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Note

STABILITY AND THERMODYNAMICS OF METAL-*p*-NITROBENZALDEHYDE THIOSEMICARBAZONE SYSTEMS

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Since Domagk et al.'s [1] original discovery of the antitubercular activity of thiosemicarbazones [2–4], much attention has been given to these compounds by chemists. Williams [5] and Furst and Haro [6] proved experimentally an increase in activity of drugs when administered as metal complexes. A number of metal chelates inhibit tumor growth [7]. In cancer treatment it has been shown that the active species is not the thiosemicarbazone itself but a metal chelate of the thiosemicarbazone [8,9]. After Mashima's work [10], coordination chemists also became interested in thiosemicarbazones and thiocarbazides as potential ligands.

A survey of the literature reveals that the chelating properties of *p*-nitrobenzaldehyde thiosemicarbazone have been scantily documented. In view of the biologically importance of the thiosemicarbazones and their derivatives, an attempt has been made to investigate the interaction of *p*-nitrobenzaldehyde thiosemicarbazone with some bivalent metal ions [Cu(II), Ni(II), Co(II), Mn(II) and Zn(II)] in solution to understand the stoichiometry, stability and thermodynamics of the systems.

EXPERIMENTAL

All the chemicals used were of B.D.H. Analar quality. The metal solutions were prepared in double distilled water and standardized by standard methods. The *p*-nitrobenzaldehyde thiosemicarbazone (Table 1), obtained by

TABLE 1

Elemental analysis of *p*-nitrobenzaldehyde thiosemicarbazone

	C	H	N	S
Found (%)	43.24	3.19	23.98	14.98
Calculated (%)	42.85	3.57	25.00	14.28

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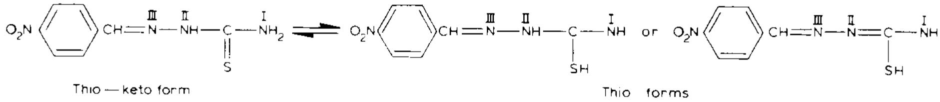
adding equimolecular quantities of *p*-nitrobenzaldehyde (Koch-Light, London) and thiosemicarbazone(LOBA), was prepared in acetone,

A Beckman pH-meter H-2 equipped with a glass and calomel electrode assembly, duly standardized with standard buffers, was used to record the pH-values of the solution. pH-metric titrations of the following solutions (total volume, 50 ml, medium, 50% acetone–water) were carried out: (a) 4×10^{-3} M HCl, 1×10^{-1} M KCl; (b) 4×10^{-3} M HCl, 1×10^{-1} M KCl, 1×10^{-3} M ligand; (c) 4×10^{-3} M HCl, 1×10^{-1} M KCl, 1×10^{-3} M ligand, 2×10^{-5} M metal with 0.1 N NaOH(50% acetone–water).

pH-Values were corrected for volume and for non-aqueous media according to Van-Uitert and Haas [11]. The shapes of the curves were as usual.

RESULTS AND DISCUSSION

The acidic nature of *p*-nitrobenzaldehyde thiosemicarbazone in solution is attributed to the fact that the thio-keto form changes to the thiol form, where sulphahydryl hydrogen is distinctly acidic and is replaced by sodium or potassium, forming soluble salts.



The protonation constant, $^{p}K^{H}$, or *p*-nitrobenzaldehyde thiosemicabazone (thiol form) was estimated following Irving and Rossotti's expression [12].

$$\bar{n}_{A} = Y - \left[\frac{(V'' - V')(N^{0} + E^{0})}{(V^{0} + V')\,\mathrm{TC}_{L}^{0}} \right]$$

where the terms have their usual meaning and the relationship

$$\log {}^{p}K^{H}n = B + \log \frac{\bar{n}_{A} - (n-1)}{(n - \bar{n}_{A})}$$

where B = pH-meter reading. Values of log $^{p}K^{H}$ at 28 and 38°C were 11.20 and 10.25, respectively.

$\bar{n}$ (formation function) was calculated using Bjerrum's expression [13].

$$[\mathrm{L}] = \frac{T_{L} - (\mathrm{ML}) - 2(\mathrm{ML}_{2}) \cdots N(\mathrm{ML}_{N})}{1 + (\mathrm{H}^{+})/K^{*}}$$

where $K^{*} = 1/{}^{p}K^{H}$, and $(\mathrm{H}^{+}) = 10^{-\mathrm{pH}}$.

The metal titration curves were well separated from the ligand titration curves, indicating the participation of the anion of *p*-nitrobenzaldehyde thiosemicarbazone is complexation. A ratio of five parts of ligand to one part of metal ion was maintained in each set to avoid hydrolysis of the metal. The metal–ligand curves were obtained by plotting $\bar{n}$ vs. pL and are complete at both ends. From these curves the stepwise formation constants were evaluated by interpolating at half $\bar{n}$ values; in Cu(II)–, Ni(II)–, and Zn(II)–*p*-nitrobenzaldehyde thiosemicarbazone systems this procedure could not be justified since the log k_1/k_2 value was less than 2.5. Pointwise calculation and the graphical method, utilizing eqns. (1) and (2) and Bjerrum's eqn. (3), were also for evaluating the constants.

$$\log k_1 = \mathrm{pL} + \log\frac{\bar{n}}{\bar{n}-1} \tag{1}$$

$$\log k_2 = \mathrm{pL} + \log\frac{\bar{n}-1}{2-\bar{n}} \tag{2}$$

$$\frac{\bar{n}}{\bar{n}-1}\frac{1}{(\mathrm{L})} + k_1 + \frac{\bar{n}-2(\mathrm{L})}{\bar{n}-1}k_1k_2 = 0\ (N=2) \tag{3}$$

Table 2 contains the mean values of constants and the thermodynamic functions of the systems.

Analysis of Table 2 reveals that the values of log pK_H of the proton complex and of log k_1, log k_2 of the metal complexes of *p*-nitrobenzaldehyde thiosemicarbazone decrease with rise of temperature; it also indicates that the lower temperature favours complexation, because of the decrease in number of collisions with the decrease in kinetic energy of molecules and hence the stability of the system is lowered. The less negative values of the free energies of formation (ΔG^0) for all the systems, excepting Cu(II)–*p*-nitrobenzaldehyde thiosemicarbazone where ΔG^0 is more negative, indicate the reaction to be a spontaneous process, and lead us to believe the reactions to be spontaneous processes. ΔH^0 values, being negative in Ni(II)–, Co(II)–, Mn(II)– and Zn(II)–*p*-nitrobenzaldehyde thiosemicarbazone systems, point to the exothermic nature of the reaction, favouring the aforsaid experimental fact that a lower temperature favours the complexation. The Cu(II)–*p*-nitrobenzaldehyde thiosemicarbazone reaction is endothermic ($+\Delta H^0$). The entropy (ΔS^0) values are negative for Ni(II)–, Co(II)–, Mn(II)–, and Zn(II)–*p*-nitrobenzaldehyde thiosemicarbazone systems, indicating unfavourable entropy. The ΔS^0 value for the Cu(II)–*p*-nitrobenzaldehyde thiosemicarbasone system is positive.

The value of $\bar{n}$ approaches 2 in all systems, pointing to the existence of 1 : 1, 1 : 2 complexes in solution. These findings further found support in the titration of different sets having 0 : 1, 1 : 1, 1 : 2, 1 : 3 (metal–ligand) ratios in that it was seen that the reaction between metals [Cu(II), Ni(II), Co(II), Mn(II) and Zn(II)] and *p*-nitrobenzaldehyde thiosemicarbazone occurs with the liberation of protons, limiting conditions being reached with 1 : 3 mixtures in all systems, indicative of the existence of 1 : 1 and 1 : 2 complexes.

The fact that coordination occurs through the terminal hydrazine nitrogen, N(III), atom and sulphur of the thiocarbonyl groups in thiosemicarbazone has been established by IR measurement and X-ray structure

TABLE 2

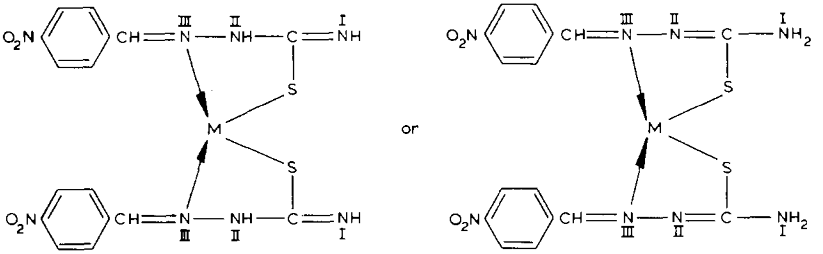
Pointwise and overall formation constants and thermodynamic functions of the complexes of *p*-nitrobenzaldehyde thiosemicarbazone with some bivalent metals

System	Temp. (°C)	Method	log k_1	log k_2	log β_2	ΔG^0 (kcal mole^{-1})	ΔH^0 (kcal mole^{-1})	ΔS^0 (cal mole^{-1} °C^{-1})
Cu(II)	28	A	10.50	6.40	16.90			
		B	9.88	6.11	15.99			
		C	10.20	6.15	16.35			
		D	10.61	6.73	17.34			
		Mean	10.29	6.25	16.65	−22.93		
	38	A	10.10	8.50	18.60			
		B	9.98	7.71	17.69			
		C		8.25				
		D	10.31	8.66	18.97			
		Mean*	10.15	8.19	18.33	−26.09	71.97	315.31
Ni(II)	28	A	10.70	9.00	19.70			
		B	11.12	8.91	20.03			
		C	11.10	9.20	20.30			
		D	11.29	9.95	21.24			
		Mean*	10.17	9.35	20.52	−28.27		
	38	A	9.00	5.10	14.10			
		B	8.49	5.27	13.76			
		C	8.95	5.20	14.15			
		D	9.17	5.21	14.38			
		Mean	8.87	5.23	14.10	−20.06	−275.00	−819.74
Co(II)	28	A	11.90	5.40	17.30			
		B	11.37	6.22	17.59			
		C		5.50				

		D	12.25	7.72	19.97		
		Mean	11.84	6.45	18.29	−25.19		
	38	A	9.00	5.60	14.60		
		B	8.71	5.57	14.28		
		C	9.00	5.65	14.65		
		D	9.17	5.88	15.05		
		Mean	8.97	5.68	14.65	−20.85	−155.92	−434.31
Mn(II)	28	A	10.70	7.00	17.70			
		B	10.49	7.43	17.92			
		C	10.45	7.25	17.70			
		D	10.78	7.74	18.52			
		Mean	10.61	7.36	17.97	−24.75		
	38	A	10.00	5.60	15.60			
		B	9.50	5.46	14.96			
		C	9.90	5.75	15.65			
		D	10.05	5.77	15.82			
		Mean	9.86	5.65	15.51	−22.07	−105.38	−267.88
Z*n*(II)	28	A	10.70	8.50	19.20			
		B	10.21	8.02	18.23			
		C	10.85	8.10	18.95			
		D	10.86	8.79	19.65			
		Mean*	10.64	8.30	18.94	−26.09		
	38	A	10.40	8.90	19.30			
		B	10.15	7.13	17.28			
		C		7.45				
		D	10.31	8.95	19.26			
		Mean*	10.23	8.04	18.27	−26.00	−28.70	−8.68

A, Bjerrum integral method; B, pointwise calculation method; C, graphical method; D, due to Bjerrum; eqn. (3).
Mean* = Mean value of methods B, C and D.

determination [14–18]. Tentative structures of metal complexes of *p*-nitrobenzaldehyde thiosemicarbazone may be written



Bis(*p*-nitrobenzaldehyde thiosemicarbazonato) M(II), where M = Cu, Ni, Co, Mn and Zn.

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