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Full Length Research Paper

Complex of nickel (II) with isonicotinohydroxamic acid

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Isonicotinohydroxamic acid (INHA) was synthesized, characterized, and its pKa determined spectrophotometrically as 8.68 ± 0.05 at 25°C and in buffers of 0.1 mol dm^{-3} ionic strength (I). A spectroscopic investigation of its reaction with Ni^{II} in aqueous solution revealed the sole formation of the 1:2 complex at equilibrium. Spectra and magnetic studies of the isolated complex indicate octahedral coordination via the (N) atom of the hydroxamate group. Microbial sensitivity test on eight microorganisms used showed no activity.

Key words: Nickel (II), spectrophotometry, buffer, hydroxamate group, octahedral coordination microbial sensitivity.

INTRODUCTION

Monohydroxamic acid form typical octahedral complexes with transition metal via coordination through the oxygen atoms and formation of reasonably ionic metal oxygen bonds (Nwabueze, 1996). Since hydroxamic acids are intimately associated with iron transport phenomena, the selectivity of this mechanism is important since other metal ions, which may be essential or which may have toxic effect on the organism are present in the environment (Crumbliss and Garisson,1988). They are known to act as antibiotic, antibiotic antagonist, tumor inhibitors and many of them are used as drugs (Kurzak et al., 1992). Hydroxamic acids have been shown to possess diverse biological activities, many of which are due to their complexing properties towards transition metal ions (Nigovic et al., 2002)

The N bonding model (suggesting deprotonation of nitrogen of the hydroxamic group) was first observed by Brown and Roche (1982) in nickel (II) complexes with glycine hydroxamic acids and since then only a few examples have been reported. Aminohydroxamic acid, coordinating through N, also occurred in polynuclear complexes with bridging hydroxamic function (Dobosz, 1999). Other examples are complexes of Ni (II) and Cu(II) with (hydroxyimino) propanohydroxamic acid exhibiting N bonding mode have been sited, thus providing a new example of the adjacent donor function facilitating this bonding mode (Dobosz, 1999).

The interaction of hydroxamic acids with nickel (II) is of importance since they act as potent and specific inhibittors of the nickelloenzyme, urease (Hase and Bobashi, 1967)

This paper is therefore a report on the work carried out on the affinity of the title ligand for nickel (II) with special emphasis on the structure and nature of bonding involved. In addition, some physico-chemical properties were investigated and included in the report.

EXPERIMENTAL

Ethylisonicotinate was obtained from Aldrich. All other reagents were of Analar R-grade. $NaNO_3$ was used for the preparation of the background electrolyte and stock solutions. Water was doubly distilled, degassed using purified N_2 and stored in glass stoppered flasks. KOH and HNO_3 used for adjusting pH were stored in glass ampoules and were standardized with potassium hydrogen phthalate and tris (hydroxymethyl) methyl amine respectively. The pH measurements were made using a radiometer Copenhangen Research pH meter calibrated with standard buffer tablets (2, 4 and 9).

Electronic spectra were recorded on ATI Maltson Genesis series FTIR™ machine as Nujol mull in the 4000 - 200cm^{-1} spectra region. Room temperature magnetic susceptibility measurements were made on MSB Auto magnetic susceptibility balance. All these analyses were done at National Research Institute for Chemical Technology (NARICT) Zaria and University of Abuja, Nigeria.

Preparation of the ligand

Isonicotinohydroxamic acid (INHA) was prepared as described in

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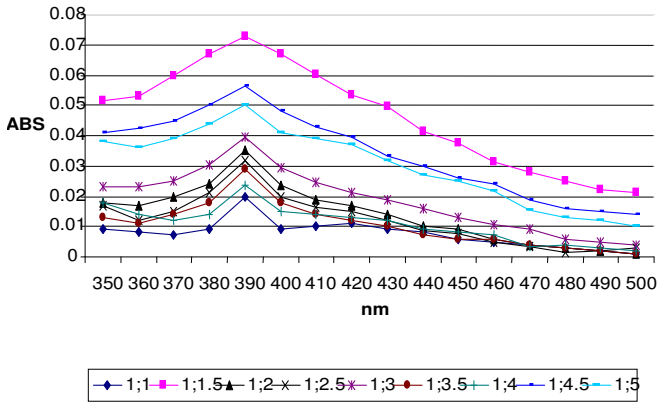


Figure 1. Isosbestic point search for Ni $^{II-}$ INHA system.

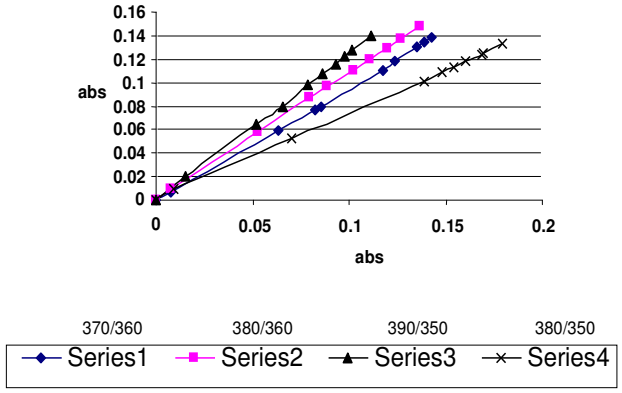


Figure 2. Graphysical rank matrix analysis for Ni $^{II-}$ – INHA system (one specie test).

literature (Jones and Scott, 1922).

Preparation of the complex

$[Ni(INHA)_2].2H_2O$ complex was prepared as follows: $NiSO_4.6H_2O$(0.53 g, 0.002 mol) in EtOH was added with stirring in INHA (0.556 g, 0.004 mol) in EtOH (20 cm^3). To this mixture a 10% solution of $NaHCO_3$ was added until a lemon green precipitate appeared. The precipitate was removed by filtration, washed with small aliquots of Et_2O and dried over silica gel in a vacuum dessicator (Yield 55%).

Equilibrium studies

The pKa value for the ligand was determined spectrophotometriccally by the method of Albert and Sergent (1971) using boric acid and borax of ionic strenght 0.1 moldm^{-3} and 0.025 mol dm^{-3} buffer for INHA ligand in this case, the ligand stock solution was 5×10^{-4} mol dm^{-3} diluted five folds in buffer solution for INHA measurments were made in eight boric/borax buffer solutions used for INHA at analytical wavelength of 200 nm. The number of complexes present in solution at equilibrium was determined by the isosbestic point method and graphical rank matrix using nine solutions containing 1:1-1:5 metal: ligand ratio (ligand concentration increasing in units of 0.5). A solution of 0.1 mol dm^{-3} made up of 0.01 mol dm^{-3} $HNO_3$and 0.09mol dm^{-3} $NaNO_3$ was used to prepare equimolar stock solution of Ni^{2+} and the ligand 2.5×10^{-3} mol dm^{-3};the same solutions was used for aldilutions in all cases, the solutions were thermostated at 25°C for 2 h in an ultrasonic bath.

Evaluation of the antimicrobial activity

The antimicrobial activity of the test compound was assayed against eight bacteria. *Staphylococcus aureus, Escherichia coli, Salmonella-typhy, Klebsiella, Streptococcus, Pseudomonias, Corrynebacterium* and *Neisseria*. Among these organisms, four of them are Gram +ve. While others are Gram -ve. All are regarded as pathogenic to humans and animals. All media and bacteria suspensions were prepared using a method adapted from that of Cruickshank (1965).

About 15 – 20 cm^3 of molten nutrient agar was poured into sterile Petri plates about 10cm in diameter. After solidification of the agar, three cups (10 mm in diameter and 5 mm deep) were removed from each agar dish and fresh bacteria suspension was then uniformly spread on each cup. At this point, each of the cups was spotted three times with test solution at concentration of 50, 100 and 200 μ g/cm^3 in dimethylsulphoxide (DMSO). After incubating the plates at 37°C overnight, the diameter of the zone of inhibition of the bacteria growth was then recorded.

A 5% phenol solution was used as a positive control and DMSO as solvent control each time the experiments were performed.

RESULTS AND DISCUSSION

The various stages in the preparation of INHA are as represented by the reactions below:

$$2Na + 2MeOH \rightarrow 2MeONa + H_2 \uparrow$$

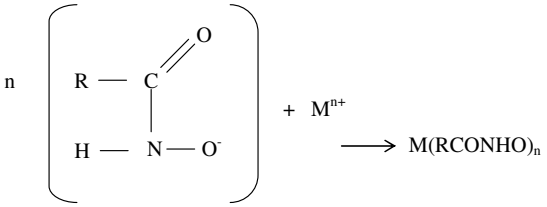
$$NH_2OH.HCl + MeONa \rightarrow NH_2OH + NaCl\downarrow + MeOH$$

$$NH_2OH + RCO_2Et \rightarrow RCON(H)OH + EtOH$$

$$RCON(H)OH + MeONa \rightarrow RCON(H)O^-Na^+ + MeOH$$

$$RCON(H)O^- - Na^+ + HCl \rightarrow RCON(H)OH + NaCl\downarrow$$

Where R = Pyridine ring for the complex of INHA model.



Where n is a neutral monodentate ligand.

The pKa value of INHA is 8.68 ± 0.05. The high basicity of the ligand may be ascribed to the positive inductive effect of the bulky pyridine ring attached to the functional group. Figure 1 shows the absorption spectra of solutions containing a constant metal but variable ligand molar concentration for INHA system, while Figure 2 shows graphical Matrix rank analysis of the absorbance data gene-

Table 1. Analytical data and physicochemcial properties of the isolated complex ( ) Calculated %.

Compound	Form. wt	Mp/Dec ^{o}C	Colour	Found M	µeff BM	λ max x $10^3 cm^{-1}$	Assignment
$Ni(INHA)_2.2H_2O$	370.17	148	Lemon Green	15.40 (15.86)	3.25	24.39 13.70	$^3A_{2g} \rightarrow {}^3T_{1g}P$ $^3A_{2g} \rightarrow {}^3T_{1g}F$

Key:
M = metal, Form.wt = Formular weight, MP/dec = Melting Point/Decomposition,
B.M = Borh Magneton

Table 2. Diagnostic I.R data for the complex (cm^{-1}).

Compound	v (NH) cm^{-1}	Δ v (NH)cm^{-1}	v (C=0) cm^{-1}	Δ v (C=0)cm^{-1}
INHA	3422.50		1605.01	
$Ni(INHA)_2.2H_2O$	3308.69	-113.90	1596.20	-9.81

Key:
INHA = Isonicotinohydroxamic acid.

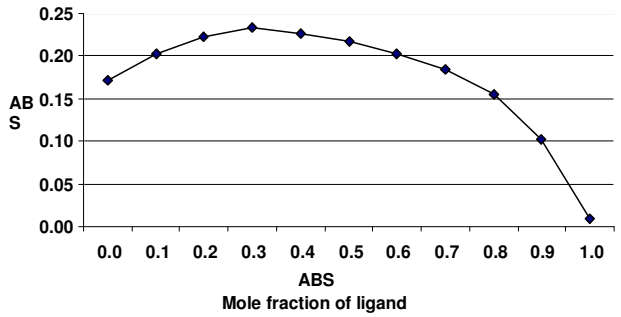
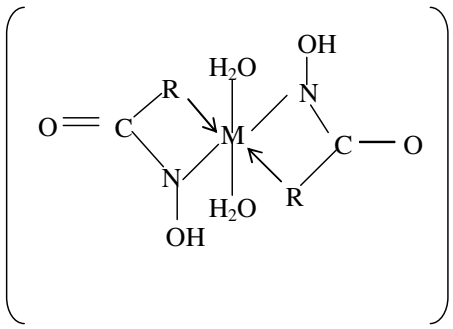


Figure 3. Continuous variations (Job's plot) method for Ni^{II} - INHA system.

generated from similar solutions for INHA system. The absence of an isosbestic point and the shape of the graph is typical of systems containing only one complex specie. In this regard, the system shows similar behavior (Hartley et al., 1980).

Several equilibrium models were tried but it was only with ML_2 model that convergence was achieved. The composition of the complex as determined by Job's plot is shown in Figure 3. The ratio of Ni^{II} to the ligand under investigation was ML_2 i.e. Ni^{II} – INHA (Hartley et al., 1980).

The colour of Nickel (II) complex is lemon green. The analytical data and some physico-chemical properties are shown in Table 1. The spectrum of $[Ni(INHA)_2].2H_2O$ shows two bands located at about 24.39 x 10^3 cm^{-1}, and 13.70 x 10^3 cm^{-1} which are due to transition from the $^3A_{2g}$ ground term to the $^3T_{1g}(P)$ and $^3T_{1g}(F)$ levels respectively (Nicholls, 1974). This spectrum and the observed magnetic moment indicate a magnetically dilute octahedral nickel (II) complex (Boadanov et al., 1972; Nicholls, 1974). The diagnostic i.r band in the free ligand was compared with the complex reported in Table 2. The **v** (C=0) vibration located at 1605.01cm^{-1} in the ligand is lowered by 9.81cm^{-1} in the complex, this together with decrease in the **v** (NH) band indicates (N) bonding of mode that is, (suggesting deprotonation of nitrogen atom of the hydroxamic group (Brown and Roche, 1982). The microbial sensitivity test carried out on the ligand and its isolated nickel (II) complex showed no activity on the microorganism under investigation. Table 3, Shows the microbial sensitivity test against eight microorganisms as indicated in the table. The ligand and the complex show no activity. On the basis of its physico-chemical properties, the shown structure in Scheme 1 is proposed for the complex. Proposed structure for (N) bonding mode for octahedrally coordinated complex.



Key: $M^{2+} = Ni^{2+}$

Scheme I

Conclusion

When we compared the pKa value of INHA (8.68±0.05 with the analogous values of benzhydroxamic acid pKa

Table 3. Microbial sensitivity test for the ligand and its isolated nickel (II) complex.

Ligand/Complex	*Staph. aureus*	*S. typhylium*	*E.coli*	*Klebsiella*	*α Hemolytic strep.*	*Neisseria*	*Pseudonomias*	*Corynebacteria*
Gram	+ve	+ve	-ve	-ve	+ve	-ve	-ve	+ve
INHA	-	-	-	-	-	-	-	-
$Ni(INHA)_2.2H_2O$	-	-	-	-	-	-	-	-

8.79 and acetohydroxamic acid pKa 9.37, it can be seen that the pKa of INHA falls within the range sited in literature. Experimental data indicates that the hydroxamate nitrogen atom is involved in the coordination to the metal complex. The carbonyl stays free for eventual hydrogen binding interaction with active site. The microbial sensitivity test shows no activity. This may be related to poor conductivity of the metal complex.

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