Metal Ion Mediated Intramolecular Stacking Interactions - Ni^{2+} with 2(2'-Pyridyl)Benzimidazole and Amino Acids

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Interaction of Ni^{2+} with 2(2'-pyridyl)benzimidazole and amino acids (alanine, phenyl alanine and tryptophan) has been investigated by potentiometric pH measurements. Ternary complexes containing phenyl alanine or tryptophan are found to be more stable than those containing alanine. The stabilization has been explained in terms of stacking interaction.

Metal ions stabilize, destabilize or modulate biological processes by introducing conformational changes through electronic effects like stacking and hydrophobic effects [1-3]. The study of intramolecular interactions in a system containing a metal ion and two different ligands has gained significant importance in recent past [4-6]. In order to identify stacking and hydrophobic effects of the ligands, we have undertaken a pH-metric investigation of the interaction of 2(2'-pyridyl)benzimidazole [2(py)benz] with $Ni(NO_3)_2$ and selected amino acids.

EXPERIMENTAL

The 2(py)benz was obtained from Aldrich Chemical Company Ltd. (USA) and amino acids (alanine, phenyl alanine & tryptophan) from Aldrich. Nickel nitrate was of AnalaR grade. The metal ion content in solution was determined volumetrically by titration with sodium salt of EDTA [7]. Potentiometric measurements were carried out at 30°C with 0.1M KNO_3 as background electrolyte in 40% dioxan - water mixture using Control Dynamics pH meter. The pH reading was corrected according to the method suggested by Van Uitert and Haas [8]. The corrected pH meter readings were plotted against 'a' (mole of base added per mole of ligand) or 'm' (mole of base added per mole of metal ion). Calculation was carried out with the help of BEST Computer Programme [9].

RESULTS AND DISCUSSION

Acid Dissociation Constants

The free ligand titration curve for the mono-protonated 2(py)benz shows a steep inflection at a=1. The acid dissociation constants of 2(py)benz and also amino acids were calculated in the buffer region a=0 to a=1. The values thus obtained are given in Table 1.

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Table 1

Protonation Constants of Free Ligands and Formation Constants of Binary & Ternary Complexes

Metal ion - Ni^{2+}; Medium - 0.1 M KNO_3 in 40% Dioxan; Temp - 30°C

Ligand	Acid Dissoc. Constant M:Q:R:S	log K	Binary Complex M:Q:R:S	log K^{M}_{ML}	Ternary Complex M:Q:R:S	Log K^{MA}_{MAL}	Δlog K	% R.S.
2(py)benz	0: 1: 0: 1	4.66±0.05	1: 1: 0: 0	6.95±0.03	(primary ligand in ternary complexes)			
Alanine	0: 0: 1: 1	9.29±0.05	1: 0: 1: 0	5.50±0.06	1: 1: 1: 0	5.08±0.05	-0.42	-7.63
Ph.alanine	0: 0: 1: 1	8.98±0.02	1: 0: 1: 0	5.10±0.01	1: 1: 1: 0	5.39±0.03	+0.29	+5.68
Tryptophan	0: 0: 1: 1	8.96±0.02	1: 0: 1: 0	5.20±0.03	1: 1: 1: 0	5.52±0.04	+0.32	+6.15

M is metal ion; Q is 2(py)benz; R is amino acid; S is protons in the specie

$\Delta \log K = \log K^{MQ}_{MQR} - \log K^{M}_{MR}$; % R.S. = ($\Delta \log K$ / $\log K^{M}_{MR}$) x 100

Binary Systems

The potentiometric curves for the binary system [1:1 Ni^{2+} - 2(py)benz] show a single steep inflection at m=1. The formation constants (log K) for the binary complex Ni^{2+} with 2(py)benz and also with amino acids were calculated in the region m=0 to m=1. The value thus obtained are included in Table 1. The stability constants decrease in the order Ni-alanine> Ni-tryptophan >Ni-phenylalanine. Ni-alanine complex is stabler than others studied, because of the comparative higher basicity of alanine.

Ternary Systems

The potentiometric titration curves of the ternary system [1:1:1 Ni^{2+} -2(py)benz - amino acid] coincides with binary titration curve of Ni^{2+} -2(py)benz in the region m=0 to m=1 with a steep inflection at m=1 ; later it deviates showing another feeble inflection at m=2. This indicates stepwise complex formation with 2(py)benz as the primary ligand. The stability constants of the ternary complexes were calculated in the region m=1 to m=2 by assuming complete formation of 1:1 Ni^{2+} -2(py)benz complex before the coordination of amino acid (secondary ligand) takes place.

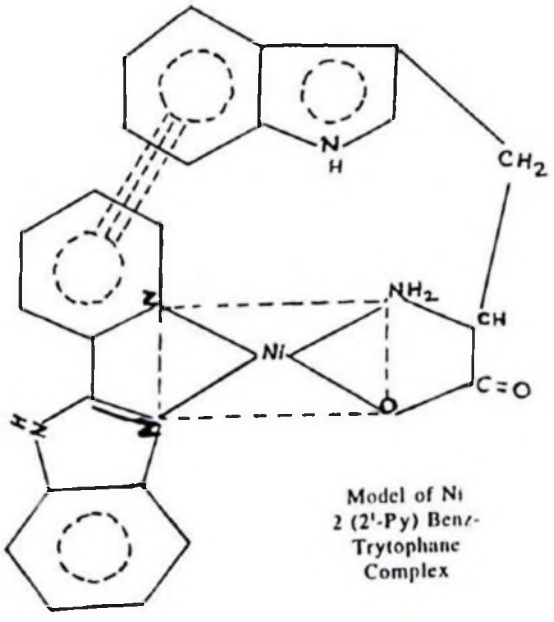
In order to obtain precise values of Δlog K, it is essential that the binary and ternary constants refer to identical experimental conditions. Acid dissociation & binary constants listed in Table I have been reported earlier in literature under different expermental conditions [10]. These constants have been redetermined in this work at 30°C & I = 0.1M KNO_3 in 40% dioxan.

Based on a purely statistical basis, negative values are expected for Δlog K, since there are more coordinating sites on the aquo metal ion as compared to the binary metal complex. For the coordination of a bidentate ligand -

amino acid - to an octahedral metal ion already bound to a bidentate ligand - 2(py)benz, the statistically expected Δ log K value is - 0.40 [11]. A more negative or positive value represents destabilization or stabilization respectively of the ternery complex.

Percentage Relative Stabilization (% R.S.) is another parameter to measure the relative ease of the formation of mixed ligand complexes. Positive or less negative value of % R.S. indicates stabilization while negative value of % R.S. indicates destabilization.

In the present study the ternary system involving phenylalanine & trytophan exhibit positive value of Δlog K and % R.S., while those involving alanine shows negative Δlog K value of -0.42 - almost the same value as expected on statistical grounds alone. The positive Δlog K values for the ternary complexes of Ni^{2+}-2(py)benz with either phenylalanine or tryptophan indicate that these amino acids bind to the Ni^{2+} -2(py)benz complex more strongly than to the aquo -Ni^{2+} complex.



Model of Ni 2 (2'-Py) Benz-Trytophane Complex

Model of the 2(py)benz - Ni^{2+} - tryptophan complex show that the phenyl group of the indole ring of the tryptophan can stack reasonably well with the pyridine ring of 2(py)benz as shown in figure 1. Such stacking interactions probably cause the increased stability observed in this system. In the case of phenylalanine, a more modest positive Δlog K value can again be attributed to stacking of the phenyl ring of the amino acid and pyridine ring of the 2(py)benz.

The more positive ΔlogK value for tryptophan as compared to that of phenylalanine may be due to the fact that the indole fragment with a wider hydrophobic surface area stacks better with 2(py)benz than phenylalanine [12].

The negative Δlog K value for ternary system involving alanine indicate the absence of stacking interactions in this system. The aromaticity (π electron cloud) is a pre-requisite to have the stacking interactions and this is absent in alanine. Further the Δlog K value of -0.42, suggests that the statistical factor alone is operating in the formation of this ternary complex.

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REFERENCES

1. J. B. Orenberg, B.E. Fischer and H. Sigel, *J. Inorg. Nucl. Chem.*, **42** (1980) 785.

2. B.E. Fischer and H. Sigel, *J. Am. Chem. Soc.*, **102** (1980) 2998

3. H. Sigel, B.E. Fischer and E. Farkas, *Inorg. Chem.*, **22** (1983) 925

4. K. Prasad and M. Srinivas Mohan, *J. Coor. Chem.*, **16** (1987) 1

5. P. Rabindra Reddy and M. Ravi Prakash Reddy, *Indian J. Chem.*, **29(A)** (1990) 1008

6. D. Srinivas Yogi, P. Venkatalah, M. Srinivas Mohan and H.B. Bhathina, *Indian J. Chem.*, **33(A)** (1994) 407

7. G. Schwarzenbech, *Complexometric Titrations*, **Interscience New York** (1957) p. 77.

8. L.G. Van Uitert and C.G. Haas, *J. Am. Chem. Soc.*, **75** (1952) 451

9. R.J. Motekaits and A.E. Martell, *Can. J. Chem.*, **60** (1982) 168, 2403

10. L.G.Sillen (Ed.), *Stability Constants of Metal-ion Complexes*, Special publication 25, **The Chemical Society, London** (1971)

11. H. Sigel, *Metal Ions in Biological Systems*, Vol 2 **Marcell Dekker New York** (1973) Ch. 2

12. M. Tabata & M. Tanaka, *Inorg.Chem.*, **27** (1988) 3190