

Potentiometric Study of Binary and Mixed Complexes of Imidazole, Histamine, Histidine and Diacetyl monooxime with Some Transition Metal Ions in Aqueous Solution

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ABSTRACT: The complexation reactions between diacetyl monooxime (Damo), imidazole (Him), histamine (Hist) and histidine (His) with Co^{2+} , Ni^{2+} and Cu^{2+} were studied potentiometrically in aqueous solution at $25^{\circ}C$ and $\mu = 0.5 M KNO_3$. The overall stability constants $\log \beta$'s of species were obtained by computer refinement of pH-volume data using BEST computer program. Several models were tested and, based on the lowest σ_{FIT} , the best one is accepted. The main species in binary complexes are MAH, MA_2 , MA_2H , MA_2H_2 , (in MA_3 and MA_4 $A = Him$), and for ternary complexes are MAB, MA_2B , MAB_2 and MABH. The $\Delta \log K_{MAB}$ and $\log X_{MAB}$ were calculated for MAB mixed complexes. The order found for the resulting stability constants vary as $Co^{2+} < Ni^{2+} < Cu^{2+}$

KEY WORDS: Potentiometry, Mixed ligand complexes, Imidazole, Histamine, Histidine, Diacetyl monooxime

INTRODUCTION

The chemistry of metalooximes has received considerable attention for many years, mainly because of the use of these complexes for separation and determination of some metal ions, and their usefulness as a model for the elucidation of the mechanism that control the activity of biologically important molecules such as vitamin B_{12} [1-4]. These compounds, specially, α -oxooximes, act as bidentate ligands via carbonyl and oximic nitrogen, forming chelating five-membered rings. In spite of their analytical usefulness, very few studies on complexation equilibria of the metal complexes of this class of reagents have

been carried out. The main drawback to this matter is the extremely low solubility of these compounds in aqueous solutions. There are many reports on the composition and structure of the solid metal complexes of different α -oxooximes [5-7].

A special attention has been paid to the complexation reaction of the imidazole and its derivatives, histamine and histidine mainly due to their importance role in biological systems [8-10]. There are several reports on complexation of binary and mixed complexes of imidazole, imidazole containing molecules and amino acids, with various metal ions

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[11-14]. The reported work on the interaction of serum albumin with zinc and other metal ions has demonstrated that the principal sites on the protein molecules responsible for metal binding are the imidazole group of histidine [14]. The effectiveness of the imidazole group for acting as metal binding site is attributed to its high flexibility, its presence at physiological pH and its capacity to form σ and π bonds with metal ions. The neutral imidazole coordinates via the tertiary nitrogen atom rather than the imino nitrogen of the heterocyclic ring [15,16].

In this investigation, we report on the potentiometric results of the complexation of binary and ternary systems of Him, Hist, His and Damo and Co^{2+} , Ni^{2+} and Cu^{2+} and the overall formation constants of the ternary complexes are being reported.

EXPERIMENTAL

Reagents

The nitrate salts of copper, nickel and cobalt (all from Merck) were used as supplied and the stock solutions were standardized by EDTA in the presence of suitable indicator. HCl, KOH, KCl, Damo, Hist, His and Him (all from Merck) were used without any further purification. Carbonate free KOH solution was standardized with potassium hydrogen phthalate. The HCl solution was standardized with standard KOH. All solutions were prepared in triply distilled deionized water.

Apparatus

Potentiometric titrations were performed by means of a Metrohm 686 Titroprocessor equipped with a 665 Dosimat y (with a 5.0 mL exchange unit), which was connected to a 386 Personal computer for data transfer and calculations. The Titroprocessor was calibrated to read hydrogen ion concentration by titration of hydrochloric acid solution at $25 \pm 0.5^\circ\text{C}$ and $\mu = 0.5$ M KNO_3 with KOH solution according to *Gran's* method [18]. Sample solutions were titrated in a double-walled glass cell maintained at $25 \pm 0.5^\circ\text{C}$ by circulating water and stirred magnetically under a continuous flow of purified nitrogen. Titrations were carried out over the pH range 2.0-10.0, using 50.0 ± 0.01 cm³ samples. In some cases the titration was

stopped in the beginning of precipitation.

Procedure and calculation

The protonation constants of the ligands in the acidic form were determined by titrating 50 mL of aqueous solution of ligand ($\sim 1.4 \times 10^{-2} - 6.0 \times 10^{-3}$) in 0.5 M KNO_3 with KOH 0.015 M solution. The conditions of measurements for the evaluation of the stability constants of binary mixtures were the same as for acidity constants, but in addition to the above mentioned materials, a fraction of KNO_3 was replaced by metal ion solution, so that the desired concentration ratio of ligand to metal ion was obtained. The conditions for the titration of ternary systems were the same as those of the binary systems, except that in this case there are two ligands simultaneously in the presence of metal ion.

The protonation constants of the ligands and formation constants of the resulting complexes were computed from titration data using the *Fortran* programs *PKAS* and *BEST* that are loaded on a Pentium 200 MHz computer [19]. The stoichiometries and formation constants of the resulting complexes were obtained by testing several possible composition models for the system under study. The model selected was that giving the best statistical fit and which was chemically consistent with the titration data. The estimated error for each constant was less than 0.1 log units. The concentration distribution diagram were obtained with the program *SPEPLOT* [19].

RESULTS AND DISCUSSION

Protonation constants

The protonation constants of Damo, Him, Hist and His were obtained under the same conditions of ionic strength and temperature which were applied for the study of binary and mixed systems. The titration data for ligands were obtained and a sample of pH-volume plot is shown in Fig. 1. The maximum number of protons attached to Damo, Him, Hist and His were 1,1,2, and 3, respectively. The overall protonation constants of ligands studied were calculated from computer refinement of the pH-volume data. The obtained values are shown in Table 1 and are in good agreement with previously reported data [13, 21]. The small differen-

Table 1: Stability constants of proton, Co^{2+} , Ni^{2+} and Cu^{2+} with Damo, Him, Hist and His in $M=0.5 M KNO_3$ at $25^\circ C$.

System	m	l	$h^{(a)}$	$\log \beta$		
				This work	Ref. 21	Ref. 22
Co^{2+} -Damo	0	1	1	9.51		
	1	1	0	2.83		
	1	2	0	5.66		
	1	3	0	8.49		
Ni^{2+} -Damo	1	1	0	3.76		
	1	2	0	7.18		
	1	3	0	11.34		
Cu^{2+} -Damo	1	1	0	6.09		
	1	2	0	11.39		
	1	3	0	16.90		
Co^{2+} -Him	0	1	1	7.05	6.95	6.55
	1	1	0	2.53		
	1	2	0	4.45		
	1	3	0	6.25		
Ni^{2+} -Him	1	4	0	8.10		
	1	1	0	3.52		3.37
	1	2	0	5.95		5.70
	1	3	0	8.15		7.90
Cu^{2+} -Him	1	4	0	9.70		9.57
	1	1	0	4.33	4.21	
	1	2	0	7.70	7.55	
	1	3	0	10.69	10.73	
Co^{2+} -Hist	1	4	0	12.95	12.91	
	0	1	1	9.93	9.39	
	0	1	2	16.20	15.34	
	1	1	0	5.56		
Ni^{2+} -Hist	1	2	0	9.83		
	1	1	1	12.08		
	1	2	1	17.22		
	1	1	0	7.01		6.36
Cu^{2+} -Hist	1	2	0	12.62		11.22
	1	1	1	12.10		11.85
	1	1	0	9.73	9.24	
	1	2	0	16.78	16.16	
Co^{2+} -His	1	2	1	22.40	21.82	
	0	1	1	9.22	8.96	
	0	1	2	15.44	14.96	
	0	1	3	17.24	17.37	
Ni^{2+} -His	1	1	0	7.05		
	1	2	0	12.74		
	1	1	1	12.27		
	1	1	0	8.60		8.84
Cu^{2+} -His	1	2	0	15.98		15.94
	1	1	1	13.04		13.08
	1	2	1	20.89		21.04
	1	1	0	10.30	10.27	
Cu^{2+} -His	1	2	0	18.53	18.49	
	1	1	1	14.78	14.38	
	1	2	1	23.87	23.89	
	1	2	2	27.97	27.81	

a) m , l and h are stoichiometric coefficients of M^{2+} , Ligand and H^+ respectively.

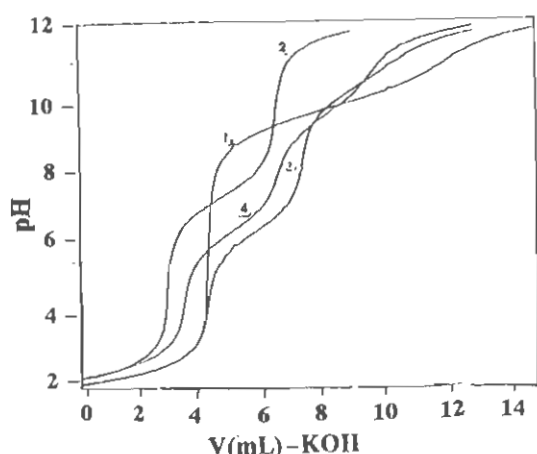


Fig. 1: Equilibrium pH titration curves of ligands: 1(Damo); 2 (Him); 3(His) and 4(Hist).

ces are within the limits of experimental errors or due to difference in experimental conditions (i.e. difference in ionic strength and temperature).

Binary complex formation equilibria

The formation constants of Co^{2+} , Ni^{2+} and Cu^{2+} with Damo, Him, Hist and His binary complexes were determined under conditions identical to those of ternary systems, values are given in Table 1 which show good agreement with the reported values [13, 21], after allowing for changes in experimental conditions as well as in methods of calculations.

M^{2+} - A binary systems (A= Damo)

In the Co^{2+} -Damo system the computer refinement of the titration data showed the presence of CoA , CoA_2 and CoA_3 species. The detectable species in Ni^{2+} and Cu^{2+} Damo are MA , MA_2 and MA_3 species. Since Damo is a bidentate (carbonyl and oximic nitrogen [3]) ligand, it is expected to form a five-membered chelate ring with metal ions. The $\log \beta_1$ of M^{2+} -Damo were found to be 2.83, 3.76 and 6.09 for Co^{2+} , Ni^{2+} and Cu^{2+} , respectively, which is confirmed by the above conclusion. Izquierdo et al. [2] reported the polynuclear complexes between some α -oxoimines with Ni^{2+} and Cu^{2+} , but in the present work no polynuclear species was observed.

Co^{2+} - B binary systems (B= Him, Hist and His)

In the Co^{2+} -Him binary system in addition to BH,

the CoB , CoB_2 , CoB_3 and CoB_4 species were also detected. The types of species in Co^{2+} -His system are CoB , CoB_2 and CoBH , in addition to BH, BH_2 and BH_3 . For Co^{2+} -Hist system the CoB , CoB_2 , CoB_2H , and CoBH species, in addition to protonated ligand were obtained. The resulting formation constants of Co^{2+} -B's systems are shown in Table 1.

Ni^{2+} - B binary systems (B= Him, Hist and His)

In the Ni^{2+} -Him system the species NiB , NiB_2 , NiB_3 and NiB_4 together with BH are remained in the final refined model. As reported by Nair et al. [12] the stepwise stability constants of Ni^{2+} -Him complexes decrease from NiB to NiB_4 . This is due to the fact that the first Him is strongly bonded to Ni^{2+} and thus decreases the tendency of the remained metal sites to bind the other three ligands. In the Ni^{2+} -His system the species of the types NiB , NiB_2 , NiBH and NiB_2H , and also BH, BH_2 and BH_3 were detected. These species were also reported by Nair et al. [12]. The Ni^{2+} -Hist system formed NiB , NiB_2 and NiBH , in addition to BH and BH_2 . The resulting formation constants of these species are listed in Table 2.

Cu^{2+} - B binary systems (B= Him, Hist and His)

The copper formed the most stable complexes amongst the metal ions with the titled ligands. The species CuB , CuB_2 , CuB_3 and CuB_4 are formed between Him and Cu^{2+} . His formed the CuB , CuB_2 and CuB_2H species. The CuBH was introduced in the initial input model but was rejected in the final refinement. For His, the CuB , CuB_2 , CuBH , CuB_2H and CuB_2H_2 species are observed. The species detected in this study, more or less (depending on experimental conditions) resemble those of previously observed ones [11, 21]. The overall stability constants for all of the above species are also included in Table 1.

Ternary complex formation equilibria

In contrast with the stability of the binary complexes, the relative stability of the ternary ones, can be expressed in several ways. The most common method is the calculation of $\Delta \log K$, that is the difference in stabilities for the addition of ligand B to the 1:1 MA complex and to the solvated metal ion as shown by Eq. (1).

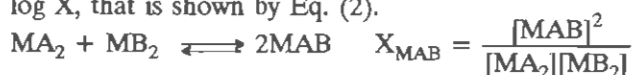
Table 2: Stability constants of ternary systems M^{2+} -Damo (A)-Him, Hist and His(B)

System	m	l_1	l_2	$h^{(a)}$	$\log \beta$	$\Delta \log K$	lig X
Co^{2+} -Damo-Him	1	1	1	0	5.60	0.24	1.09
	1	2	1	0	7.48		
	1	2	2	0	12.74		
Co^{2+} -Damo-Hist	1	1	1	0	8.33	-0.06	1.17
	1	1	2	0	11.26		
	1	1	1	1	18.26		
Ni^{2+} -Damo-Him	1	1	1	0	6.83	-0.45	0.53
	1	1	2	0	10.25		
	1	2	2	0	14.10		
Ni^{2+} -Damo-Hist	1	1	1	0	10.46	-0.31	1.12
	1	1	2	0	15.13		
	1	2	1	0	16.55		
Ni^{2+} -Damo-His	1	1	1	0	13.31	0.95	3.46
	1	2	1	0	14.10		
	1	1	1	1	19.62		
Cu^{2+} -Damo-Him	1	1	1	0	10.53	0.11	1.97
	1	1	2	0	13.91		
	1	2	2	0	18.09		
Cu^{2+} -Damo-Hist	1	1	1	0	15.33	-0.49	2.49
	1	1	2	0	20.75		
	1	2	1	0	19.14		
Cu^{2+} -Damo-His	1	1	1	0	15.69	-0.70	1.46
	1	1	1	1	20.31		

a) m, l_1 , l_2 and h are stoichiometric coefficients of M^{2+} , Ligand (A), Ligand (B) and H^+ respectively.

$$\Delta \log K = \log K_{MAB}^{MA} - \log K_{MA}^M = \log K_{MBA}^{MB} - \log K_{MB}^M \quad (1)$$

Another parameter generally used for indicating the stabilization of the ternary complexes relative to the binary ones, is the disproportionation constant, log X, that is shown by Eq. (2).



$$\log X_{MAB} = 2\log \beta_{MAB} - (\log \beta_{MA_2} + \log \beta_{MB_2}) \quad (2)$$

On the statistical calculations [22], the positive log X values indicate the remarkable stability of the mixed complexes over the binary complexes.

Co^{2+} - Damo (A)-Him, Hist and His(B) ternary systems

Various types of ternary species were observed for these systems. The MAB, MA_2B and MA_2B_2 species were detected for Co^{2+} -Damo-Him system. It is important to pay a special attention to MA_2B_2 species that have an octahedral structure. Two Damo ligands have

a square planar configuration around metal ion [1], and two Him ligands approached the metal ion from axial position. The species MAB, MAB_2 and MABH were detected for Co^{2+} -Damo(A)-Hist(B) and Co^{2+} -Damo(A)-His(B), respectively.

The $\Delta \log K$ values obtained for MAB species in the Co^{2+} -Damo(A)-Him, Hist and His(B) systems; are more positive than their corresponding statistical values [22,23]. This is indicative of the preferential formation of ternary complexes relative to binary parent complexes. The values of log X for mixed systems of Co^{2+} -Damo(A)-Him, Hist and His(B) show this trend as illustrated in Table 2.

Ni^{2+} - Damo(A)-Him, Hist and His(B) ternary systems

The Ni^{2+} -Damo(A)-Him(B) showed the presence of three ternary species MAB, MAB_2 and MA_2B_2 . The species formed for Ni^{2+} -Damo(A)-Hist(B) are MAB, MAB_2 and MA_2B and for Ni^{2+} -Damo(A)-

His(B) they are MAB, MA₂B and MABH. The overall stability constants obtained from refinement of potentiometric data and $\Delta \log K$ and $\log X$ are shown in Table 2. The species MA₂B₂ are also observed for this system. As it is expected, from Irving-Williams order [24], the overall stability constants of Ni²⁺-A-B's systems are greater than Co²⁺-A-B's system.

Cu²⁺ - Damo(A)-Him, Hist and His(B) ternary systems

The species detected for Cu²⁺-Damo(A)-Him, Hist and His(B)'s systems are MAB, MAB₂, MA₂B₂; MAB, MAB₂, MA₂B; and MAB, MABH respectively. The stability constants and statistical information of the above species are listed in Table 2. The only detectable protonated complex of ternary system is M²⁺-Damo(A)-His(B), which could be predicted from structure of His ligand (His is a terbasic ligand with -NH₂, =N- and COOH group). The extra proton in CuABH resides on the primary amino group of His. This can be inferred from comparison of the parent metal and proton stability constants of involved species in CuABH system. In order to characterize this, $\log P$ and $\log P'$ were calculated by Eqs. (3) and (4).

$$\log P = \log \beta_{CuBH} - \log \beta_{BH} \quad (3)$$

$$\log P' = \log \beta_{CuABH} - (\log \beta_{BH} - \log \beta_{CuA}) \quad (4)$$

The obtained values for $\log P$ and $\log P'$, 5.56 and 5.0, are comparable and indicate that in both complexes the extra proton reside on the same position of the His ligand. The same arguments were also given by Nair et al. on the protonated complexes of copper-histidine systems [21].

The stability of Cu²⁺-A-B's species in some cases are 2-3 log units greater than the same species in Co²⁺ and Ni²⁺ ternary systems. This complies well with the Irving-William's [24] order for stability of transition metal complexes.

Distribution diagram plots

The concentration distribution diagrams of all binary and mixed systems were obtained in terms of percent metal ions as a pH function. The sample concentration distribution diagram plots of M²⁺-A-B's systems in which M²⁺ = Cu²⁺, A = Damo and B =

Him, Hist and His are shown in Figs. 2-4, respectively. In some cases, the concentration of mixed species rise up 60%. Among the mixed species, the MAB in Hist and His has more concentration than the other mixed species and as far as Him is concerned, the MA₂B₂ has marked priority over other mixed species. As can be seen from distribution plots, the formation of most species are condensed within the 6-9 pH range, which corresponds to physiological pH.

It is interesting to note that, the percent of species obtained for mixed components is by far higher than those expected from statistical inferences. This also shows the higher stability of the mixed species over parent binary ones.

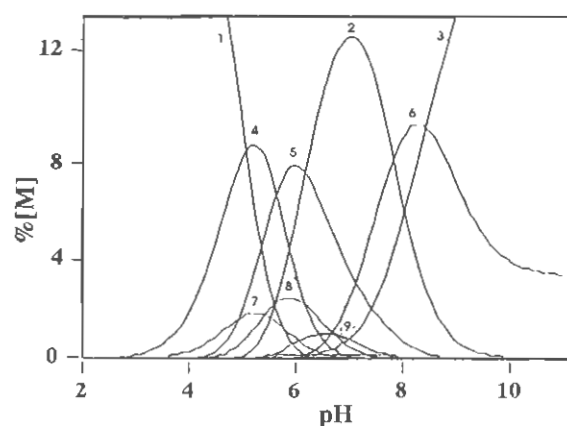


Fig. 2: The species diagrams of Cu²⁺-Damo(A)-Him(B) at concentration ratio of 4.4:1:1; 1(M); 2(MAB₂); 3(MA₃); 4(MB); 5 (MAB); 6(MA₂B₂); 7(MA); 8(MB₂); 9(MA₂).

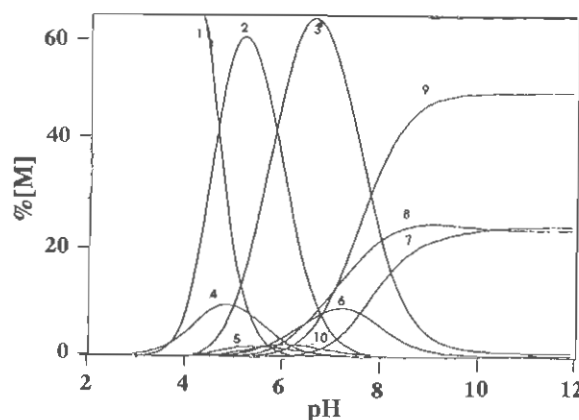


Fig. 3: The species diagrams of Cu²⁺-Damo(A)-Hist(B) at concentration ratio of 4.5:1:1; 1(M); 2(MB); 3(MAB); 4(MA₃); 5 (MB₂H); 6(MB₂); 7(MAB₂); 8(MA₃); 9(MA₂B); 10(MA).

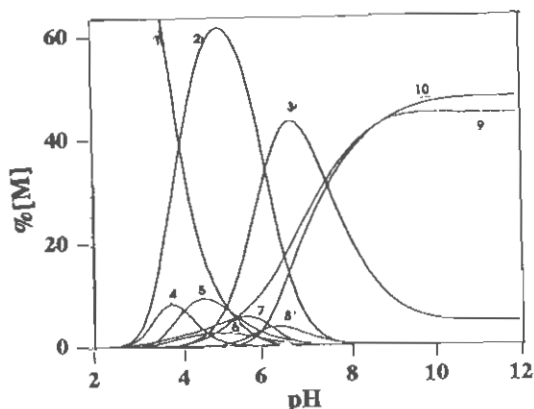


Fig. 4: The species diagrams of Cu^{2+} -Damo(A)-His(B) at concentration ratio of 4.4:1:1; 1(M); 2(MB); 3(MAB); 4(MB_2H_2); 5(MB_2H); 6(MABH); 7(MA); 8(MA_2); 9(MB_2); 10(MA_3).

From the comparison of Figs. 2 and 3, it can be concluded that the percent of MAB species in Cu^{2+} -Damo(A)-His(B) system is higher than Cu^{2+} -Damo(A)-His(B). From Table 2, it may be deduced that an increase in stability of binary systems causes a decrease in the stability of ternary systems and vice versa.

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