

Chemical Modelling Studies On The Interaction Of Phenyl Acetic Acid Hydrazide And α -Alanine With Divalent Transition Metal Ion

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Abstract: Chemical modeling studies on the ternary systems of Ni(II) with Phenyl acetic acid hydrazide and α -alanine were carried out potentiometrically in aqueous medium using Calvin-Wilson titration technique and the data was analyzed using Miniquad-75 program. Phenyl acetic acid hydrazide was found to act as a bidentate ligand bonding through carbonyl oxygen and terminal nitrogen. In the presence of α -alanine this resulted in the formation of a variety of mixed ligand species of the type $MLXH$, MLX , $MLXH_{-1}$, ML_2XH , ML_2X , ML_2XH_{-1} , ML_2XH_{-2} , MLX_2H_2 , MLX_2H , MLX_2 and MLX_2H_{-1} where, $M = Ni(II)$ $L =$ Phenyl acetic acid hydrazide and $XH = \alpha$ -alanine. These ternary species were found to be more stable than the corresponding binary complexes.

Keywords: Binary complexes, chemical modeling, potentiometric studies, speciation, ternary system.

I. Introduction

Many reactions of biological importance involve the intermediate formation of mixed-ligand species, in which a metal ion is simultaneously bound to two or more ligands. The specificity and selectivity of the vital enzymatic reactions have been attributed to the formation of such a type of ternary species. In order to understand the effect of complexation on these biologically important reactions, one must know the actual form of the species formed in the biological fluids. Therefore, the speciation studies, which throw light on the actual form of a particular substance in solution have been received much attention in recent years. Acid Hydrazides belong to a group of nitrogenous organic compounds that find extensive applications in chemical analysis, industry, agriculture and chemotherapy. As a result of their antimicrobial, antifungal and antibacterial properties [1-3], acid hydrazides are of great biological importance. The formation of metal complexes plays an important role in the enhancement of their biological activity [4-8]. Dihydrazide coated tablets are used to obtain an intentional late-burst release of the drug [9]. In view of the important factors connected to the formation of mixed ligand complexes in solution, the authors have taken up a study on the interaction of Phenyl acetic acid hydrazide and α -alanine with divalent transition metal ions. These systems can serve as useful models for a better understanding of naturally occurring phenomenon.

II. Experimental

Reagents: All inorganic chemicals (BDH) were of analytical reagent grade and were used without further purification. Phenyl acetic acid hydrazide (Fluka) was prepared freshly in dimethylformamide (DMF) just before the titrations as it is not soluble in water. Apparatus: The pH-metric titrations were carried out with a Control Dynamics pH meter model APX 175 E/C in conjunction with a 0-14 pH range glass electrode and a calomel electrode.

A tip less double walled Pyrex glass vessel of 100 ml capacity fitted with a Perspex lid, through which the electrodes, gas inlet and outlet tubes and burette tip were admitted, was used for carrying out the potentiometric titrations. The temperature of the solution was maintained by passing water from a thermostat through the annular space between the walls of the titration cell. The experimental solution was earthed by means of a platinum wire sealed in a glass tube. In order to prevent the introduction of an earth loop, the pH meter, thermostat and magnetic stirrer were earthed to the same terminal. Purified nitrogen gas was passed through the experimental solution both before and during titration to expel carbon dioxide.

III. Data Acquisition And Analysis

Requisite volumes of hydrochloric acid (to give an overall concentration of 2.0×10^{-2} mole.dm⁻³), sodium chloride (ionic strength was maintained at 0.1 mole.dm⁻³) and water in the presence and absence of metal ions and ligands in a total volume of 50 cm³ was titrated with ~ 0.2 mole.dm⁻³ sodium hydroxide. A number of titrations were performed with different concentration ratios of metal ion, hydrazide and amino acid. In all the titrations freshly prepared solutions of hydrazide and amino acid were employed. The data from

different experiments with different metal to ligand ratios were refined separately using Miniquad-75 program[10], to yield species relevant to that particular composition. This method has been found to be superior[11] compared to the analysis of the entire data from all the titrations at a time, as the main part of the error in the stability constants derives from the variability from one titration to another. Therefore, the authors processed the data from the different compositions separately using Miniquad-75 program.

IV. Results And Discussion

Knowledge on the distribution of various protonated species of the ligands and the binary species is an essential prerequisite in order to understand the various interactions that exist in a solution containing a metal ion and several ligands. Therefore, as a prelude to the determination of formation constants of metal-ligand and mixed -ligand complexes, the author has taken up a study on the protonation equilibria and metal-ligand systems of both Phenyl acetic acid hydrazide (PAAH) and α -alanine under the present experimental conditions. The results of analysis are presented in table 1.

The best-fit models of the Phenyl acetic acid hydrazide contain only one protonation constant corresponding to the protonation at the terminal nitrogen atom. In high alkaline conditions aroyl hydrazines are known to lose a proton[12] (fig.1) from the enolic form. In the case of PAAH, this type of dissociation leading to the formation of LH_1 species, is well above the pH region of study as there is no indication of the deviation of ligand titration curve from that of free acid above equivalence point. However, in the presence of a metal ion this ligand may lose this enolic proton forming MLH_1 , ML_2H_1 , and ML_2H_2 type of species.

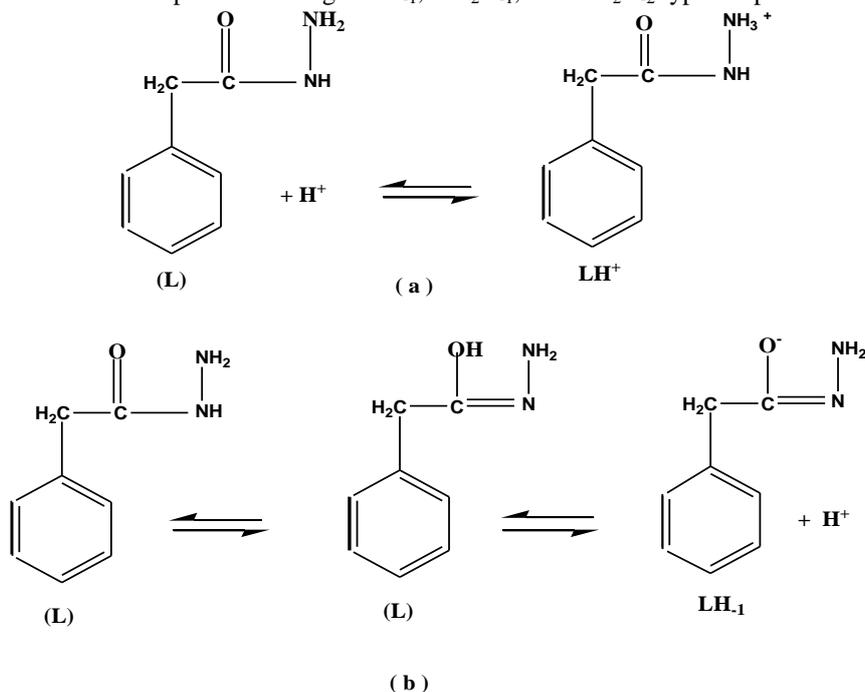


Fig.1

Fig.2.3: PROTON-LIGAND EQUILIBRIA OF PAAH

The best-fit models for metal ion-PAAH systems (table 1) indicate the formation of such species for Ni(II) system. The species ML , MLH_1 , MLH_2 , ML_2 and MLH_2 (fig. 2) contain metal ion bonded to ligand and enolic form of ligand.

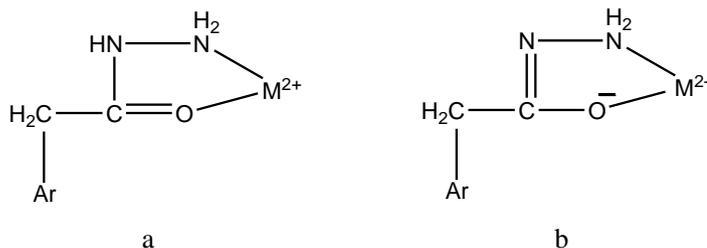
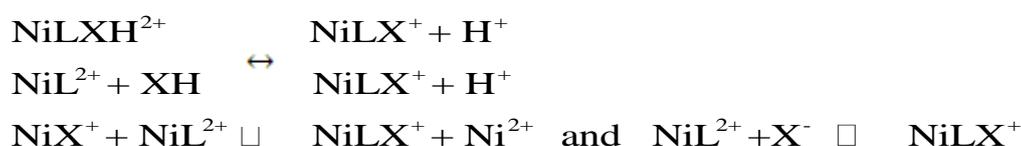


Fig.2 Metal complexes, ML and MLH_1 of Hydrazides

The deviations of experimental titration curves from that of simulated, assuming the formation of only simple complexes suggest the formation of other species. Therefore, the presence of all the plausible species including mono, bis, protonated and hydroxylated species were tested and the best-fit models obtained for all these amino acids in 30 % DMF were included in table 1. These models indicate the formation of ML, ML₂H, ML₂ and MLH₁ in addition to simple mono-nuclear complexes. Therefore, it is evident that all the metal ions interacted with the ligand both in the mono-dentate and bidentate forms, leading to the formation of various protonated species in addition to simple complexes. The sum of squares of residuals in mass balance equations 'U', χ^2 and R are well within the range allowed. The species distribution diagrams for all the systems were depicted in figs.4 to 6.

4.1 Metal Ion-PAAH- A-Alanine Systems

The best-fit model for 1:1:1 solution (table 1) indicates the formation of NiLXH, NiLX and NiLXH₁ species in addition to simple complexes. From the magnitude of the formation constant of the species NiLXH, it is clearly evident that the zwitter ion form of the alanine is involved in bonding. This species exists in solution in the pH range 2.0 to 7.5 with a (fig. 4) broad maximum centered on ~ 4.2 pH. The formation of NiLX species started at ~4.0 pH and reached a maximum of 77.1 % at 7.5 pH. The formation of deprotonated NiLXH₁ species started at ~7.0 pH and reached a maximum of 90.3 % in the pH region of study. The formation of NiLX species may be considered to be due to the following equilibria,



In 1:2:1 solution, seven mixed ligand species viz., NiLXH, NiLX, NiLXH₁, NiL₂XH, NiL₂X, NiL₂XH₁ and NiL₂XH₂ were observed (table 1) in addition to simple binary species. The pH range of formation of the species NiL₂XH (fig. 5) indicates that the alanine in zwitter ion form, bonding through -COO⁻ group is involved in complex formation.

The best-fit model for 1:1:2 solution (table 1) indicates the formation of NiLXH, NiLX, NiLXH₁, NiLX₂H₂, NiLX₂H, NiLX₂ and NiLX₂H₁ mixed ligand species. The deprotonated species may be due to the involvement of enolic form PAAH in bonding or due to hydroxylation of the species. In all other species, PAAH acts as a bidentate ligand bonding through carbonyl oxygen and terminal nitrogen, whereas, alanine is bonded to the metal ion both in bidentate(X) and monodentate(XH) forms.

In all the cases the experimental titration curves differed from the simulated ones indicating the presence of mixed ligand species. The data was subjected to analysis by Miniquad-75 program. The results of the analysis indicated the presence of MLXH, MLX, MLXH₁ in 1:1:1 solutions, ML₂XH, ML₂X, ML₂XH₁, ML₂XH₂ in 1:2:1 solutions and MLX₂H₂, MLX₂H, MLX₂, MLX₂H₁ in 1:1:2 solutions. The distribution diagrams indicate the formation of all these species in considerable amounts.

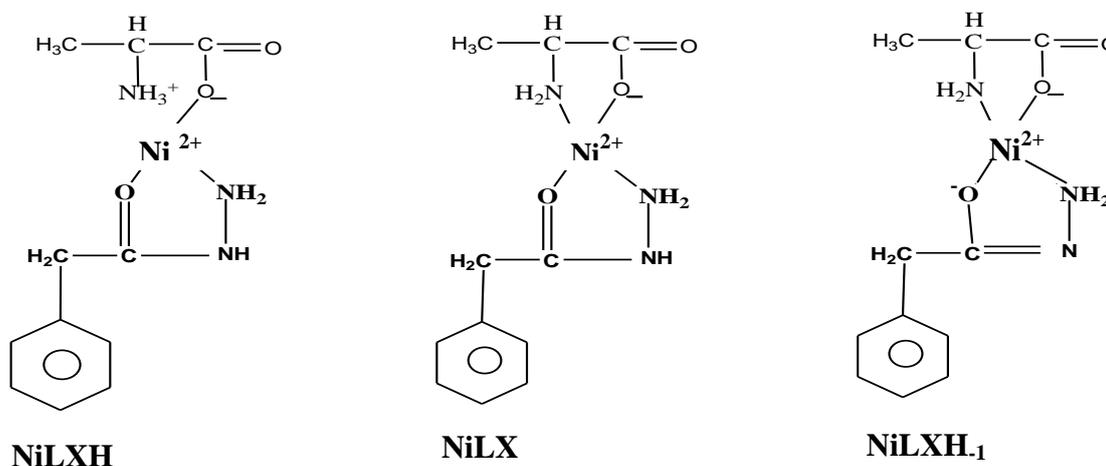
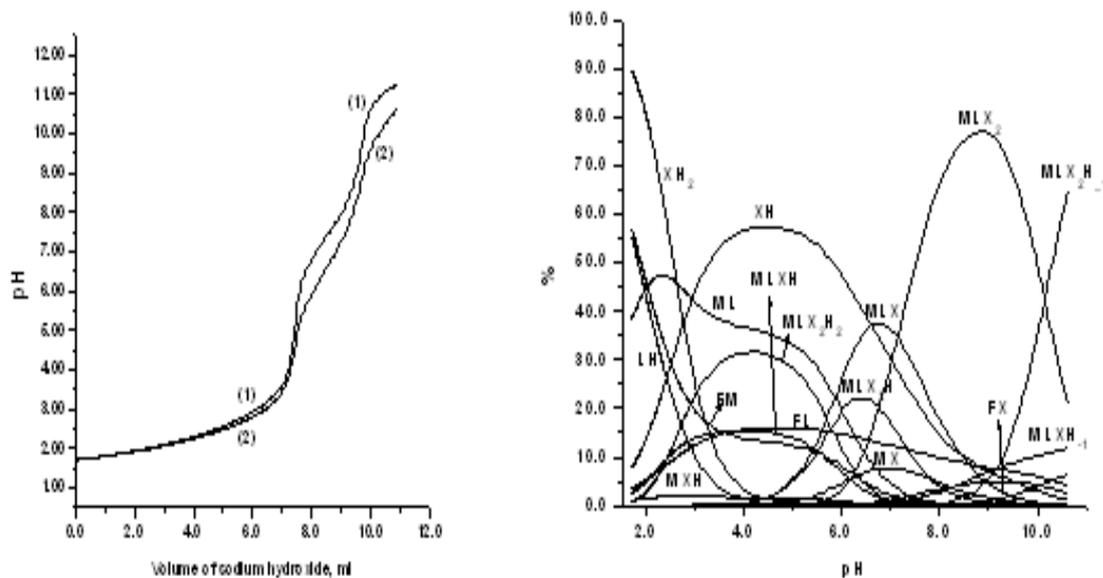


Fig.3 Ni-PAAH and Alanine Structures



a. 1. Simulated titration curve
2. Experimental titration curve

b. Species distribution diagram

[PAAH]=.00500 mole dm⁻³ [ALANINE]= .0100 mole dm⁻³ [Ni²⁺] = .00493 mole dm⁻³
 [HCl] =.03151 mole dm⁻³ [NaOH] = .21270 mole dm⁻³ TOTAL VOLUME=50.0 cm³
 Temp.: 30.0 ±0.1°C μ = 0.1M

Fig. 6 Ni (II)-PAAH-ALANINE SYSTEM (1:1:2)

Table: 1
Best-Fit Models For Nickel(II)-Paah-Alanine Systems In 30% Aquo-Dmf Solution

Metal ion	Composition (M:L:X)	Species mlxh	log β _{mixh}	
Ni ²⁺	1:1:1	0101	2.904	U/NP = 2.741 X 10 ⁻⁸
		0011	9.880	χ ² = 19.03
		0012	12.639	R =0.00632
		1100	3.590	Skewness= 1.56
		1010	6.026	Kurtosis=9.63
		1011	11.262	
		1111	15.398 (29)	
		1110	9.984 (20)	
		111-1	1.187 (30)	
	1:2:1	1200	6.214	U/NP = 2.348 X 10 ⁻⁸
		120-2	-9.082	χ ² = 5.51
		1211	17.662 (6)	R =-0.00967
		1210	12.387 (11)	Skewness= -0.10
		121-1	3.924(7)	Kurtosis=7.32
		121-2	-3.216(11)	
	1:1:2	1020	10.676	U/NP = 2.112X 10 ⁻⁸
		1122	27.899 (16)	χ ² = 10.24
		1121	22.124(14)	R =-0.00101
		1120	15.359(11)	Skewness= 0.05
		112-1	5.212(14)	Kurtosis=7.33

*Figures in the parentheses are the standard deviations in the least significant digit.

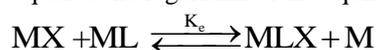
The slight deviation between the calculated and experimental titration curves (figs. 4, 5 and 6 respectively for 1:1:1, 1:2:1 and 1:1:2 compositions) in the lower pH region of Ni(II)-PAAH-alanine systems indicate the presence of protonated ternary species. The large deviation above ~6.0 pH indicates the presence of simple and deprotonated species.

The best-fit models obtained after refinement are presented in table 1. The species that are converged include NiLXH, NiLX, NiLXH₋₁, NiL₂XH, NiL₂X, NiL₂XH₋₁, NiL₂XH₋₂, NiLX₂H₂, NiLX₂H, NiLX₂ and NiLX₂H₋₁ in addition to proton-ligand and binary species.

The relative stability of a mixed ligand complex in comparison with its parent binary complexes is best quantified [13,14] by considering Δ log K obtained using the equation,

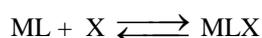
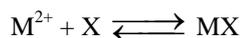
$$\Delta \log K = \log \beta_{ML_iX_x} - (\log \beta_{ML_i} + \log \beta_{MX_x})$$

The difference, Δ log K, is also equal to the logarithm of the equilibrium constant of the equilibrium,



$$\Delta \log K = \log K_e = \log \frac{[MLX].[M]}{[MX].[ML]}$$

In this formulation, the stabilities of reactions between ligand "X" and aqua metal ion and ligand,"X" and ML are compared.



Since more coordination positions are available on the aquo metal ion in comparison with 'ML' the first reaction is statistically more probable in comparison with the second one, leading to -ve values of Δ log K. This is normally observed in simple binary systems where log K₁ is always greater than log K₂. On the contrary in the case of mixed -ligand complexes for certain combination of ligands log K is found to be +ve or greater than the statistically expected value indicating the tendency towards mixed ligand complex formation. This formulation can be extended to the formation of multi-metal species. The Δ log K values obtained are shown in tables 2,3,4 and 5.

Table: 2
ΔLog K And Log X Values For The Fomation Of Mlx Species

Metal Ion-Paah-Alanine Systems:(A)

Metal ion	log β ₁₁₀₀ (A)	log β ₁₀₁₀ (B)	C = A+B	log β ₁₁₁₀ (D)	Δlog K = D-C
Ni ²⁺	3.590	6.026	9.616	9.984	0.368

(b)

Metal ion	log β ₁₂₀₀ (A)	log β ₁₀₂₀ (B)	C = A+B	log β ₁₁₁₀ (D)	log X = 2D-C
Ni ²⁺	6.214	10.676	16.890	9.984	3.078

Table-3
ΔLog K And Log X Values For The Fomation Of Mlxh And Ml₂xh Species
Metal Ion-Paah-Alanine Systems:

(A)

Metal ion	log β ₁₁₀₀ (A)	log β ₁₀₁₁ (B)	C = A+B	log β ₁₁₁₁ (D)	Δlog K = D-C
Ni ²⁺	3.590	11.262	14.852	15.398	0.546

(b)

Metal ion	log β ₁₂₀₀ (A)	log β ₁₀₁₁ (B)	C = A+B	log β ₁₂₁₁ (D)	Δlog K = D-C
Ni ²⁺	6.214	11.262	17.476	17.662	0.186

Table-4

**ΔLog K And Log X Values For The Fomation Of Ml₂x And Mlx₂ Species
Metal Ion-Paah-Alanine Systems:**

(a)

Metal ion	log β ₁₂₀₀ (A)	log β ₁₀₁₀ (B)	C = A+B	log β ₁₂₁₀ (D)	Δlog K = D-C
Ni ²⁺	6.214	6.026	12.240	12.387	0.147

(b)

Metal ion	log β ₁₁₀₀ (A)	log β ₁₀₂₀ (B)	C = A+B	log β ₁₁₂₀ (D)	ΔlogK= D-C
Ni ²⁺	3.590	10.676	14.266	15.359	1.093

Table: 5

ΔLogk Values For The Formation Of Deprotonated Species

(a) Ml₂xh-2 Species

Metal ion	Ligand1 (L)	Ligand 2 (XH)	log β ₁₂₀₋₂ (A)	log β ₁₀₁₀ (B)	C = A+B	log β ₁₂₁₋₂ (D)	Δlog K=D-C
Ni ²⁺	PAAH	alanine	-9.082	6.026	-3.056	-3.216	-0.160

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