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# THERMAL STUDIES ON THE CHELATION BEHAVIOUR OF BIVALENT METAL COMPLEXES OF BIOLOGICALLY ACTIVE 2-HYDROXY-1-NAPHTHALDEHYDE MONOSEMICARBAZONE (HNAS)

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## ABSTRACT

Thermal behaviour of bivalent metal complexes with 2-hydroxy-1-naphthaldehyde monosemicarbazone (HNAS) has been studied potentiometrically in 75% (v/v) aqueous dioxan medium at various temperatures. The method of Bjerrum and Calvin [J. Bjerrum, Metal Amino Formation of Aqueous Solution, Hasse, Copenhagen, 1941, p. 298; M. Calvin and K.W. Wilson, J. Am. Chem. Soc., 67 (1945) 2003] as modified by Irving and Rossotti [H.M. Irving and H.S. Rossotti, J. Chem. Soc. (1954) 2904] has been used to calculate the values of $\bar{n}$ and pL. The stability constants have been calculated on an IBM 360 FORTRAN IV computer using the weighted least-squares method. The values of $S_{\min}$ have also been calculated. The order of stability constants was found to be $UO_2 > Cu > Ni > Co > Zn > Pb > Cd > Mn > Mg$. The other thermodynamic parameters ($\Delta G$, $\Delta H$ and $\Delta S$) have been calculated from the stability constants obtained for different temperatures at constant ionic strength.

## INTRODUCTION

The semicarbazones and thiosemicarbazones of certain aldehydes and ketones have significant antimicrobioal activities [1-5]. Domagk et al. [6] first reported the anti-tubercular activities of metal semicarbazones and thiosemicarbazones. Since then many papers have appeared on the pharmacology of these compounds. The activity of semicarbazones is thought to be due to their power of chelation with traces of metal ions present in biological systems.

As part of an extended study undertaken in our laboratories on the thermal behaviour of metal complexes of biologically active ligands, we describe here the thermal stabilities of bivalent metal complexes with 2-hydroxy-1-naphthaldehyde monosemicarbazone (HNAS) at different temperatures in 75% (v/v) aqueous dioxan medium.

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## EXPERIMENTAL

### *Apparatus*

A digital pH-meter (ECIL model pH 5651) with a glass electrode (0–14 pH range) was used for pH measurements. The pH-meter was standardised with potassium hydrogen phthalate and phosphate buffers before performance of the titrations. All measurements were made at a definite temperature maintained constant by using a MLW (West Germany) (NBE type) thermostat. An IBM 360 FORTRAN IV computer was used for most of the calculations.

### *Chemicals*

2-Hydroxy-1-naphthaldehyde monosemicarbazone (HNAS) was prepared by dissolving the requisite amount of 2-hydroxy-1-naphthaldehyde in a minimum amount of alcohol and adding to it an aqueous solution containing semicarbazide hydrochloride and an equal amount of anhydrous sodium acetate. The mixture was refluxed for 1 h and HNAS was precipitated by adding dilute hydrochloric acid to the solution. The HNAS thus obtained was recrystallised from ethanol. HNAS solution was prepared in freshly distilled dioxan. The purity of HNAS was checked by TLC and elemental analysis. The decomposition temperature of HNAS is 214° C.

The solutions of bivalent metal ions, viz. Mg(II), Mn(II), Cd(II), Pb(II), Zn(II), Co(II), Ni(II), Cu(II) and $UO_2$(II) were standardised by conventional methods.

TMAH ($Me_4NOH$) (Merck) in 75% dioxan (aqueous) was used as a titrant. The solution was standardised with oxalic acid $(COOH)_2$. Perchloric acid ($HClO_4$) was standardised with $Na_2CO_3$ and diluted to the required molarity (0.05 M). $NaClO_4$ (Merck) was used to maintain the ionic strength.

Dioxan (Merck) was freed from peroxide by refluxing it with sodium metal for 24 h and was freshly distilled over sodium before use. All other chemicals were of reagent grade.

### *Titration technique*

Investigations were carried out at four temperatures, viz. 20, 30, 40 and 50° C at 0.1 M $NaClO_4$ ionic strength. For each set of experiments, the final volume was made up to 20 ml, maintaining the 75% aqueous dioxan medium. The following solutions (total volume = 19.67 ml instead of 20 ml, due to contraction in volume on mixing dioxan and water) were titrated potentiometrically against standard 0.05 M TMAH, in 75% aqueous dioxan (v/v) to determine $\bar{n}$ and pL values of the complexes: (i) 0.8 ml of $HClO_4$ (0.05 M) + 1.0 ml of $NaClO_4$ (2 M) + 0.5 ml of $KNO_3$ or $K_2SO_4$ (0.01

M) + 2.7 ml of $H_2O$ (double distilled) + 15.0 ml of dioxan; (ii) 0.8 ml of $HClO_4$ (0.05 M) + 1.0 ml of $NaClO_4$ (2 M) + 0.5 ml of $KNO_3$ or $K_2SO_4$ (0.01 M) + 0.2 ml of $H_2O$ + 10.0 ml of ligand solution (0.01 M) + 7.5 ml of dioxan; (iii) 0.8 ml of $HClO_4$ (0.05 M) + 1.0 ml of $NaClO_4$ (2 M) + 0.5 ml of metal solution (0.02 M) + 0.2 ml of $H_2O$ + 10.0 ml of ligand solution (0.01 M) + 7.5 ml of dioxan.

The titrations were carried out in a covered, double-walled glass cell in an atmosphere of $N_2$, which was presaturated with solvent (75% dioxan in $H_2O$) before being passed into the reaction solution.

From the titration curves of solutions (i) and (ii), the values of $\bar{n}_H$ were calculated at various pH values. The p*K*a value of the ligand was found by plotting log $(\bar{n}_H/1-\bar{n}_H)$ vs. pH and the values thus obtained were 10.45, 10.25, 10.02, 9.75 at 20, 30, 40 and 50 °C, respectively, with $\mu = 0.1$ M $NaClO_4$. From the titration curves of solutions (i), (ii) and (iii), $\bar{n}$ values of the metal complexes were determined at various pH values, the corresponding pL values were calculated. The $\bar{n}$ and pL data were analysed using the weighted least-squares method developed by Sullivan et al. [10] on an IBM 360 FORTRAN IV computer to get $\beta_n$ values. The weighted least squares treatment determined by the set of $\beta_n$ values which make the function $U$

$$U = \sum_{n=0}^{N} (y - x - nz)\beta_n x^n$$

nearest to zero, by minimising $S$,

$$S = \sum_{i=1}^{I} W_i U^2(x_i y_i z_i)$$

with respect to variation in $\beta_n$. $S_{\min}$ has the same statistical distribution as $\chi^2$ with $K$ degrees of freedom and the weight defined in accordance with Sullivan et al. [11]. $S_{\min}$ can be equated to $\chi^2$. The stability constants thus calculated are given in Table 1. The values of $\Delta H$ were calculated by the graphical method of Yatsimirskii and Vaslev [12], while values of $\Delta G$ and $\Delta S$ were calculated by conventional methods.

## RESULTS AND DISCUSSION

In the present investigations it has been noticed that the values of acid dissociation constants p*K*a and stability constants decrease with increasing temperature of the medium and acidity of metal ions. The order of stability constants (log $K_1$) of metal complexes of HNAS is found to be $UO_2$ > Cu > Ni > Co > Zn > Pb > Cd > Mn > Mg. The order is in good agreement with the order found by Meller and Maley [13] and Irving and Williams [14,15].

TABLE 1

Stability constants of bivalent metal complexes of 2-hydroxy-1-naphthaldehyde monosemicarbazone (HNAS)

| Metal ion | Weighted least squares method | | | $S_{min}$ |
|---|---|---|---|---|
| | log $K_1$ | log $K_2$ | log $\beta_2$ | |
| $\mu = 0.1$ M $NaClO_4$, temp. = 20 ± 0.5 °C | | | | |
| $H^+$ | 10.45 | – | – | – |
| $UO_2$(II) | 9.98 | 9.36 | 19.34 | 0.1164 |
| Cu(II) | 9.10 | 8.25 | 17.35 | 0.2512 |
| Ni(II) | 8.93 | 7.99 | 16.92 | 0.2233 |
| Co(II) | 8.60 | 7.58 | 16.18 | 0.0098 |
| Zn(II) | 7.82 | 6.43 | 14.25 | 0.0196 |
| Pb(II) | 6.05 | 5.80 | 11.85 | 0.0549 |
| Cd(II) | 5.65 | 4.23 | 9.88 | 0.0302 |
| Mn(II) | 5.03 | 4.17 | 9.20 | 0.0341 |
| Mg(II) | 3.22 | 3.03 | 6.25 | 0.0051 |
| $\mu = 0.1$ M $NaClO_4$, temp. = 30 ± 0.5 °C | | | | |
| $H^+$ | 10.25 | – | | – |
| $UO_2$(II) | 9.73 | 8.57 | 18.30 | 0.0108 |
| Cu(II) | 8.81 | 7.40 | 16.21 | 0.0331 |
| Ni(II) | 8.75 | 7.05 | 15.80 | 0.0058 |
| Co(II) | 8.15 | 6.73 | 14.88 | 0.0225 |
| Zn(II) | 7.51 | 6.14 | 13.65 | 0.0229 |
| Pb(II) | 5.66 | 4.50 | 10.16 | 0.0340 |
| Cd(II) | 5.57 | 4.00 | 9.57 | 0.0045 |
| Mn(II) | 4.99 | 3.73 | 8.72 | 0.0271 |
| Mg(II) | 2.94 | 2.55 | 5.49 | 0.0053 |
| $\mu = 0.1$ M $NaClO_4$, temp. = 40 ± 0.5 °C | | | | |
| $H^+$ | 10.02 | – | – | – |
| $UO_2$(II) | 9.54 | 8.58 | 18.12 | 0.0073 |
| Cu(II) | 8.64 | 7.23 | 15.87 | 0.0344 |
| Ni(II) | 8.27 | 7.02 | 15.30 | 0.0314 |
| Co(II) | 7.71 | 6.48 | 14.19 | 0.0152 |
| Zn(II) | 7.25 | 5.52 | 12.77 | 0.0012 |
| Pb(II) | 5.54 | 4.39 | 9.93 | 0.0627 |
| Cd(II) | 5.19 | 4.19 | 9.38 | 0.0528 |
| Mn(II) | 4.85 | 3.53 | 8.38 | 0.0024 |
| Mg(II) | 2.87 | 1.38 | 4.25 | 0.0001 |
| $\mu = 0.1$ M $NaClO_4$, temp. = 50 ± 0.5 °C | | | | |
| $H^+$ | 9.75 | – | – | – |
| $UO_2$(II) | 9.39 | 7.95 | 17.34 | 0.0357 |
| Cu(II) | 8.37 | 7.09 | 15.46 | 0.3732 |
| Ni(II) | 7.86 | 6.59 | 14.45 | 0.3170 |
| Co(II) | 7.53 | 6.27 | 13.80 | 0.0559 |
| Zn(II) | 7.07 | 5.88 | 12.95 | 0.0198 |
| Pb(II) | 5.43 | 4.16 | 9.59 | 0.1408 |
| Cd(II) | 5.07 | 4.74 | 9.81 | 0.0518 |
| Mn(II) | 4.64 | 3.64 | 8.28 | 0.0038 |
| Mg(II) | 2.44 | 2.42 | 4.86 | 0.0050 |

In these studies the stability constant decreases as the temperature increases along with the p$K$a value. These results are in good agreement with those of Pitzer [16]. The log $K_1$, log $K_2$, log $\beta_2$ and $S_{\min}$ values at different temperatures ($\mu = 0.1$ M) are given in Table 1. In all cases the values of log $K_1$ are greater than those of log $K_2$.

The regularity of this stability constant can be correlated with a monotonic decrease in the ionic radii and monotonic increase in the second ionisation potential, which in passing from Mn to Cu may be taken to indicate that either coordination has not altered the electronic ground state of the metal ions or that any modifications are of secondary importance. For these chelates, $\bar{n}$ values greater than 2.0 have not been obtained. We therefore conclude that not more than two chelates, i.e. 1 : 1 and 1 : 2 (M : L) are found in each system.

Finally, in view of the very low ($5 \times 10^{-4}$ M) concentration of metal ions used in the titration, it has been assumed that the possibility of formation of polynuclear complexes is negligible.

The thermodynamic parameters ($\Delta G$, $\Delta H$ and $\Delta S$) were calculated by using the following relationships

$$\Delta G = -RT \ln K$$

$$\mathrm{d} \log K/\mathrm{d}(1/T) = -\Delta H/2.303R$$

$$\Delta S = (\Delta H - \Delta G)/T$$

The overall free energy change and enthalpy and entropy changes at 20 ± 0.5 °C are reported in Table 2. The negative free energy change ($\Delta G$) in each case indicates that the chelation is spontaneous. Further, $\Delta G$ becomes more negative with increase in temperature suggesting an increase in the extent of complex formation at lower temperature. The enthalpy changes are exothermic. The change in entropy upon complexation is related both to

TABLE 2

Thermodynamic parameters of bivalent metal complexes of 2-hydroxy-1-naphthaldehyde monosemicarbazone (HNAS) at $\mu = 0.1$ M $NaClO_4$ and temp. = $20 \pm 0.5$ °C

| Metal ions | $-\Delta G$ (kcal $mol^{-1}$) | $-\Delta H$ (kcal $mol^{-1}$) | $\Delta S$ (kcal $K^{-1}$ $mol^{-1}$) |
|---|---|---|---|
| $UO_2$(II) | 13.38 | 7.85 | +0.0188 |
| Cu(II) | 12.20 | 10.71 | +0.0050 |
| Ni(II) | 11.97 | 20.67 | −0.0297 |
| Co(II) | 11.53 | 18.69 | −0.0244 |
| Zn(II) | 10.48 | 10.71 | −0.0007 |
| Pb(II) | 8.11 | 4.35 | +0.0128 |
| Cd(II) | 7.57 | 3.51 | +0.0138 |
| Mn(II) | 6.74 | 4.77 | +0.0067 |
| Mg(II) | 4.31 | 10.99 | −0.0227 |

changes in the number of particles in the system and to changes in the mode of vibration of particles in the system.

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