

Kinetic Study of Transition Metal Complexes with Benzodiazepine Drug (Nifoxipam)

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Abstract

The ligand metal complexes of nifoxipam (NX) with Cr(III), Mn(II) and Ni(II) have been synthesized. Metal to ligand ratio in all complexes has been found to be 1:1. All the complexes have been assigned octahedral stereo chemistry. The thermodynamic parameters such as ΔG , ΔH and ΔS are calculated from the curve of $\log K_s$ verse temperature. It is found that Ni (II) and Mn (II) are the most stable complexes from the data of formation constant and Gibbs free energy.

Key words: Metal ions, kinetic study, metal complexes, nifoxipam.

Introduction

Transition metal complexes of Schiff bases concerning interaction of metal ions with nitrogen and oxygen organic moieties have been of great interest for many years since they are becoming an effective biochemical, analytical and antimicrobial reagents. Many reports have shown that some drugs have greater activity when administered as metal complex as that as free organic compounds [1-3]. Literatures revealed that benzodiazepine and its derivate ives are reported to have, analgesic and anti-inflammatory activity, cardiovascular activity, anti-neoplastic activity, anti- fungal activity, enzyme inhibition activity, antianthelmintic activity, anti-filarial agent, anti- viral activity and anti- ulcer activity [6-8]. Literature survey reveals that very little work, however, have been reported on conductimetric studies of benzodiazepine metal complexes involving pyridine moiety [9]. Literature survey reveals that very little work, however, have been reported on conductimetric studies of macro cyclic metal complexes involving pyridine moiety(Skoog, 1998)..In the present article we reported the preparation and kinetic study of nifoxipam metal complexes with Cr(III), Mn(II) and Ni(II).

Experimental

Physical measurements and analysis Melting points were recorded on a Gallen Kamp melting point apparatus and were corrected. Molar conductance of the solutions of the complexes in DMF ($10^{-3}M$) were measured on PW9526 digital conductivity meter.

Study of complex formation in solution The complexes of the ligand (L) with the selected metal ions [Cr(III), Mn(II) and Ni(II)] were studied in solution using ethanol as solvent, in order to determine (M:L) ratio in the prepared complexes, following molar ratio determine by Job's method [10]. Series of solutions were prepared having a constant concentration (C) $10^{-3}M$ of the hydrated metal chlorides and the ligand (L) at deferent concentration. The [M: L] ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of [M: L].

Stability constant of the complexes (Ks) The stability constant of the (1:1) [M: L] complex, was evaluated using the following equation [9]:

$$K_s = 1 - \alpha / \alpha_2 c \text{ ---- (1)}$$

Where α is the degree of the dissociation of ionization of (C1-C7) was determined by the equation (2):

$$\alpha = (A_s - A_m) / A_m \text{ ----(2)}$$

Or conduct metrically by the equation (3):

$$\alpha = \Lambda_m / \Lambda^\circ \text{ ---- (3)}$$

Λ_m : molar conductance of the complex solution in $10^{-3}M$ (DMF).

Λ° : molar conductance in infinite dilution, and C is the concentration of the complex. The absorbance of the solutions was measured at (λ_{max}) of the maximum absorption, furthermore the molar absorptivity) for the complexes was calculated from absorptivity

$$\Lambda_m = \epsilon_{\max} \cdot b \cdot c \quad \text{--- (4)}$$

where Λ_m is the average of three measurements of the absorption containing the same amount of metal ion and fivefold excess of ligand and b is the depth of the quartz cell, usually equal to 1 cm .

Λ_m = molar conductance were measured in units of $\text{ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$.

SD = standard deviation which is estimated after carrying out three data of experiments. As evident in Table, that stability constant K_s for Ni (II) complex is compared with Cr (III) complex which investigates the presence of d8 configuration and agrees with Irving Williamson [11].

A: molar absorptivity have been measured in $\text{L}^{-1} \cdot \text{mole}^{-1} \cdot \text{cm}$.

B: formation constant of complexes were determined by spectroscopic method.

The stability constant (K_s) was evaluated using the following equations:

$$K_s = (1-\alpha)/\alpha 2c \quad \text{--- (5)} \quad A = \Lambda_m - A_s / \Lambda_m \quad \text{--- (6)}$$

(α) Is the degree of the dissociation (c) is the concentration of the complex in (mole/L) units, (A_s and Λ_m) are the absorbance values of the solution were measured at (λ_{\max}) of the maximum absorption. The molar absorptivity (ϵ_{\max}) (eq.7) has been calculated using equation:

$$A = \epsilon_{\max} \cdot b \cdot C \quad \text{--- (7)} \quad (A)$$

Is the average of three measurements of the absorption containing the same amount of metal ion and three fold excess of ligand, (b) is the depth of the quartz cell usually equal 1cm(Skoog, 1998.).

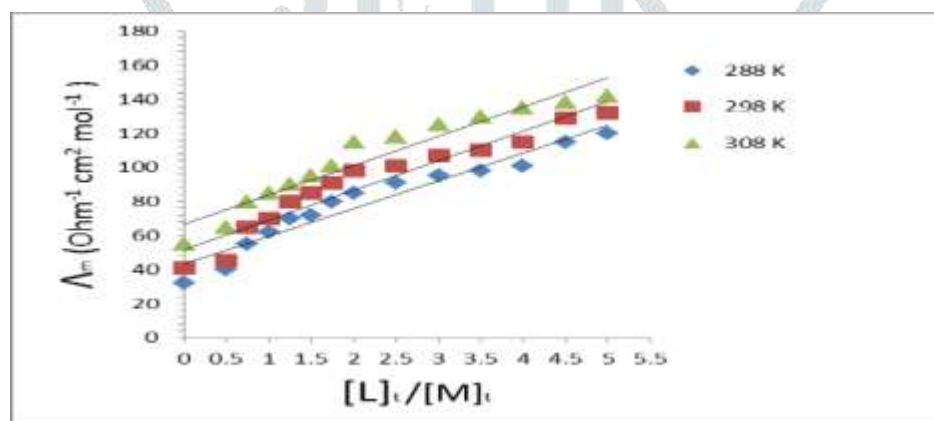


Figure Molar conductance mole-ratio for Mn(II) complex in pure DMF at different temperature.

RESULTS AND DISCUSSION

The UV-Visible spectra of the ligand and their metal complexes were recorded for their solutions in ethanol and DMSO as solvents in the range (200 – 1000) nm. In the case of all complexes, the assignments agree with the proposed stereo chemistry. The results indicate that the molar ratio of (1:1) for complexes yielded high stability. Furthermore the molar absorptivities for all complexes is rather high.

By using the relation $\Lambda_m = K/C$ the molar conductance of the complex (Λ_m) can be calculated where is the molar concentration of 10^{-3} molar of their solutions at ($25 \pm 2^\circ\text{C}$) were measured. It is calculated from the results that Cr(III) , Mn(II) and Ni(II) are electrolytes in 1:1 and 1:2 ratio respectively [12]. The thermodynamic of new metal complex have been measured conductometrically that $\Delta G = -12500$ KJ/mole for Mn(II) complex. In addition the stability constant of Mn(II) complex in DMF various temperature was obtained from variation of molar conduction as a function of ligand/metal cation mole ratios using a Gen plot computer program [13]. Sufficiently, large value of ΔG for Mn(II) complex showed that spontaneous formation of the complexes [14,15]. The thermodynamic parameters Table, free energy ΔG , enthalpy change ΔH and entropy change ΔS were calculated by the following relationships [16] :

$$\Delta G = -RT \ln K_{eq} \quad \text{--- (8)}$$

And from changing the values K_{eq} with $1/T$

$$\left(\frac{d \log K_{eq}}{dt} \right) = \left(\frac{\Delta H}{2.303RT^2} \right) \quad \text{--- (9)}$$

The value of ΔH were estimated. Finally ΔS value was calculated from Gibbs equation:

$$\Delta G = \Delta H - T\Delta S \text{ ---- (10)}$$

Table: Stability constants, and molar absorptivities of the complexes

Complex	As	Am	A	λ_{\max}	Ks(L.I-1)	ϵ_{\max}
Cr (III)	0.57	0.470	0.144	521	12 x 10 ⁵	321
Mn(IV)	0.55	0.23	0.300	265	3.5 x 10 ⁴	8900
Ni(II)	0.46	0.321	0.378	560	9.11 x 10 ⁴	289

Where is As the average of three measurements of the absorption of solution containing a stoichiometric amount of ligand and metal ion.

Table: Thermodynamic parameters for metal complexes in DMF solutions

complex	Λ_m Ohm-1.cm ² .mol ⁻¹	$-\Delta G \text{ C} \pm \text{SD KJ/mole}$	$\Delta H \text{ C} \pm \text{SD KJ/mole}$	$\Delta S \text{ C} \pm \text{SD KJ/mole}$
Cr (III)	177	15.85 ± 2.80 (13.263)	-55.5 ± 6.4	-333 ± 18.9
Mn(IV)	95	18.95 ± 0.44 (14.50)	23.66 ± 8.00	342.5 ± 30.1
Ni(II)	68	20.51 ± 0.56 (25.3*103)	92.71 ± 7.8	671.5 ± 2.500

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