchlorate (0.01*M* in 0.02*M* perchloric acid) + 5.0 ml sodium perchlorate (1.0*M*) + 5.0 ml ligand (0.01*M* of *GCN*, *TRN* or *PDL*) + 35.0 ml water, (*D*) 5.0 ml perchloric acid (0.02*M*) + 5.0 ml sodium perchlorate (1.0*M*) + 5.0 ml *BIPY* (0.01*M*) + 35.0 ml water. (*E*) 5.0 ml metal perchlorate (0.01*M* in 0.02*M* perchloric acid) + 5.0 ml sodium perchlorate (1.0*M*) + 5.0 ml *BIPY* (0.01*M*) + 35.0 ml water, (*F*) 5.0 ml metal perchlorate (0.01*M* in 0.02*M* perchloric acid) + 5.0 ml sodium perchlorate (1.0*M*) + 5.0 ml *BIPY* (0.01*M*) + 5.0 ml secondary ligand (0.01*M* of *TRN* or *PDL*) + 30.0 ml water; total volume in each case 50.0 ml. These mixtures were individually titrated against standard alkali, whereby six titration curves viz. *A*, *B*, *C*, *D*, *E*, and *F* were obtained in each case (Figs. omitted).

In *M-PHEN-L* systems investigations in 50% aqueous-ethanol (*v/v*) medium became imperative as *M-PHEN* complexes could not be examined in aqueous medium due to occurrence of opacity, turbidity, precipitation etc. Titration mixtures were thus prepared similarly as above but the volume in each case was raised to 50.0 ml by suitable addition of water and/or alcohol in such a way that 50% aqueous-ethanol (*v/v*) medium was maintained in each case.

With *NTA* as a primary ligand, the studies were again carried out in aqueous medium and mixtures were prepared similarly. *NTA* is not a neutral ligand like *BIPY* or *PHEN* and contains dissociable protons for which an allowance was made in the calculations.

Also, as *PDL* sample was available only in form of its hydrochloride, an allowance was given in calculations for the excess acidity in all the systems investigated.

Calculations

Binary M-L Complexing Systems

From the titration curves the average number of protons bound per free ligand ion ($\bar{n}_A$), average number of ligands attached per metal ion ($\bar{n}$) and free ligand exponent (pL) were calculated, whereby the formation curves corresponding to proton-ligand (Fig. 1) and metal-ligand (Fig. 2) systems were obtained. Approximate values of the formation constants were evaluated by interpolation at half $\bar{n}_A$, $\bar{n}$-value method and more precise values were determined by the average value method.

Ternary M-A-L Complexing Systems

The corresponding curve departs from the secondary ligand titration curve only after the complete formation of 1:1 ($M:A$) species and before the hydroxo complex formation of $(M \cdot BIPY)^{2+}$ or

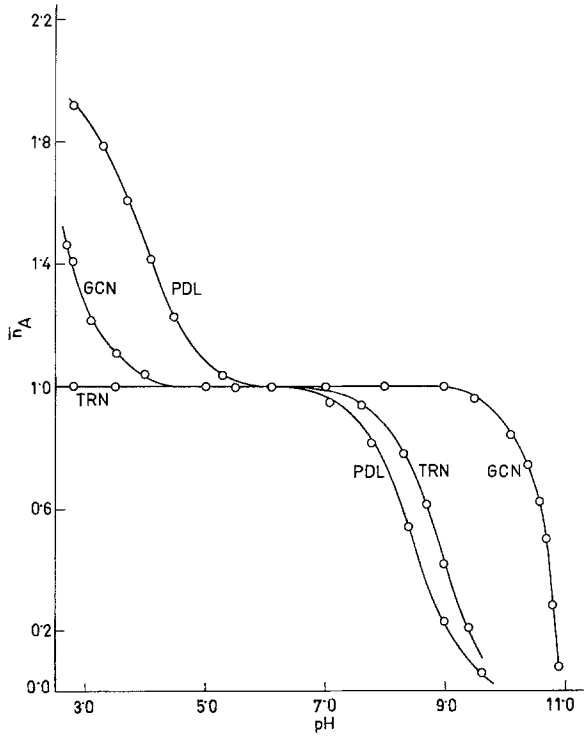


Fig. 1. Formation curves: Protonation Systems of *GCN*, *TRN*, and *PDL*

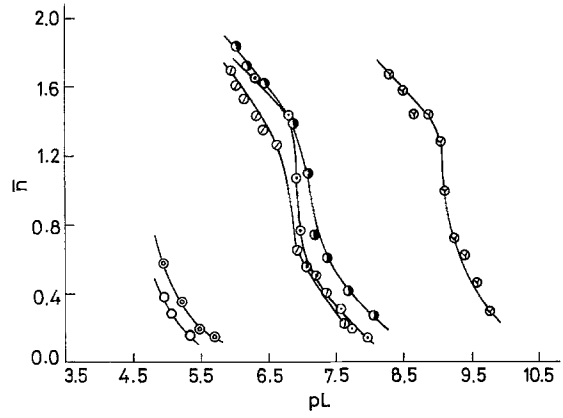


Fig. 2. Formation curves: [*M-L*]
-⊗-⊗- UO_2(VI)—*GCN*, -⊙-⊙- Cu(II)—*GCN*, -○-○- Cu(II)—*TRN*, -◑-◑- UO_2(VI)—*TRN*, -⊙-⊙- Cu(II)—*PDL*, -⊘-⊘- UO_2(VI)—*PDL*

$(M \cdot PHEN)^{2+}$ species; $(M \cdot NTA)^-$ species not undergoing any hydroxo complex formation even at higher pH values. Thus, the average number of secondary ligand molecules attached per $(M \cdot BIPY)^{2+}$, $(M \cdot PHEN)^{2+}$ or $(M \cdot NTA)^-$ions, $\bar{n}_{mix}$, were calculated in analogy to [14].

From the values obtained for $\bar{n}_{mix}$, the free ligand exponents pL_{mix} were calculated[14].

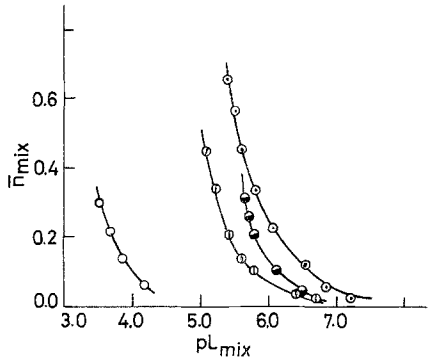


Fig. 3. Formation curves: $[M\text{-}A\text{-}L]$
-◒-◒- Cu(II)—*PHEN*—*TRN*, -⊙-⊙- Cu(II)—*PHEN*—*PDL*,
-⊘-⊘- Cu(II)—*BIPY*—*PDL*, -○-○- Cu(II)—*NTA*—*TRN*

The parameters $\bar{n}_{mix}$ and pL_{mix} were treated similarly as in the binary systems in order to get the formation curves (Fig. 3) and the values of the formation constants.

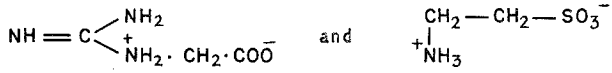
Results and Discussion

Proton Ligand Systems of GCN, TRN and PDL

Amongst the ligands chosen in the present investigation *GCN* is an amino acid, and *TRN* also behaves like an amino acid

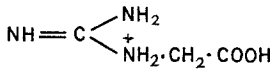
(GCN) (TRN)

possessing the following zwitterionic structures:

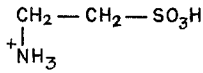


(+GCN−) (+TRN−)

In the initial stage of titration the following species will be formed by protonation:



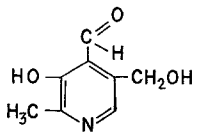
and



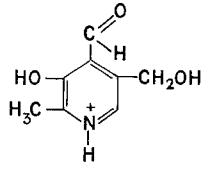
(^{+}GCN) (^{+}TRN)

Though in the case of *GCN* the value of protonation constants corresponding to the cationic imino group, $-\overset{+}{N}H_2$, *and* the carboxylic acid group, —COOH, could be obtained, *TRN* provided only one value of protonation constant under the experimental conditions (Table 1).

In case of *PDL* the basic nitrogen of the pyridine ring is protonated during the initial stage of the titration. Values of protonation constants, corresponding to the cationic tertiary nitrogen *and* the phenolic group are recorded in Table 1.



(PDL)



($^{+}$PDL)

Binary Metal Complexes of GCN, TRN and PDL

In *M-PDL* systems the initially colourless reaction mixture gradually acquired a greenish tinge and subsequently changed to dark green during the addition of alkali. However, the exact pH of colour changes could not be detected under experimental conditions. In cases of *M-GCN* and *M-TRN* systems no colour changes were observed. It was noted that UO_2(VI) forms complexes with *GCN*, *TRN* and *PDL* in two steps. With Cu(II) both the steps could be studied only with *GCN*, while with *TRN* and *PDL* the second step formation constant K_2 could not be studied due to occurrence of opacity, turbidity, precipitation etc. Values of step formation constants corresponding to various equilibria are recorded in Table 1.

The absence of protonated and polynuclear species was confirmed by using several concentrations of the reactants; the results obtained were identical. In a majority of *M-L* systems, precipitation occurred soon after the *M*:*L* (1:1) stage of complexation was complete, and no studies beyond this stage were possible. Hence, ML_2 and the hydroxo species likely to be formed after this stage could not be considered.

Ternary Metal Complexes of TRN and PDL

Amongst various ternary complexing systems undertaken in the present investigation only a few copper(II) complexes could be studied. Others could not be pursued any further either due to occurrence of

Table 1. *Stability constants of binary and ternary chelates*

Reactions	log (Equil. Const.) Method[a]	Method[b]
$L = GCN$		
$L^- + H^+ \rightleftharpoons LH$	10.75	10.85
$LH + H^+ \rightleftharpoons LH_2^+$	—	2.59
$Cu^{2+} + L^- \rightleftharpoons Cu\,L^+$	7.20	7.22
$Cu\,L^+ + L^- \rightleftharpoons Cu\,L_2$	6.65	6.53
$UO_2^{2+} + L^- \rightleftharpoons UO_2\,L^+$	9.45	9.50
$UO_2\,L^+ + L^- \rightleftharpoons UO_2\,L_2$	8.75	8.68
$L = TRN$		
$L^- + H^+ \rightleftharpoons LH$	8.90	8.82 (8.88)[c]
$Cu^{2+} + L^- \rightleftharpoons Cu\,L^+$	—	4.67 (5.90)[c]
$UO_2^{2+} + L^- \rightleftharpoons UO_2\,L^+$	7.50	7.68
$UO_2L^+ + L^- \rightleftharpoons UO_2L_2$	6.70	6.92
$(Cu \cdot PHEN)^{2+} + L^- \rightleftharpoons (Cu \cdot PHEN \cdot L)^+$	—	5.24[c]
$(Cu \cdot NTA)^- + L^- \rightleftharpoons (Cu \cdot NTA \cdot L)^{2-}$	—	3.08
$L = PDL$		
$L^- + H^+ \rightleftharpoons LH$	8.60	8.44 (8.52)[c]
$LH + H^+ \rightleftharpoons LH_2^+$	3.95	3.93 (4.14)[c]
$Cu^{2+} + L^- \rightleftharpoons Cu\,L^+$	5.00	4.93 (5.22)[c]
$UO_2^{2+} + L^- \rightleftharpoons UO_2\,L^+$	7.10	7.14
$UO_2\,L^+ + L^- \rightleftharpoons UO_2\,L_2$	6.25	6.20
$(Cu \cdot BIPY)^{2+} + L^- \rightleftharpoons (Cu \cdot BIPY \cdot L)^+$	5.05	4.90
$(Cu \cdot PHEN)^{2+} + L^- \rightleftharpoons (Cu \cdot PHEN \cdot L)^+$	5.55	5.60[c]

[a] Interpolation at half $\bar{n}$ value method.
[b] Average value method.
[c] In 50% aqueous-ethanol.

opacity, turbidity, precipitation etc., or the conditions required for the technique to be applicable could not be fulfilled.

In the complexing systems which could be studied, it is interesting to note that in case of *BIPY* as a primary ligand the values of log $K^{Cu \cdot BIPY}_{Cu \cdot BIPY \cdot L}$ ($K^{Cu \cdot BIPY}_{Cu \cdot BIPY \cdot L}$ = stoichiometric mixed ligand formation constant) are not much lower than the corresponding log K_1 (K_1 = first step formation constant of the secondary ligand binary complexes) (Table I). However, from statistical considerations, the value of log

$K^{Cu \cdot BIPY}_{Cu \cdot BIPY \cdot L}$ should be appreciably lower than log K_1 as the concentration of electrons around the metal ion in $(Cu \cdot BIPY)^{2+}$ would be more than in $[Cu \cdot (H_2O)_n]^{2+}$ owing to the bipyridine molecule being more strongly coordinating than water. The reason for the $(Cu \cdot BIPY)^{2+}$ species is, that the M-N bond is influenced not only by $L \rightarrow M$ σ-interaction, but there also occurs to some extent $M \rightarrow L$ $(d\pi \rightarrow p\pi)$-interaction which does not permit the concentration of electrons on the metal ion to increase significantly.

Mixed ligand complexes involving 1,10-phenanthroline as a primary ligand (Table 1) exhibit similar behaviour as those in the ternary complexing systems of bipyridine, perhaps due to the structural similarities of *PHEN* with *BIPY*.

It can be seen from Table 1 that the mixed ligand formation constant $\log K^{Cu \cdot NTA}_{Cu \cdot NTA \cdot L}$ corresponding to the association of the secondary ligand (L) with $(Cu \cdot NTA)^-$ ions is much less than $\log K_1$. This may be expected on the basis that there occurs a *Coulomb* repulsion between the secondary ligand anions and the *NTA* anions, during the mixed ligand complex formation tending to lower the stability of the mixed ligand chelates, whereas no such repulsion is encountered during the process of formation of $M:L$ (1:1) species.

References

1 *D. R. Williams*, Chem. Rev. **72**, 203 (1972).
2 *R. D. Gillard*, Inorg. Chim. Acta Rev. **1967**, 69.
3 *D. N. Chaturvedi* and *C. M. Gupta*, Z. analyt. Chem. **260**, 120 (1972).
4 *D. N. Chaturvedi* and *C. M. Gupta*, Analyst **98**, 895 (1973).
5 *J. S. Fruton* and *S. Simmonds*, General Biochemistry, p. 812. Tokyo: C. E. Tuttle. 1962.
6 *J. S. Fruton* and *S. Simmonds*, General Biochemistry, p. 833. Tokyo: C. E. Tuttle. 1962.
7 *H. Sherman*, The Vitamins. ch. 14. New York: Academic Press. 1954.
8 *G. R. Gale, J. A. Howle*, and *E. M. Walker, jr.*, Cancer Res. **31**, 950 (1971).
9 *R. O. Williams* and *L. A. Loebb*, J. Cell Biol. **58**, 594 (1973).
10 *G. A. Nolan*, Toxicol. Appl. Pharmacol. **23**, 238 (1972).
11 *L. G. Sharf*, Nature (London) **239**, 231 (1972).
12 *H. Irving* and *H. S. Rossotti*, J. Chem. Soc. **1953**, 3397; **1954**, 2904.
13 *M. V. Chidambaram* and *P. K. Bhattacharya*, J. Inorg. Nucl. Chem. **32**, 3271 (1970); Ind. J. Chem. **9**, 1294 (1971).
14 *R. K. Mittal, M. Chandra*, and *A. K. Dey*, Mh. Chem. **109**, 853 (1978).