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## Enthalpy changes associated with formation of some complexes of chlorobenzoylthioacetophenone with their therapeutic uses

Kunal Kumar, Nishant Soren &amp; Hashmat Ali\*

University Department of Chemistry, Sido Kanhu Murmu University, Dumka, Jharkhand, India

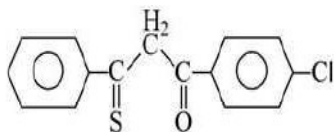
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**Abstract-** The complexes of para-chlorobenzoylthioacetophenone with Manganese, Nickel, Palladium have great Therapeutic uses. These complexes have been found curative in many acute diseases including breast cancer. Para-chlorobenzoylacetophenone the ligand chosen for the present research work is an organic compound of Monothio- $\beta$ -diketone class of compounds. This organic ligand behaves as uninegatively charged bidentate chelating agent. The overall Stability Constants of the said complexes have been determined potentiometrically. Thereafter, Standard Changes in Enthalpy accompanying complex formation were determined to know its contribution in complexation as also its therapeutic uses.

**Key words:** Overall Stability constant, Medicinal values, Enthalpy, Therapeutic uses, Free energy

### INTRODUCTION

The ligand (I) chosen for complexation with bivalent manganese, nickel, palladium and platinum is p-chlorobenzoylthioacetophenone. It belongs to Monothio- $\beta$ -diketone<sup>1-3</sup> class of compounds and behaves as a uninegatively charged bidentate ligand through its enol or enethiol<sup>4-6</sup> form to form stable six-membered chelate<sup>7</sup>.



**Fig. 1- p-chlorobenzoylthioacetophenone**

However, no attempt has been made so far to study the Standard Change in Enthalpy ( $\Delta H^\circ$ ) accompanying the

formation of above complexes as also to know the therapeutic uses of these complexes.

In this present communication we report the Stability Constants<sup>8-10</sup> of the complexes of p-chlorobenzoylthioacetophenone with bivalent Mn, Ni, Pd & Pt at three different temperatures 10°C, 20°C and 30°C and changes taking place accompanying the said complexation together with therapeutic significance of the complexes. Stability constant is determined by Calvin-Bjerrum's potentiometric technique<sup>11-13</sup> as modified by Irving and Rossotti<sup>13,14</sup>.

### MATERIALS & METHODS

The ligand, p-chlorobenzoylthioacetophenone was synthesised by Claisen condensation of o-ethylthiobenzoate with p-chloroacetophenone in presence of sodamide as shown below.

\*Corresponding author :

Phone : 9534064385

E-mail : dr.hashmatiali96@gmail.com

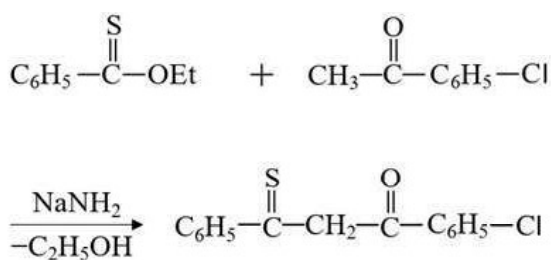


Fig. 2- Synthesis of p-chlorobenzoylthioacetophenone

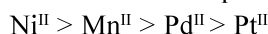
The standard solution of ligand was prepared in dioxan.<sup>15,16</sup> Metal chloride solutions were also standardised. The temperatures were kept constant at 10°C, 20°C and 30°C respectively for three different experimental sets. Following three mixtures were prepared:

- (i) 5 ml 0.4 M HCl + 5 ml M KCl
- (ii) Mixture (i) + 5 ml 0.02 M Ligand solution
- (iii) Mixture (ii) + 5ml 0.004 M Metal ion solution

Table 1- Stepwise and Overall Stability Constant Data of Metal Complexes at 10°C, 20°C and 30°C.  
[Log = pKa= 10.92 at t = 10°C, 10.77 at t = 20°C & 10.68 at t = 30°C].

Metal Ions	Temperatures								
	10°C			20°C			30°C		
	Log K <sub>1</sub>	Log K <sub>2</sub>	Log β	Log K <sub>1</sub>	Log K <sub>2</sub>	Log β	Log K <sub>1</sub>	Log K <sub>2</sub>	Log β
Ni <sup>2+</sup>	10.59	09.75	20.34	10.37	09.48	19.85	10.31	09.45	19.76
Mn <sup>2+</sup>	09.48	08.79	18.27	09.32	08.69	18.01	09.24	08.55	17.79
Pd <sup>2+</sup>	09.11	08.51	17.62	09.12	08.39	17.51	08.83	08.29	17.12
Pt <sup>2+</sup>	08.93	08.39	17.32	08.77	08.23	17.00	08.63	08.14	16.77

From the above table, it is obvious that the Stability Constants of Metal complexes follow the trend:



The value of Standard change in Free energy ( $\Delta G^\circ$ ) at a given temperature was obtained by the thermodynamic expression,  $\Delta G^\circ = -2.303 RT \log \beta$ , where,  $\Delta G^\circ$  = Standard Change in Free energy accompanying the complexations,  $\beta$  = Overall Stability Constant and R = Constant.

The  $\Delta G^\circ$  values at three different temperatures for each metal complex formed are arranged in Table-2.

Table 2-  $\Delta G^\circ$  values of Bivalent Metal Complexes at three different temperatures.  
( $\mu = 0.1$  M KCl and Medium = 75% aqueous Dioxan)

Metal ions	$-\Delta G^\circ$ (kcal/mol)		
	Temperatures		
	10 ± 1°C	20 ± 1°C	30 ± 1°C
Ni <sup>2+</sup>	26.34	26.61	27.40
Mn <sup>2+</sup>	23.66	24.15	24.67
Pd <sup>2+</sup>	22.82	23.48	23.74
Pt <sup>2+</sup>	22.43	22.79	23.25

Total volume in each case was maintained 50 ml.

The mixtures were titrated in duplicate against 0.2 M KOH solution. The pH was measured in O<sub>2</sub>-free nitrogen atmosphere. The pH-meter readings and the volume of alkali added was plotted in each case and referred to (1) Acid, (2) Ligand and (3) Complex Titration Curves respectively.

$\bar{n}_A$  values at various B-values were obtained from acid and ligand titration curves. Plot of  $\bar{n}_A$  vs B gave the Formation Curve of the Ligand-Proton Complex wherefrom pKa value of ligand was obtained by Half-Integral method. Values of  $\bar{n}$  and pL were known by Ligand and Complex titration curves and Formation curves of the complexes were drawn by plotting  $\bar{n}$  vs pL. These curves gave the values of Stepwise Stability constants, Log K<sub>1</sub> and Log K<sub>2</sub> obtainable through Half-Integral method. Results are reported below in Table-1 below.

Thus, decrease in Standard Free energy change value is lower at 10°C than at 20°C which in turn is lower than those at 30°C for each complex and in the case of each metal ion.

Determination of  $\Delta H^\circ$ :

The Standard change in Enthalpy<sup>17,18</sup>, ( $\Delta H^\circ$ ) accompanying the above complex formation reaction was determined with the help of following isobar equation.

$$\frac{d \ln \beta}{dT} = \frac{\Delta H^\circ}{RT^2}$$

The above equation may be rearranged as:

$$\frac{d(\log \beta)}{d(1/T)} = \frac{-\Delta H^\circ}{2.303R}$$

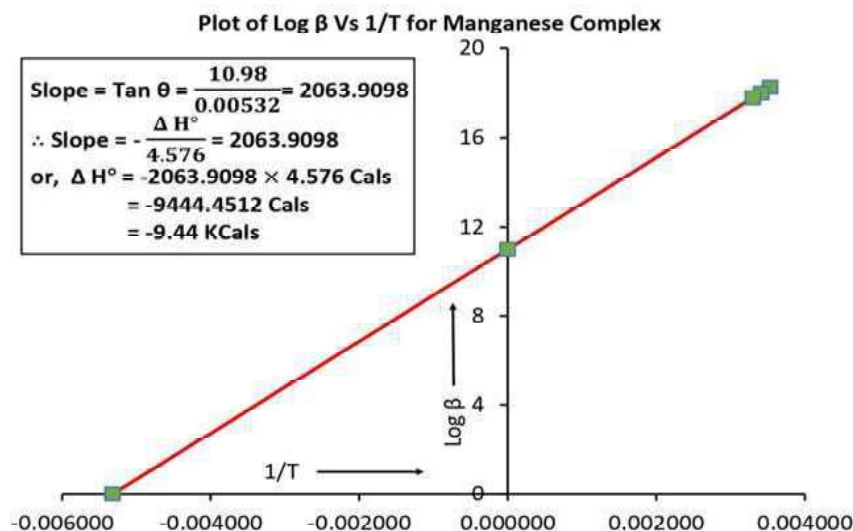
Taking R = 1.987 cal/deg./mol, we have

$$\frac{d(\log \beta)}{d(1/T)} = \frac{-\Delta H^\circ}{4.576}$$

The gradient of the tangent drawn at the point corresponding to a particular temperature on the curve obtained by plotting the values of Log β as a function of

$1/T$  will be equal to  $\frac{-\Delta H^\circ}{4.576}$ . Gibbs-Helmholtz equation was employed to determine the value of  $\Delta H^\circ$ . The values of

$\Delta H^\circ$  obtainable by the above ways are furnished below in Table-3.



**Fig. 3- Standard change in Enthalpy for Manganese Complex**

Similar, graphs were obtained for Nickel Complex, Palladium Complex and Platinum Complex.

**Table 3-  $\Delta H^\circ$  values of Bivalent Metal Complexes in Kcals  $\text{mol}^{-1}$  at three different temperatures.**

Metal ions	$-\Delta H^\circ (\text{kcal mol}^{-1})$		
	By Linear Plot Method	By Gibbs-Helmholtz equation at $30 \pm 1^\circ\text{C}$	Average values
$\text{Ni}^{2+}$	11.58	11.08	11.33
$\text{Mn}^{2+}$	09.44	09.35	09.39
$\text{Pd}^{2+}$	09.70	10.00	09.85
$\text{Pt}^{2+}$	10.85	10.77	10.81

## RESULTS & DISCUSSIONS

From the Thermodynamic expression,  $-RT \ln \beta = \Delta G^\circ$ , it follows that  $\beta$  (overall stability constant) increases as  $\Delta G^\circ$  (Standard change in Free energy) becomes more negative and hence a more stable metal complex is formed. In the present investigation, we find that like Stability order mentioned in Table. 1, the decrease in Free energy change follows the same trend:  $\text{Ni}^{II} > \text{Mn}^{II} > \text{Pd}^{II} > \text{Pt}^{II}$ . Thus, the complexes formed are Free energy stabilized. So, far as Standard change in Enthalpy is concerned, Linear Plot Method(LPM) as well as use of Gibbs-Helmholtz equation gives similar values for  $\Delta H^\circ$  for all the complexes formed. The highest as well as the lowest values are shown by the

complexes of Nickel and Manganese respectively which are the members of first transition elements series. However, compared to Palladium, a member of second transition series, Platinum belonging to third transition elements series has unexpectedly higher value of Standard change in Enthalpy. The average values of  $\Delta H^\circ$  obtainable from LPM and by utilising G-H equation for the complexes of Nickel, Platinum, Palladium and Manganese are 11.33, 10.81, 09.85 and 09.39 Kcals/mol respectively in decreasing order as shown in Table 3.

## CONCLUSION

The negative values of  $\Delta H^\circ$  for each metal complex as listed in Table-3 signifies that the complex formation reactions are exothermic in nature. Thus, all the complexes formed are enthalpy stabilised. Though there is discrepancy in the values of  $\Delta H^\circ$  obtained in the case of complexes of Mn (a member of 1<sup>st</sup> transition series) and Pd (a member of 2<sup>nd</sup> transition series) compared to those of Pt,  $\Delta H^\circ$  contribute much in stabilising the metal complexes in each case and at each temperature.

Having good Enthalpy change values, the above bivalent transition metal complexes have great medicinal values and have been found curative in many acute diseases especially in breast cancer. These have been found essential in storage and transport of oxygen and as electron transfer agent needed in cancer chemotherapy.

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