# Stabilities of Some Bivalent Transition Metal Ions with 2-Hydroxy naphthaldehyde Semicarbazones and Thiosemicarbazones in Dioxane-Water Mixtures: A Potentiometric Study

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**Summary.** Equilibria between 2-hydroxy naphthaldehyde derivatives (semicarbazone and thiosemicarbazone) and proton or some bivalent metal ions have been investigated potentiometrically at a constant ionic strength and different compositions of the mixed solvent (dioxane : water). The method of Bjerrum and Calvin [1, 2], as modified by Irving and Rossotti [3], has been used to determine the values of $\bar{n}$ and $pL$. The stability constants have been calculated following Sullivan et al. [4] to give $\beta_n$ values. The values of $S_{min} = \chi^2$ have also been calculated. The order of stability constants was found to be $UO_2^{2+} > Cu^{2+} > Ni^{2+} > Co^{2+} > Zn^{2+} > Pb^{2+} > Cd^{2+} > Mn^{2+} > Mg^{2+}$. The effect of varying the dielectric constant of the medium on the stability constants of the complexes has also been investigated at an ionic strength of $0.100\,M$ $NaClO_4$ and a temperature of $20 \pm 0.5$°C.

**Keywords.** Bivalent metal ion; 2-hydroxy-1-naphthaldehyde derivatives; formation constant; potentiometry.

**Die Stabilitäten einiger bivalenter Übergangsmetallionen mit 2-Hydroxynaphthaldehyd-Semicarbazonen und -Thiosemicarbazonen in Dioxan-Wasser-Mischungen: Eine potentiometrische Studie**

**Zusammenfassung.** Es wurden die Gleichgewichte zwischen 2-Hydroxynaphthaldehyd-Semicarbazonen und -Thiosemicarbazonen einerseits und Proton oder zweiwertigen Übergangsmetallionen andererseits potentiometrisch bei einer konstanten Ionenstärke und verschiedenen Zusammensetzungen von Dioxan und Wasser als gemischtem Lösungsmittel untersucht. Die Methode von Bjerrum und Calvin nach der Modifikation von Irving und Rossotti wurde zur Evaluierung der Werte für $\bar{n}$ und $pL$ verwendet. Die Stabilitätskonstanten und $\beta_n$-Werte wurden nach Sullivan et al. berechnet. Die Werte $S_{min} = \chi^2$ wurden ebenfalls bestimmt. Die Reihenfolge der Stabilitätskonstanten war $UO_2^{2+} > Cu^{2+} > Ni^{2+} > Co^{2+} > Zn^{2+} > Pb^{2+} > Cd^{2+} > Mn^{2+} > Mg^{2+}$. Außerdem wurde der Effekt wechselnder Dielektrizitätskonstanten des Lösungsmittels auf die Stabilitätskonstanten der Komplexe bei einer Ionenstärke von $0.100\,M$ $NaClO_4$ und einer Temperatur von $20 \pm 0.5$°C untersucht.
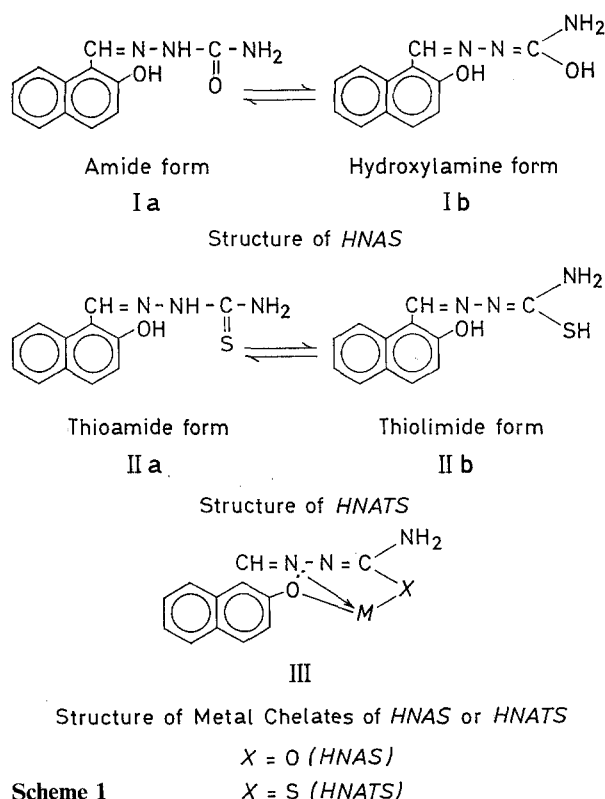
## Introduction

The derivatives of 2-hydroxy naphthaldehyde are potential analytical [5] and biological [6] reagents. The semicarbazones and thiosemicarbazones of certain al-

dehydes and ketones have significant antitubercular activities [7 − 11]. Domagk et al. [12] reported for the first time the antitubercular activities of metal semicarbazones and thiosemicarbazones. Since then a number of papers have appeared on the pharmacology of these compounds. The activity of semicarbazones and thiosemicarbazones is thought to be due to their power of chelation with traces of metal ions present in biological system.

As part of an intensive study undertaken in our laboratory on the chelation behavior of metal complexes of biologically active O-hydroxy naphthaldehyde and its derivatives [13, 14], we describe here the effect of varying the dielectric constant of the medium on the chelation behaviour of bivalent metal complexes of semicarbazone and thiosemicarbazone of 2-hydroxy naphthaldehyde (*HNAS* and *HNATS*) using potentiometric technique.

## Materials and Methods

The semicarbazone or thiosemicarbazone of 0-hydroxy naphthaldehyde (*HNAS* and *HNATS*) was prepared by reacting the requisite amount of 2-hydroxy naphthaldehyde (Aldrich Chemical Company, Inc. U.S.A.) dissolved in the minimum amount of absolute ethanol with semicarbazides and thiosemicarbazide hydrochloride (Fluka A.R.) in water containing glacial acetic acid. The reaction mixture was refluxed for 2 h (semicarbazone derivative) or 4 h (thiosemicarbazone derivative) filtered and cooled in ice. The semicarbazone or thiosemicarbazone of 0-hydroxy naphthaldehyde (*HNAS* or *HNATS*) was precipitated by adding dilute hydrochloric acid and recrystallized from ethanol. The purity of these newly prepared compounds was checked by thin layer chromatography, elemental analysis, melting point, IR and $^1$H-NMR spectra.



Amide form                     Hydroxylamine form
I a                                      I b
Structure of *HNAS*

Thioamide form                 Thiolimide form
II a                                     II b
Structure of *HNATS*

III
Structure of Metal Chelates of *HNAS* or *HNATS*

X = O *(HNAS)*
Scheme 1              X = S *(HNATS)*

On the basis of the analyses and using the spectral study of Varshney et al. [15], the tentative structures of *HNAS* (amide form in solid and hydroxylamine form in solution), *HNATS* (thioamide form in solid and thiolimine form in solution), and the metal chelates of *HNAS* and *HNATS* are as shown in Scheme 1.

The *HNAS* or *HNATS* solution was prepared in freshly distilled 1,4-dioxane (E. Merck). The solution of bivalent metal ions, viz. $UO_2^{2+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Zn^{2+}$, $Pb^{2+}$, $Cd^{2+}$, $Mn^{2+}$, and $Mg^{2+}$ were standardized by conventional methods. $Me_4NOH$ (*TMAH*) (E. Merck, AG, Darmstadt) was used as titrant in varying the percentage (v/v) of dioxane in the mixed solvent. Its solution was standardised with oxalic acid.

$HClO_4$ was standardised with $Na_2CO_3$ and diluted to the required molarity (0.05 M) with conductivity $H_2O$. $NaClO_4$ (E. Merck) was used to maintain the ionic strength. 1,4-Dioxane, A.R. (B.D.H.) was purified by the method given by Vogel [16].

A digital *pH* meter (ECIL, model pH 5651) in conjunction 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 performing the titration. All measurement were made at a definite temperature maintained constant by using an MLW (West Germany) (NBE type) thermostat. A PC-XT computer was used for most of the calculations.

The following solutions were titrated potentiometrically against standard 0.05 M *TMAH* in 75% (v/v) dioxane-water medium.

$0.8\ cm^3\ HClO_4$ (0.05 M) + $1.0\ cm^3\ NaClO_4$ (2.0 M) + $2.7\ cm^3$ double distilled water + $15\ cm^3$ dioxane + $0.5\ cm^3\ KNO_3$ or $K_2SO_4$ (0.02 M). (A)

$0.8\ cm^3\ HClO_4$ (0.05 M) + $1.0\ cm^3\ NaClO_4$ (2.0 M) + $0.2\ cm^3$ double distilled water + $0.5\ cm^3\ K_2SO_4$ or $KNO_3$ (0.02 M) + $10.0\ cm^3$ ligand (*HNAS* or *HNATS*) (0.01 M) + $7.5\ cm^3$ dioxane. (B)

$0.8\ cm^3\ HClO_4$ (0.05 M) + $1.0\ cm^3\ NaClO_4$ (2.0 M) + $0.2\ cm^3$ double distilled water + $0.5\ cm^3$ metal ion solution (0.02 M) + $10.0\ cm^3$ ligand (*HNAS* or *HNATS*) (0.01 M) + $7.5\ cm^3$ dioxane. (C)

The details of the titration procedure adopted were given in an earlier paper [14]. Investigations were carried out at a definite ionic strength 0.1 M $NaClO_4$ at $20 \pm 0.5°C$ varying the solvent composition [75%, 60%, 50%, and 40% (v/v) dioxane-water medium]. For each set of experiments, the final volume was made upto $20\ cm^3$. Each set was titrated against 0.05 M *TMAH*. The titrations were carried out in a covered double-walled glass cell in an atmosphere of $N_2$, which was presaturated with the mixed solvent (dioxane in water), before being passed into the reaction solution. The concentration of $HClO_4$, *HNAS* or *HNATS*, and metal ions were 0.002 M, 0.005 M, and 0.0005 M, respectively.

The *pH* values in aquo-organic solvent mixture were corrected using the method of Van Uitert and Hass [17] and volume corrections were also applied according to the method of Rao and Mathur [18].

From the titration curves of solutions A and B, the parameter $\bar{n}_H$, the average number of proton bound per free ligand ion, were determined by the expressions described by Irving and Rossotti [3] in order to evaluate the $pK_a$ value of the ligand. The values of log $(\bar{n}_H/1-\bar{n}_H)$ versus *pH* gave linear plots having intercepts equal to $pK_a$ and slopes to unity. During complexation, the phenolic group of *HNAS* or *HNATS* dissociates first and the $pK_a$ value of the ligand (*HNAS* or *HNATS*) corresponds to the dissociation of this group. Thus, *HNAS* or *HNATS* acts as a monobasic acid.

The values of $\bar{n}$, the average number of ligand molecules bound per metal ion and *pL*, the free ligand exponent, were calculated on a PC-XT computer using the

titration curves of solutions A, B, and C. The corresponding values of stability constants have been calculated using the weighted least squares method of Sullivan et al. [4]. The weighted least squares method determines the set of $\beta_n$ values which makes the function $U$,

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

nearest to zero by minimizing $S$,

$$\left[ S = \sum_{i=1}^{I} U^2(x_i, y_i, z_i) \right].$$

With respect to the variation in $\beta_n$, we report the $S_{min}$ values for the different metal chelates. $S_{min}$ has the same statistical distribution as $\chi^2$ with $K$ degrees of freedom and with a weight defined in accordance with Sullivan et al. [19]. $S_{min}$ is equal to $\chi^2$.

### Results and Discussion

The order of the stability constants of the metal complexes with $HNAS$ or $HNATS$ is as follows: $UO_2^{2+} > Cu^{2+} > Ni^{2+} > Co^{2+} > Zn^{2+} > Pb^{2+} > Cd^{2+} > Mn^{2+} > Mg^{2+}$.

This order is in good agreement with that found by Mellor and Maley [20] and by Irving and Williams [21, 22]. The $\log K_1$, $\log K_2$, $\log(K_1/K_2)$, $\log \beta_2$, and $S_{min}$ values at 20°C for bivalent metal ion chelates at different solvent composition for $HNAS$ and $HNATS$ are summarised in Table 1. In all the systems, the values of $\log K_1$ is greater than $\log K_2$.

As the tendency of a metal ion to take up ligand is proportional to the number of vacant sites, the ratio between consecutive stability constants ($\log K_1/\log K_2$) is determined statistically to a certain extent [2]. For anionic ligands the coulombic attraction is more for $M^{2+}$ as compared to $ML^+$. Therefore $\log K_1 - \log K_2$ is usually positive [23]. Table 1 shows that for all systems studied here $\log K_1 - \log K_2$ is positive and lies within $0.08 - 2.25$ log units.

The results show that the stability of the metal chelates increases continuously from $Mn^{2+}$ to $Cu^{2+}$ and falls again at $Zn^{2+}$. Furthermore, the order of stability constant is independent of the ligand. Minor deviations can be predicted on theoretical grounds. The regularity of this stability sequence can be correlated with a monotonic decrease in the ionic radii and monotonic increase in the second ionisation potential which, in passing from $Mn^{2+}$ to $Cu^{2+}$, 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 $1:2$ (metal : ligand) are formed in each system. In view of the very low $(5.0 \cdot 10^{-4} M)$ concentration of metal ions used in the titration, it has been assumed that the possibility of polynuclear complex formation is negligible.

The dissociation constant $pK_a$ and the stability constants of the metal complexes

**Table 1.** Stability constants of some bivalent transition metal chelates with derivatives of 2-hydroxy naphthaldehyde (*HNAS* or *HNATS*) in various dioxane-water (% $v/v$) media at 0.1 $M$ NaClO$_4$ and a temperature of 20 ± 0.5°C

| Complexing ion | Stability constants + $S_{min}$ | Weighted least squares method | | | | | |
|---|---|---|---|---|---|---|---|
| | | *HNAS* | | | *HNATS* | | |
| | | 75% ($v/v$) | 60% ($v/v$) | 40% ($v/v$) | 75% ($v/v$) | 60% ($v/v$) | 50% ($v/v$) |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| H$^+$ | $pK_a$ | 10.45 | 10.30 | 10.25 | 10.98 | 10.54 | 10.41 |
| UO$_2^{2+}$ | $\log K_1$ | 9.97 | 9.29 | 8.53 | 10.09 | 9.99 | 9.39 |
| | $\log K_2$ | 9.36 | 7.41 | 6.35 | 8.38 | 8.65 | 7.85 |
| | $\log(K_1/K_2)$ | 0.61 | 1.88 | 2.18 | 1.71 | 1.34 | 1.54 |
| | $\log \beta_2$ | 19.33 | 16.70 | 14.88 | 18.47 | 18.64 | 17.24 |
| | $S_{min}$ | 0.1163 | 0.0474 | 0.0151 | 0.0217 | 0.0220 | 0.0774 |
| Cu$^{2+}$ | $\log K_1$ | 9.10 | 8.96 | 7.37 | 9.78 | 9.28 | 9.11 |
| | $\log K_2$ | 8.25 | 7.14 | 5.48 | 8.89 | 7.90 | 7.41 |
| | $\log(K_1/K_2)$ | 0.85 | 1.82 | 1.89 | 0.89 | 1.38 | 1.70 |
| | $\log \beta_2$ | 17.35 | 16.10 | 12.85 | 18.67 | 17.18 | 16.52 |
| | $S_{min}$ | 0.2512 | 0.0271 | 0.0495 | 0.0558 | 0.0162 | 0.0164 |
| Ni$^{2+}$ | $\log K_1$ | 8.93 | 7.92 | 7.19 | 9.60 | 9.06 | 8.59 |
| | $\log K_2$ | 7.99 | 5.67 | 5.24 | 8.22 | 7.49 | 7.18 |
| | $\log(K_1/K_2)$ | 0.94 | 2.25 | 1.95 | 1.38 | 1.57 | 1.41 |
| | $\log \beta_2$ | 16.92 | 13.59 | 12.43 | 17.82 | 16.55 | 15.77 |
| | $S_{min}$ | 0.2232 | 0.0138 | 0.0161 | 0.0580 | 0.0057 | 0.0324 |
| Co$^{2+}$ | $\log K_1$ | 8.60 | 7.08 | 6.89 | 9.00 | 8.63 | 7.86 |
| | $\log K_2$ | 7.58 | 5.30 | 4.85 | 7.08 | 7.26 | 5.90 |
| | $\log(K_1/K_2)$ | 1.02 | 1.78 | 2.04 | 1.92 | 1.37 | 1.96 |
| | $\log \beta_2$ | 16.18 | 12.38 | 11.74 | 16.08 | 15.89 | 13.77 |
| | $S_{min}$ | 0.0097 | 0.0587 | 0.0249 | 0.0149 | 0.3568 | 0.0299 |
| Zn$^{2+}$ | $\log K_1$ | 7.82 | 6.38 | 6.23 | 8.35 | 7.92 | 7.25 |
| | $\log K_2$ | 6.43 | 4.47 | 4.15 | 6.59 | 6.03 | 5.53 |
| | $\log(K_1/K_2)$ | 1.39 | 1.91 | 2.08 | 1.76 | 1.89 | 1.72 |
| | $\log \beta_2$ | 14.25 | 10.85 | 10.38 | 14.94 | 13.95 | 12.78 |
| | $S_{min}$ | 0.0196 | 0.0056 | 0.0026 | 0.0370 | 0.0112 | 0.0017 |
| Pb$^{2+}$ | $\log K_1$ | 6.05 | 5.81 | 5.78 | 7.64 | 6.74 | 6.30 |
| | $\log K_2$ | 5.80 | 4.00 | 3.76 | 5.81 | 5.05 | 4.89 |
| | $\log(K_1/K_2)$ | 0.25 | 1.81 | 2.02 | 1.83 | 1.69 | 1.41 |
| | $\log \beta_2$ | 11.85 | 9.81 | 9.54 | 13.45 | 11.79 | 11.19 |
| | $S_{min}$ | 0.0548 | 0.0051 | 0.0042 | 0.0049 | 0.0526 | 0.0628 |
| Gd$^{2+}$ | $\log K_1$ | 5.65 | 4.96 | 4.80 | 6.55 | 5.96 | 5.80 |
| | $\log K_2$ | 4.23 | 3.41 | 3.62 | 4.87 | 3.84 | 4.43 |
| | $\log(K_1/K_2)$ | 1.42 | 1.55 | 1.18 | 1.68 | 2.12 | 1.37 |
| | $\log \beta_2$ | 9.88 | 8.37 | 8.42 | 11.42 | 9.80 | 10.23 |
| | $S_{min}$ | 0.0302 | 0.0048 | 0.0344 | 0.0769 | 0.0040 | |

Table 1. (continued)

| Complexing ion | Stability constants + $S_{min}$ | Weighted least squares method | | | | | |
|---|---|---|---|---|---|---|---|
| | | HNAS | | | HNATS | | |
| | | 75% (v/v) | 60% (v/v) | 40% (v/v) | 75% (v/v) | 60% (v/v) | 50% (v/v) |
| $Mn^{2+}$ | $\log K_1$ | 5.03 | 4.66 | 4.31 | 5.67 | 5.11 | 4.65 |
| | $\log K_2$ | 4.17 | 3.14 | 2.71 | 4.25 | 3.19 | 3.54 |
| | $\log (K_1/K_2)$ | 0.86 | 1.52 | 1.60 | 1.42 | 1.92 | 1.11 |
| | $\log \beta_2$ | 9.20 | 7.80 | 7.02 | 9.92 | 8.30 | 8.19 |
| | $S_{min}$ | 0.0341 | 0.0009 | 0.0005 | 0.0019 | 0.0016 | 0.0012 |
| $Mg^{2+}$ | $\log K_1$ | 3.21 | 3.16 | 2.83 | 3.39 | 3.38 | 3.33 |
| | $\log K_2$ | 3.04 | 2.80 | 2.61 | 3.31 | 2.23 | 2.87 |
| | $\log (K_1/K_2)$ | 0.17 | 0.36 | 0.22 | 0.08 | 1.15 | 0.46 |
| | $\log \beta_2$ | 6.25 | 5.96 | 5.44 | 6.70 | 5.61 | 6.20 |
| | $S_{min}$ | 0.0051 | 0.0007 | 0.0026 | 0.0024 | 0.0004 | 0.0217 |

in various concentrations of an organic solvent (dioxane) are given in Table 1. The dielectric constant $\varepsilon$ of the medium was changed by varying the percentage of the organic component of the medium. It can be seen from Table 1, that the $pK_a$ values increase with an increase in the percentage of organic solvent in the medium. The values of $\log K_1$ and $\log K_2$ have also become similar. The same has been observed by Shin-ichi Ishiguro et al. [24]. They observed that values of the formation constants of the nickel(II) ethylenediamine complexes increased with the dioxane content in the solvents. Gergely and Kiss [25] made similar observations while studying the stability constants of copper and nickel complexes of alanine in dioxane-water and methanol-water media. The stability of complexes containing either an $O-H$ or an $O-M$ link increases with increasing organic content of solvent [25−28] due to the decrease in the dielectric constant of the bulk solvents. As the dielectric constant decreases, the ion-ion interaction involving the proton (or metal ion) and the anionic oxygen donor of the ligand increases to a greater extent than the ion-dipole interaction between the proton (or metal ion) and the solvent molecules. The observed increases in stabilities may be due to the $O$-$M$ link being strongly affected.

For a given mixed aqueous organic solvent [dioxane:water − 40%, 50%, 60%, and 75% (v/v)], the $pK_a$ value of 2-hydroxy naphthaldehyde derivatives (HNAS and HNATS) increases with increase in organic solvent content of mixed aquo-organic soluent: 40% < 50% < 60% < 75% (v/v) for dioxane-water mixtures.

This may be due to a decrease in the dielectric constant of the medium, an increase in proton solvation and a decrease in hydrogen bonding ability of the solvent.

The experimental results shown in Table 1 reveal that the $pK_a$ values of both ligands (HNAS and HNATS) and the stability constant of their metal chelates are in the order HNAS > HNATS.

The variation in $pK_a$ of ligands and stability constants of their complexes can be explained on the basis of following factors [29]: (i) steric effects, (ii) electronic effects, and (iii) size and electronegativity of the coordinated atoms.

The increase in electron density on the coordinating atoms enhances the basicity, that is the nucleophilic character of the donor atom, thus favouring the formation of a coordinate σ-bond and causing its greater stability.

## Acknowledgements

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