

Studies on Nickel(II)-Pyridoxamine-Imidazole Containing Mixed Ligand Complex Systems

Neelakantan, M.A.[†]*

Department of Chemistry, National Engineering College, K.R Nagar, Kovilpatti – 628 503, Tamil Nadu, INDIA

Sivasankaran Nair, M.

Department of Chemistry, Manonmaniam Sundaranar University, Abhishekapatti, Tirunelveli – 627 012, Tamil Nadu, INDIA

ABSTRACT: *The stability constants of species present in the systems Ni(II)-pyridoxamine(pym)(A) and Ni(II)-pyridoxamine(pym)(A)-imidazole containing ligands(B) [B = imidazole(him), benzimidazole(bim), histamine(hist) and L-histidine(his)] have been determined pH-metrically using the MINQUAD computer program. The existence of the species NiAH, NiA and NiA₂ was proven for the Ni(II)-pym(A) system, whereas for the Ni(II)-pym(A)-B systems NiABH₂, NiABH, NiAB and NiAB₂ species were identified. The pym ligand(A) binds the metal ion via its phenolic oxygen and amino methyl nitrogen atoms in the NiAB and NiAB₂ species, and the binding of ligand B in these complexes is similar to their binding in the respective binary species. The site of protonation in NiABH and NiABH₂ species is explained. A more positive $\Delta \log K$ values for NiAB compared to NiAB₂ species is discussed. The computer simulated distribution of the complexes in solution has been evaluated. The mixed ligand pyridoxamine complex of Ni(II) with L-histidine was prepared and characterized by conventional methods.*

KEY WORDS: *Mixed ligand complex, Stability constant, Speciation, Pyridoxamine, Imidazole containing ligands.*

INTRODUCTION

For a long time it has been shown that metal ions play an important role in biological systems, as exemplified by many instances in which enzymes are known to be activated by metal ions [1]. Vitamin B-6 exists in the forms pyridoxal, pyridoxine and pyridoxamine. The coenzyme pyridoxamine 5'-phosphate plays a vital role in the function of a number of enzymes

that catalyze essential chemical reactions in the human body. About 70-80% of the vitamin B-6 in the body is located in muscle, bound to glycogen phosphorylase, an enzyme involved in releasing glucose from glycogen. Vitamin B-6 is one of the most versatile enzyme cofactors involved in breaking more types of chemical bonds and also in so many aspects of

* To whom correspondence should be addressed.

+ E-mail: maneels@rediffmail.com

1021-9986/04/1/97

7/\$/2.7

metabolism [2]. Hence mode of coordination of pyridoxamine with nickel(II) in presence of other ligands becomes important. Imidazole nitrogen donor atoms of histidyl residues are the most common binding sites in various metalloenzymes [3]. Therefore ligands containing imidazole rings can potentially mimic the binding sites and catalytic activities of the enzymes.

In order to understand fully the mixed ligand complexes involving enzymes and proteins, our laboratories have been investigating the mixed ligand complexes of amino acids, peptides and antibiotics for some time [4-8]. In the present investigation we have made a detailed study with regard to the mode of binding of the pyridoxamine(A) with Ni(II), and with Ni(II) in the presence of imidazole containing ligands, imidazole(him), benzimidazole(bim), histamine(hist) and L-histidine(his) in aqueous solution at 37 °C and $I = 0.15 \text{ mol dm}^{-3} (\text{NaClO}_4)$, using pH metric method.

EXPERIMENTAL

All the ligands used in this work were obtained from Fluka AG, Buchs, Switzerland. The hist ligand used was in the diprotonated form. Nickel perchlorate and other solutions were prepared as described earlier [5-7]. The pH titrations were carried out at 37 °C and $I = 0.15 \text{ mol dm}^{-3}$ under nitrogen with a digital pH meter (accuracy of $\pm 0.01 \text{ pH}$ unit) as described earlier [4-8]. All solutions were prepared with double distilled water using grade A glassware. The stability constants for the ternary complex systems were refined by MINIQUAD 75 computer program [9] on a HCL Magnum II 68030 twin processor minicomputer fixing the binary stability constants (Table 1) as non-refinable parameters.

Synthesis of Ni(II)-pym(A)-his(B) mixed ligand complex

The green powder of $[\text{Ni}(\text{pym})(\text{his})\cdot\text{H}_2\text{O}]$ was separated from its very concentrated solution. This solution was obtained by mixing 20 cm^3 aqueous solution of $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ (0.498g, 2 mmol) and 20 cm^3 aqueous solution of pym (0.336g, 2 mmol), then 20 cm^3 aqueous solution of his (0.31g, 2 mmol) was slowly added. The pH of the resultant solution was adjusted with NaOH to 7.5. The resulting solution was constantly stirred for 12 hours. The

complex was isolated after 2 weeks standing at room temperature. The nickel content was estimated gravimetrically by the dimethylglyoxamime method. (Found: Ni, 14.56; C, 42.06; H, 5.84; N, 17.45, $\text{Ni}(\text{C}_{14}\text{H}_{21}\text{N}_5\text{O}_4)\cdot\text{H}_2\text{O}$ requires Ni, 14.67; C, 42.03; H, 5.79; N, 17.51).

RESULTS AND DISCUSSION

Ni(II)-pym(A) systems

In the Ni(II)-pym(A) system NiAH, NiA and NiA₂ species were identified. The compounds of vitamin B-6 can act either as unidentate ligand and bind the metal ion through the heterocyclic nitrogen or as a bidentate ligand and chelate the metal ion through the phenolic oxygen and the nitrogen or oxygen at one of the adjacent group in the 4 - position [10,11]. The $\log \beta_{\text{NiA}}$ value of 6.58 in Ni(II)-pym(A) demonstrates pym binds the metal in a bidentate manner. As the aminomethyl in pym is more basic than hydroxymethyl group, pym binds the metal via its phenolic oxygen and amino methyl nitrogen atoms forming a 6 - membered chelate ring. This type of coordination is considered in Cu(II)/Zn(II)/Cd(II)-pym(A) and dimethyl tin-pym(A) complex systems [11,12]. The $\log K_{\text{NiA}}^{\text{NiA}}$ value of 4.73 in Ni(II)-pym(A) indicates the bidentate binding of both pym(A) in NiA₂ species(Struct.1). The $\log \beta_{\text{NiAH}}$ value of 7.37 in the Ni(II)-pym(A) complex follows the trend of pK_a value for the amino group of free pym. This indicates that the amino group of pym is protonated, and binds the metal ion via phenolic OH in the NiAH species.

Ni(II)-pym(A)-him, bim, hist and his (B) systems

In the Ni(II)-pym(A)-bim(B) system, NiAB and NiAB₂ species have been identified, while in the Ni(II)-pym(A)-him(B) system, NiABH in addition to the above species were identified. The NiABH₂, NiABH and NiAB species have been detected in Ni(II)-pym(A)-hist and his(B) systems.

Stability and structure of NiAB and NiAB₂ species

The ligand pym(A) binds Ni(II) in a bidentate manner via its phenolic oxygen and aminomethyl nitrogen. The $\log K_{\text{NiAB}}^{\text{NiB}} / \log K_{\text{NiAB}_2}^{\text{NiB}_2}$ values obtained

Table 1: Stability constants for the proton and parent binary complexes of Ni(II) with pym(A), him, bim, hist, and his(B) at 37 °C and I = 0.15 mol dm⁻³ (NaClO₄).

Parameter	Ligand B				
	Pym	him ^a	bim ^b	hist ^a	his ^a
log β _{HB}	10.48(1)	6.55(2)	5.68(1)	9.39(8)	8.96(3)
log β _{H₂B}	18.52(5)	----	----	15.34(1)	14.96(5)
log β _{H₃B}	22.01(9)	----	----	----	17.37(9)
log β _{NiBH}	13.95(6)	----	----	11.85(3)	13.08(5)
log β _{NiB}	6.58(4)	3.37(5)	2.37(4)	6.36(2)	8.84(7)
log β _{NiB₂H}	----	----	----	17.86(4)	21.04(7)
log β _{NiB₂}	11.31(8)	5.70(9)	4.11(9)	11.22(2)	15.94(4)
log β _{NiB₃}	----	7.90(9)	----	----	----
log β _{NiB₄}	----	9.57(11)	----	----	----
pK ^H _{NiBH}	7.37	----	----	5.49	4.24
pK ^H _{NiB₂H}	----	----	----	6.64	5.10
log K ^{NiB} _{NiB₂}	4.73	2.13	1.74	4.86	7.10
log K ^{NiB₂} _{NiB₃}	----	2.20	----	----	----
log K ^{NiB₃} _{NiB₄}	----	1.67	----	----	----
log K ^{NiBH} _{NiB₂H}	----	----	----	6.01	7.96
log P	----	----	----	2.46	4.12
Ref: ^a 5; ^b 6					

in these systems (Table 2) bear favorable comparison with log K₁ value obtained in Ni(II)-pym(A) system (Table 1). Similarly, log K^{NiA}_{NiAB} values obtained in Ni(II) - pym (A) - him / bim (B) systems (Table 2) are comparable to log K₁ values obtained (Table 1) in Ni(II)-B binary systems. This demonstrates that primary and secondary ligands bind the metal ion in a similar manner as their binding in their respective binary species. Thus, in the NiAB species in Ni(II)-pym(A)-him and bim(B) systems, pym primary ligand would bind nickel through its phenolic oxygen and aminomethyl nitrogen and third coordination site will be occupied by imidazole nitrogen of him/bim secondary ligands. The fourth position in this species would be occupied by solvent water molecule. In NiAB₂ species in these two systems the imidazole

nitrogen of the second him / bim ligand will occupy the fourth position. The higher log β values obtained in NiAB and NiAB₂ species in Ni(II)-pym(A)-him(B) system compared to that values in the corresponding bim(B) system can be explained by considering the higher basicity of him compared to that of bim ligand. The Δ log K values computed for NiAB and NiAB₂ species in Ni(II)-pym(A)-him/bim(B) systems (Table 2) are more positive compared to the statistically expected values [13] indicating marked stabilization of these mixed ligand complexes. The same trends have also been reflected in species distribution profiles (Fig.1). The Δ log K values of NiAB species in Ni(II)-pym(A)-him / bim(B) systems are more positive compared to those values for the respective NiAB₂ species. The relative stabilities of

Table 2: Stability constants for the Ni(II)-pym(A)-him, bim, hist and his(B) ternary complex systems at 37 °C and I = 0.15 mol dm⁻³ (NaClO₄).

Parameter	Ligand B			
	Him	bim	hist	his
$\log \beta_{\text{NiABH}_2}$	----	----	25.85(3)	27.12(3)
$\log \beta_{\text{NiABH}}$	16.65(2)	----	21.47(2)	23.56(2)
$\log \beta_{\text{NiAB}}$	9.98(4)	7.83(8)	13.67(4)	15.47(6)
$\log \beta_{\text{NiAB}_2}$	12.01(6)	10.04(9)	----	----
$\text{pK}_{\text{NiABH}_2}^{\text{H}}$	----	----	4.38	3.56
$\text{pK}_{\text{NiABH}}^{\text{H}}$	6.67	----	7.80	8.09
$\log K_{\text{NiAB}}^{\text{NiA}}$	3.40	2.25	7.09	8.89
$\log K_{\text{NiAB}}^{\text{NiB}}$	6.61	6.47	7.31	6.63
$\log K_{\text{NiABH}}^{\text{NiBH}}$	2.70	----	7.52	9.61
$\log K_{\text{NiAB}_2}^{\text{NiB}_2}$	6.31	5.93	----	----
$\Delta \log K_{\text{NiABH}_2}$	----	----	0.05	0.09
$\Delta \log K_{\text{NiABH}}$	-0.67	----	1.16	0.77
$\Delta \log K_{\text{NiAB}}$	0.03	-0.11	0.73	0.05
$\Delta \log K_{\text{NiAB}_2}$	-0.27	-0.65	---	----

the NiAB and NiAB₂ species depend on the size of the chelate ring formed by the primary ligand(A). Also the higher values for NiAB species is due to (i) the loss of π -bonding in going from an in plane coordinated imidazole to two out of plane cis coordinated imidazole as observed in the cis-bis(imidazole) complexes and (ii) the statistical effect resulting from the reduction in available binding sites for the coordination of the second him / bim ligand.

In Ni(II)-pym(A)-hist(B) system, the $\log K_{\text{NiAB}}^{\text{NiB}}$ and $\log K_{\text{NiAB}}^{\text{NiA}}$ values obtained (Table 2) bear favorable comparison to the respective $\log K_1$ values in Ni(II)-pym(A) and Ni(II)-hist(B) binary systems (Table 1). This demonstrates the bidentate binding of primary ligand pym(A) and secondary ligand hist(B) in NiAB species exactly similar to their binding in the respective binary species. The $\log \beta_{\text{NiAB}_2}$ value in Ni(II)-pym(A)-hist(B)

system is higher(≈ 1.6 log units) than the value obtained in Ni(II)-pym(A)-him(B) system, though in both these complexes the metal ion has a coordination number of 4. The enhanced stability observed in the hist(B) system may be due to the fact that the hist binds Ni(II) forming a 6-membered ring, while the binding of him with Ni(II) in NiAB₂ species does not involves chelate formation. The $\log \beta$ value of 15.47 for NiAB species in his(B) ligand system is higher compared to 13.67 obtained in the hist (B) secondary ligand system which suggests that his(B) binds the metal ion in a tridentate manner in its NiAB species(Struct.2). The $\Delta \log K_{\text{NiAB}}$ values obtained indicates higher stability for the NiAB complexes.

Stability and structure of NiABH and NiABH₂ complexes

NiABH species has been identified in Ni(II)-pym(A)-him, hist and his(B) systems and its formation has been found to be more favored above pH 4. In Ni(II)-him(B)

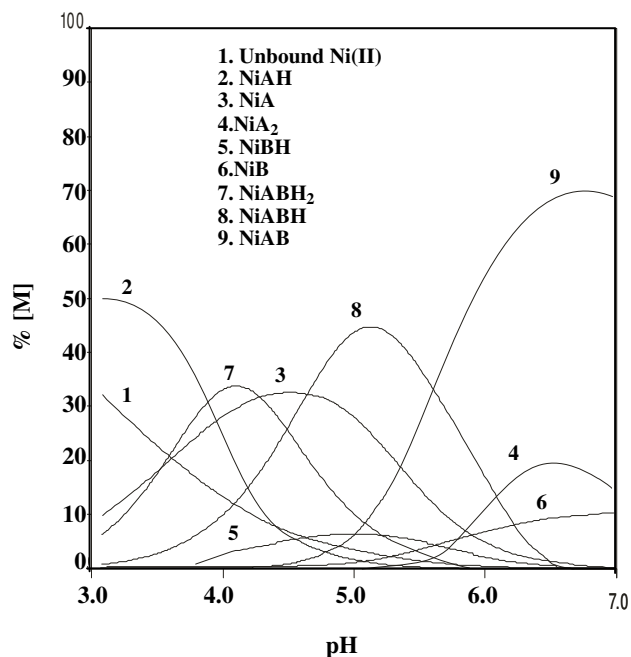


Fig.1: Distribution diagram for the Ni(II)-pym(A)-hist(B) ternary complex system, $C_M = 0.003$; $C_A = C_B = 0.006 \text{ mol dm}^{-3}$. Curves for NiB_2H and NiB_2 could not be drawn due to their low concentrations.

binary system no protonated binary species has been detected (Table 1), while the monoprotated binary species NiAH species has been detected in Ni(II)-pym(A) system. The $\text{pK}_{\text{NiABH}}^{\text{H}}$ value of 6.67 obtained in Ni(II)-pym(A)-him(B) system bears favorable comparison with $\text{pK}_{\text{NiAH}}^{\text{H}}$ value of 7.37 obtained in Ni(II)-pym(A) binary system, where the proton is attached with the aminomethyl group of the ligand. Thus the NiABH species in Ni(II)-pym(A)-him (B) system it can be concluded that the extra proton resides with the pym(A). However, the $\text{pK}_{\text{NiABH}}^{\text{H}}$ values obtained in Ni(II)-pym (A) - hist / his (B) systems (Table 2) follow the trends of $\log \beta_{\text{NiBH}}$ values in Ni(II)-hist/his(B) systems (Table 1). Hence, it can be expected that the extra proton in NiABH species in Ni(II)-pym(A)-hist and his (B) systems can reside with the hist/his(B)(Struct.3). At lower pH values NiABH₂ species has been found to be favored in Ni(II)-pym(A)-hist and his(B) systems. With regard to the site of the protonation in these NiABH₂ complexes, it may be inferred that one proton is attached with pym(A) and the other resides with hist / his(B) (Struct.4).

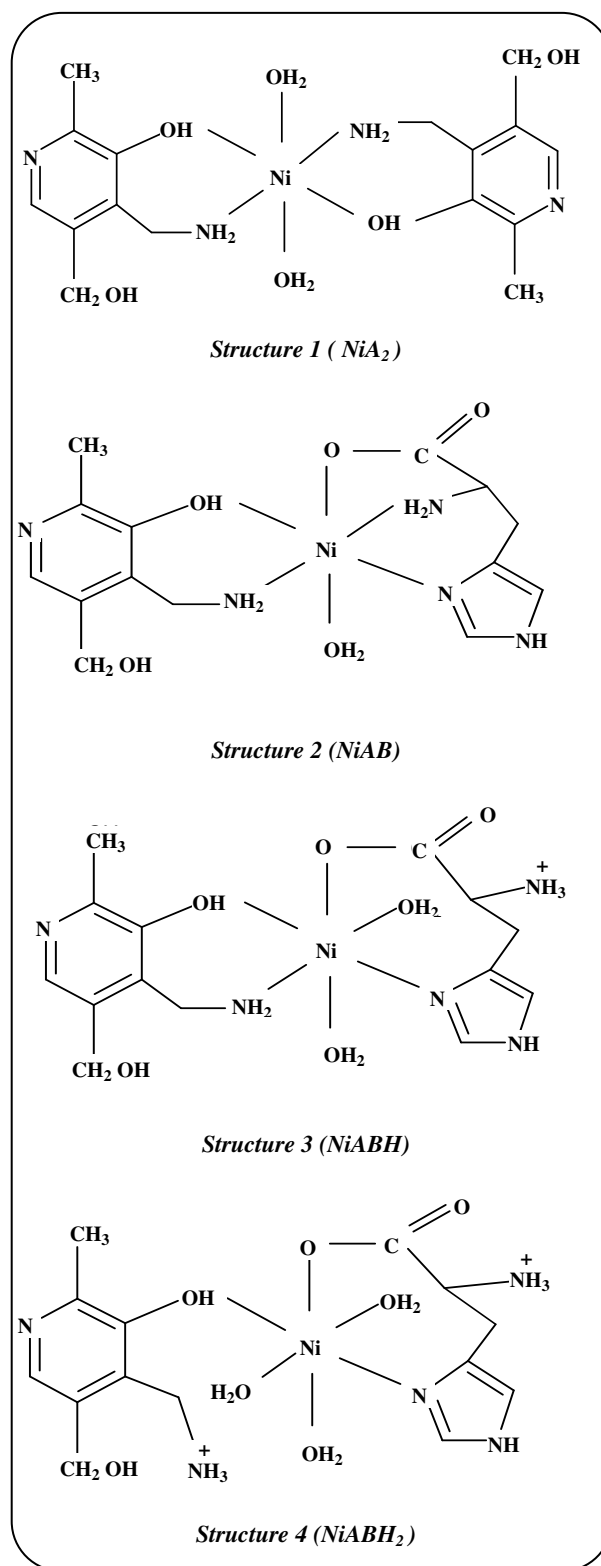


Fig. 2: The Structural representation of NiA_2 in the Ni (II)-pyridoxamine (A) and NiAB , NiABH and NiABH_2 species in the Ni (II)-pyridoxamine (A)-histidine (B) systems.

Characterization of Ni(II)-pym(A)-his(B) mixed ligand complex

The results of chemical analysis of the mixed ligand complex agree with the formula of [Ni(II)(pym)(his)H₂O]. The IR spectra shows a broad band in the range of 3460 – 3355 cm⁻¹, which can be ascribed to the stretching vibration of water molecule. The group of bands appearing in the region of 3330–3020 cm⁻¹ in the spectra of the complex can be attributed to the stretching vibrations of the coordinated NH₂ group. The distinct band appearing in the region 1655-1600 cm⁻¹ is typical of coordinated carboxylate stretching [14]. Accordingly, the absence of any band in the region of 1750-1700 cm⁻¹ in the IR spectra of isolated ternary complex suggests the coordination of the COO⁻ group of his to the Ni(II). Thus, in this complex pym is bidentate and his is tridentate with Ni(II). The band in the region 1396 -1367 cm⁻¹ can likely be ascribed to the symmetric stretching vibrations of the coordinated carboxylate.

Acknowledgement

One of the authors (MAN) wishes to thank Dr. Kn. K. S. K. Chockalingam, Principal, National Engineering College for his constant encouragement.

Received : 24th November 2002 ; Accepted : 2nd January 2004

REFERENCES

- [1] Sigel, H., "Metal ions in biological systems", **1**, 37 edited by A Sigel (M Dekker, NY) (1971 – 1997); Williams, D.R., "The metals of Life" , Van Nostrand Rein Hold, New York (1971); "Transition metal sulfur chemistry, Biological and industrial significance", edited by Stiefel, E.I., and Matsumoto, K., Oxford (2001).
- [2] Leklem, J.E., "Handbook of Vitamins", Marcel Decker Inc, New York, (1991); "Nutrition in Health and Disease", Williams and Wilkins (1999).
- [3] Karlin, K. D., and Tyeklar, Z., "Bioinorganic Chemistry", Chapman and Hall, NewYork (1993).
- [4] Nair, M.S., and Neelakantan, M.A., *J. Indian Chem. Soc.*, **77**, 373 (2000); **77**, 394 (2000).
- [5] Nair, M.S., Arasu, P.T., Pillai, M.S., and Natarajan, C., *J. Chem. Soc. Dalton Trans.*, 917 (1993).
- [6] Nair, M.S., Arasu, P.T., Pillai, M.S., and Natarajan, C., *Trans Met. Chem.*, 1111 (1995).
- [7] Nair, M.S., Arasu, P.T., Pillai, M.S., and Natarajan, C., *Talanta*, **40**, 1411 (1993).
- [8] Nair, M.S., and Neelakantan, M.A., *Indian J. Chem, Sect. A*, **38**, 575 (1999).
- [9] Gans, P., Vacca, A., and Sabatini, A., *Inorg. Chim. Acta*, **18**, 23 (1976).
- [10] El-Ezaby, M.S., and Al. Sogair, *Polyhedron*, **1**, 791(1982); **2**, 245 (1983).
- [11] Chiacchierini, E., Ascenzo, G.D., De Angelis, G., Margi, A.L., and Peetrone, V., *Ann. Chim(Rome)*, **67**, 195 (1977).
- [12] Shoukry, M. M., Khairy, E. M., and Mohamed, M.M., *Talanta*, **44**, 1149 (1997).
- [13] Sigel, H., Tribolet, R. B., and Yamuchi, O., *Comments Inorg Chem*, **9** (1990).
- [14] Nakamoto, K., "Infrared and Raman Spectra of Inorganic and Coordination compounds", John Wiely, New York (1978).