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Thermodynamic Parameters of the Uncatalyzed Complxation Reaction between Ni (II) Ion and Bioactive Isatin-Bishydrazone

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Abstract
The stoichiometries and stability constants of Nickel (II) ions with 2-pyridyl-3-Isatin bishydrazone have been determined spectrophotometrically at different temperatures 20^0C, 25^0C, 30^0C, 35^0C and 40^0C by using Job's continuous variation method. In all cases, the Job's curves displayed a maximum at a mole fraction X_{ligand} =0.5 indicating the formation of complex with 1:1 metal to ligand ratio. It was observed that metal-ligand stability constant decreases with increasing temperature indicating exothermic nature of the reaction. The thermodynamic parameters i.e., ΔG^0, ΔH^0 and ΔS^0 have also been calculated.
Keywords: Isatin-bishydrazone ligands, Ni(II) complexes, thermodynamic parameters, Stability constant, spectrophotometrically.

1. Introduction

Hydrazones form an interesting class of chelating ligands which contain an azomethine group linked to a nitrogen atom and find extensive application in various fields [i,ii], and also form an important class of organic compounds with a wide variety of biological properties [iii,iv,v,vi,vii]. Development of a new chemotherapeutic hydrazones is now attracting the attention of medicinal chemist [viii]. Many studies have reported regarding the biological activities of hydrazones, including their anticancer [ix], antibacterial [x], antifungal, and herbicidal activities [xi,xii].

Isatin (1-H-indole-2, 3-dione) and its derivatives possess a broad range of biological and pharmacological properties [xiii,xiv,xv,xvi,xvii] and are widely used as starting materials for the synthesis of a broad range of heterocyclic compounds and as substrates for drug synthesis [xviii]. A variety of biological activities are associated with Isatin- hydrazones including CNS (the central nervous system) activities as potentiation of pentobarbitone induce nercosis [xix], Analgesic [xx], anticonvulsant [xxi], antidepressant [xxii], anti-inflammatory [xxiii], antimicrobial, and effects on the central nervous system [xxiv], Isatins are capable of crossing the blood–brain-barrier [xxv]. Although metal complexes of monohydrazones derived from isatin have been extensively investigated, those formed from bishydrazones have received comparatively less attention so far [xxvi,xxvii].

On the other hand, hydrazones of 2-pyridyl (2-acetyl pyridine, 2-benzoyl pyridine and pyridine-2-carboxaldhyde) and their metal complexes have good biological applications such as antimicrobial [xxviii,xxix], anti-inflammatory [xxx,xxxi,xxxii], and anticancer [xxxiii,xxxiv,xxxv] reagents.

Although much attention has been directed to study the metal complexes derived from Isatin-hydrazones [xxxvi,xxxvii], no investigations have appeared in the literature to describe the metal complexes of the hydrazones derived from Isatin-monohydrazone and 2-pyridyl (pyridine-2-carboxaldhyde, 2-acetyl pyridine and 2-benzoyl pyridine). Therefore the need to create novel Isatin -hydrazones derivatives for emerging drug targets is an active area of medicinal chemistry. Thus, our interest in the synthesis, structural characterization of new Schiff bases [xxxviii] we synthesized and characterized new isatin-bishydrazone compounds derived from isatin monohydrazone and 2-pyridyl which showing notable biological activity. Thus in the present work, we aim to study there stiochiometry with complexation with Ni(II) ions, in addition to spectrophotometrically study of the stability constants of these complexes at different temperatures 20^0C, 25^0C, 30^0C, 35^0C and 40^0C by using Job's continuous variation method, with finding the thermodynamic parameters of the new complexes.

2. Experimental

2.1. Chemicals

All chemicals were used as produced without further purification. Isatin, 2-acetyl pyridine, 2-benzoyl pyridine and pyridine-2-carboxaldhyde were obtained from Sigma-Aldrich Company Ltd. Hydrazine hydrate and hydrated Nickel chloride ($NiCl_2.6H_2O$) was obtained from BDH Company. All other reagents and solvents (methanol, ethanol and DMF) were purchased from commercial sources and were of analytical grade.

2.2. Synthesis of the ligands.

Isatin-bishydrazone ligands, namely [(pyridine-2-Carboxaldhyde)-3-isatin]-bishydrazone (cpish), [(2-acetyl pyridine)-3-isatin]-bishydrazone (apish) and [(2-benzoyl pyridine)-3-isatin]-bishydrazone (bpish) were prepared in two steps [38]: the first step is the synthesis of Isatin-monohydrazone, followed by condensation with the 2-pyridyl, giving the Isatin-bishydrazone Ligands.

2.3. Determination of the stoichiometry, formation constant and thermodynamic parameters of the complexes.

2.3.1. Determination the stoichiometry and formation constants of the synthesized complexes.

The stoichiometry of the various complexes formed in solutions via the reaction of metal (II) with the studied Isatin-bishydrazone ligands was determined by applying the spectrophotometric continuous variation methods [xxxix,xl]. By preparing a stock solution of $1x10^{-2}$ M from the metal salt, and preparing a stock solution $1x10^{-2}$ M from the ligand by dissolving the calculated weight of the metal salt or the ligand in the required volume of the appropriate solvent, then by forming a set of solutions containing different independent mole fractions of the components; metal salt and the Ligand, keeping the total concentration of the two constituents unvaried at $1x10^{-2}$ M. Then by measure the absorbance of each solution at the λ_{max} of the complex. By plotting the Absorbance (Abs.) for each compound vs. the mole fraction of the ligand ([L] / ([L]+[M])).

2.3.2. Evaluation of the thermo-dynamic parameters of the synthesized complexes.

In order to find out the thermodynamic parameters of the synthesized complexes, the contentious variation method used to evaluate the apparent formation constant was repeated over wide range of temperatures (20 – 40°C). All the spectrophotometric measurements were carried out in 1 cm cells in the thermostatted cell Jacket compartment of Jasco UV-Visible spectrophotometer (model V-530). The thermostatted cell holder was supplied by an ultrathermostate water circulator (CRIOTERM model 190) to control the temperature at 25ºC ± 0.1 ºC and at different temperatures (20-40 ºC).

3. Results and discussion

3.1. Identification of the prepared compounds.

3.1.1. Physico-chemical measurements

The stoichiometric analysis (C, H and N), of the new compounds was performed using elemental analyzer Perkin-Elmer model 40c, at the Micro-analytical Centre at Cairo-University, Egypt. The IR spectra were recorded on Shimadzu FTIR model 8101 in the region 4000–400 cm^{-1} using dry KBr discs. The electronic spectra of the compounds in methanol were recorded in the region 200–800 nm using a 10 mm matched quartz cells on Jasco UV-Visible spectrophotometer model V-530. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 solvent (solvent peak ≈ 3.8 ppm) on a Bruker Advance 400 instrument. And found to be in good agreement with the reported values [38].

3.2. Stoichiometry, stability and thermodynamic parameters of the complexes.

3.2.1. Determination of the stoichiometry of the complexes.

The stoichiometry of the various Ni(II) Isatin-bishydrazone complexes was determined by applying the spectrophotometric molar ratio [xli,xlii,xliii] and continuous variation [xliv,xlv] methods, which suggested the possible formation of 1:1 complexes. The curves of continuous variation method (*c.f.* Fig. 1) displayed maximum absorbance at mole fraction X ligand ≈ 0.5, indicating, the formation of the complex between the metal ion and the ligands in 1:1 (metal : Ligand) molar ratio. Moreover, the data resulted from applying the mole ratio method support the same metal ion to ligand ratio of the prepared complexes (*c.f.* Fig. 2).

3.2.2. Evaluation of the apparent formation constants of the synthesized complexes.

The formation constants (K_f) of the studied Ni(II) Isatin-bishydrzone complexes formed in solution were obtained from the spectrophotometric measurements by applying the continuous variation method according to the following relations [xlvi].

$$K_f = \frac{A/A_m}{\left(1 - A/A_m\right)^2 C}$$

Where A_m is the absorbance at the maximum formation of the complex, A is the actual absorbance of the complex and C is the initial concentration of the metal. As mentioned in Table (1), the obtained K_f values indicate the high stability of the prepared complexes. The values of K_f for the studied complexes increase in the following order: Ni-bpish > Ni-apish > Ni-cpish.

3.2.3. Evaluation of thermodynamic parameters of the synthesized complexes.

Moreover, the values of overall change in free energy ($\Delta G^{\#}$), enthalpy ($\Delta H^{\#}$) and entropy ($\Delta S^{\#}$) accompanying complexation reaction have been determined using Gibbs-Helmholtz equation [xlvii].

$$\Delta G^{\#} = -RTLnK_f$$

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$$

$$\Delta H^{\#} - T\Delta S^{\#} = -RTLnK_f$$

$$-\Delta H^{\#} + T\Delta S^{\#} = RTLnK_f$$

$$-\Delta H^{\#} + T\Delta S^{\#} = 2.303RTLogK_f$$

$$-\frac{\Delta H^{\#}}{2.303RT} + \frac{\Delta S^{\#}}{2.303R} = LogK_f$$

$$LogK_f = \frac{\Delta S^{\#}}{2.303R} - \frac{\Delta H^{\#}}{2.303R}\frac{1}{T}$$

By plotting the values of (LogK_f) vs. (1/T), obtaining a straight line, from the slope we can evaluate the ($\Delta H^{\#}$) and from intercept we can calculate $\Delta S^{\#}$, (*c.f.* Fig. 3). The evaluated values of $\Delta G^{\#}$, $\Delta H^{\#}$ and $\Delta S^{\#}$ are given in Table (1).

The negative values of $\Delta G^{\#}$ reflect spontaneity of the reaction [xlviii]. The change in enthalpy ($\Delta H^{\#}$) being negative, the reaction occurred is exothermic and formation of complex is favorable, this also suggests that the metal-ligand bonds are fairly strong [xlix]. Since the values of $\Delta S^{\#}$ is positive the reaction will tend to proceed spontaneously [l]. Positive entropy changes accompanying a given reaction are due to the release of bound water molecules from the metal chelates [li]. During formation of metal chelates, water molecules from the primary hydration sphere of the metal ion are displaced by the chelating ligand. Thus there is an increase in the number of particles in the system i.e., randomness of the system increases as shown in the following equation.

$$[M.(H_2O)_x]^{n+} + L \rightarrow [L - M(H_2O)_m]^{n+} + (H_2O)_{x-m}$$

Williams [lii] has pointed out that usually a high entropy value was associated when positively charged metal ions and ligands combined involving the displacement of water molecules, which then become a part of the solvent. Since the water molecules bound to the metal ions are highly distorted and oriented, the entropy is low.

4. CONCLUSION

The value of logk_f for Ni(II)-Isatinbishydrazone complexes calculated at spectrophotometrically. Exothermic nature of the reactions was observed from the value of stability constant. The composition of the complex was 1:1 metal to ligand ratio.

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Fig. (1)- Continuous variation plot of Ni(II)-Isatin-bishydrazone complexes.

Fig. (3)- Molar ratio plot of Ni(II)-Isatin-bishydrazone complexes.

Fig (4)- The variation of the stability constant (Logk_f) of the formation of the Ni(II)-Isatin-bishydrazone complexes, calculation of the thermodynamic parameters.

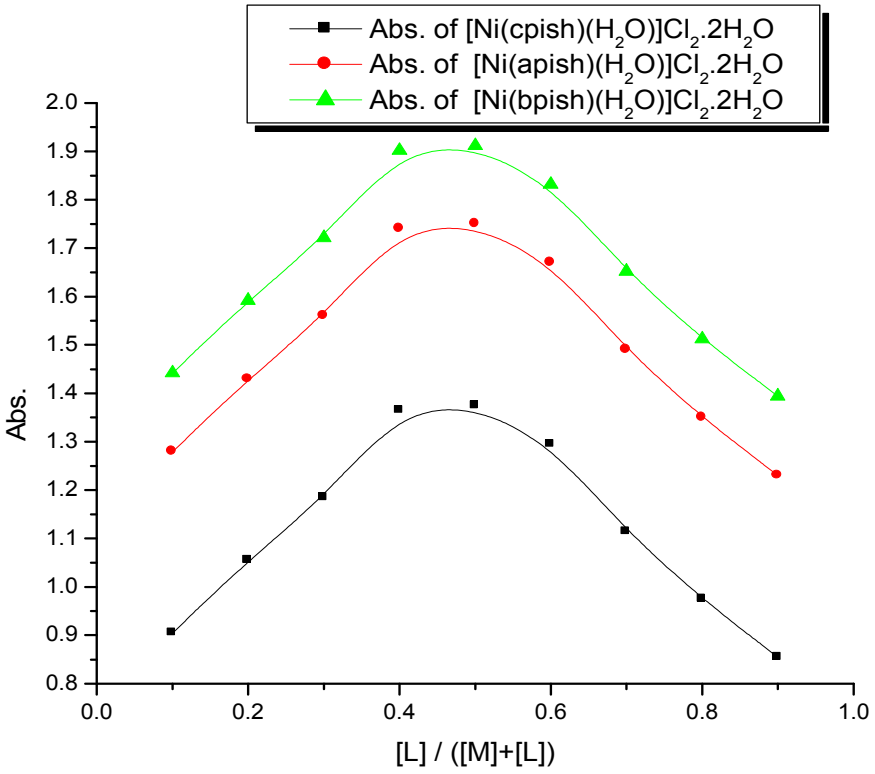

Fig. (1)- Continuous variation plot of Ni(II)-Isatin-bishydrazone complexes.

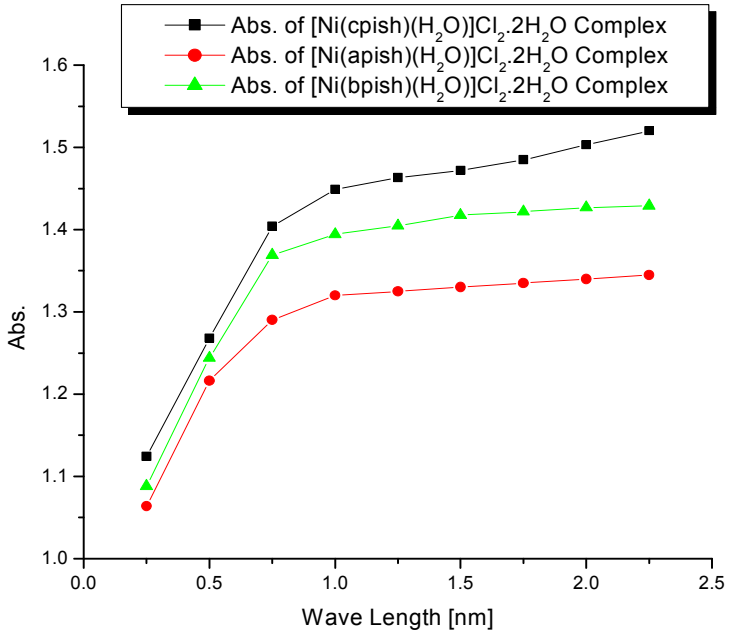

Fig. (2.a)- Molar ratio plot of Ni(II)-Isatin-bishydrazone complexes.

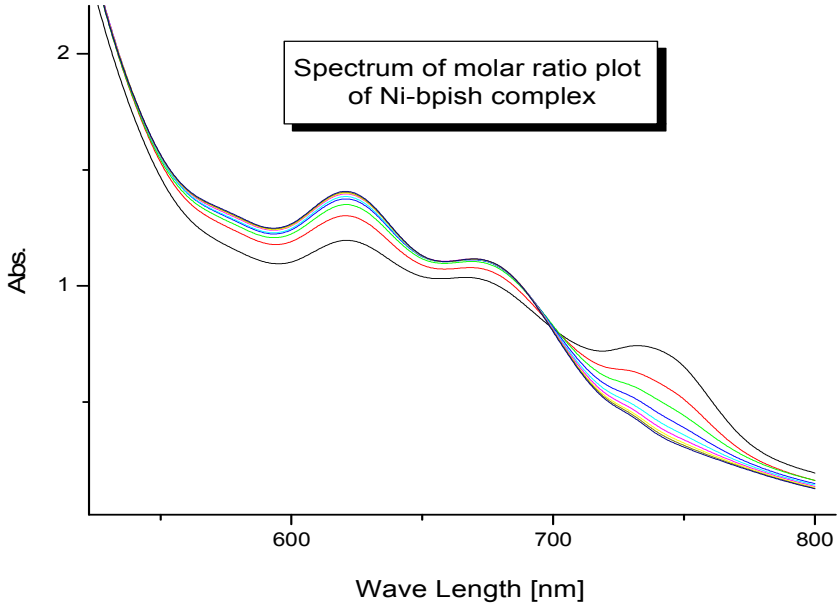

Figure (2.b)- Spectrum of molar ratio plot of Ni-bpish complex

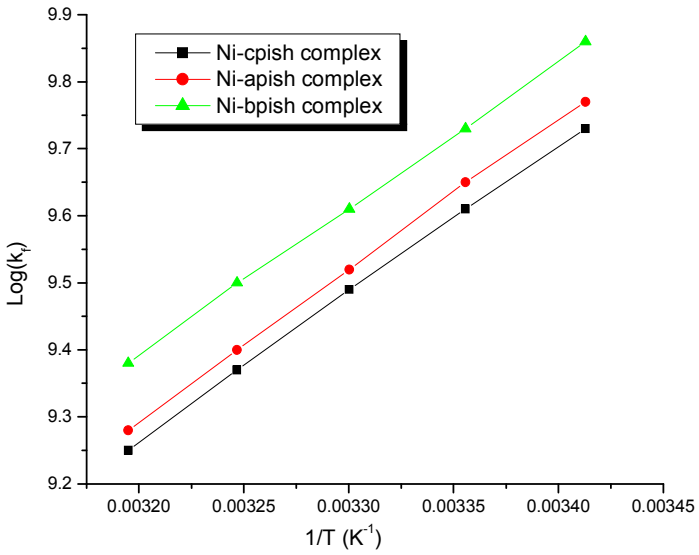

Fig (3.a)- The variation of the stability constant (Logk_f) of the formation of the Ni(II)-Isatin-hydrazone complexes, calculation of the thermodynamic parameters.

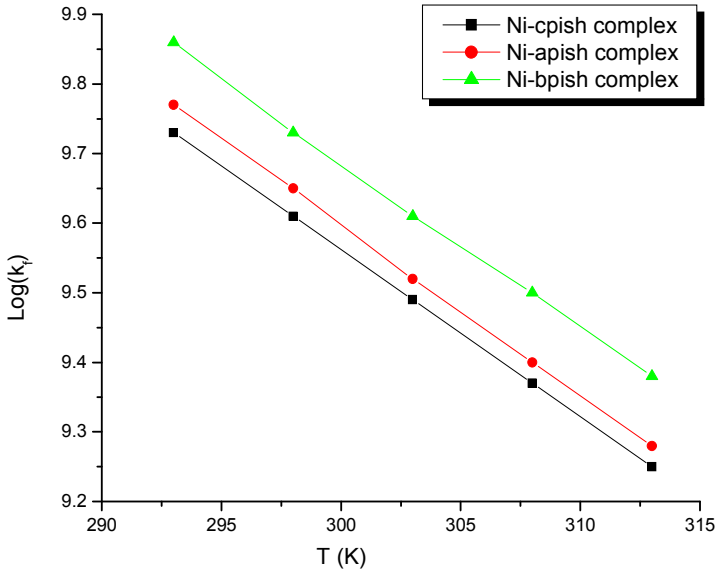

Figure (3.b)- The variation of the stability constant ($LogK_f$) with temperature for the Ni(II)-Isatin-hydrazone complexes.

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Table (1): Stability constants and Thermodynamic parameters.

Complex	Temp. (°C)	K_f (x 10^9)	Log(k_f)	$\Delta H^{\neq}$ (KJ/mol)	$\Delta S^{\neq}$ (KJ/mol.K)	$\Delta G^{\neq}$ (KJ/mol)
Ni-cpish complex	20	5.34	9.73	-42.134	0.042575	-54.6083
	25	4.09	9.61			-54.8212
	30	3.08	9.49			-55.0341
	35	2.34	9.37			-55.2469
	40	1.77	9.25			-55.4598
Ni-apish complex	20	5.89	9.77	-43.193	0.039729	-54.8335
	25	4.47	9.65			-55.0321
	30	3.35	9.52			-55.2307
	35	2.53	9.40			-55.4294
	40	1.93	9.28			-55.628
Ni-bpish complex	20	7.20	9.86	-41.8005	0.046089	-55.3044
	25	5.43	9.73			-55.5348
	30	4.09	9.61			-55.7653
	35	3.14	9.50			-55.9957
	40	2.39	9.38			-56.2262

,$\Delta G^{\neq} = \Delta H^{\neq} - T\,\Delta S^{\neq}$.

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