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Short Communication

Spectrophotometric determination of the stability constants of 4-substituted thiosemicarbazides with Co^{2+}, Ni^{2+} and Cu^{2+} system

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Abstract

Formation of 1:2 complexes have been found out by the spectrophotometric studies. The apparent equilibrium constants are determined by general absorbance-extinction-concentration scheme and also by the method of Turner and Anderson at 31°C ± 1°C and at constant ionic strength (0.0075 M).

Key words: Thiosemicarbazide, chelate, stability, constant.

1. Introduction

Thiosemicarbazides have been reported as antitubercular[1,2] and antifungal[3] agents *in vitro*. Since these activities are known to be due to the involvement of trace metals found in the cell[4], the interaction of metal ions like Ni^{2+}, Co^{2+} and Cu^{2+} with thiosemicarbazides seems to be interesting. Spectrophotometric technique has been used in the present investigation as it is quick and reliable to determine the equilibrium constants of metal-ligand interactions in solutions.

2. Experimental

4-(m-Methoxy-phenyl) thiosemicarbazide[5] and 4-(p-Ethoxyphenyl) thiosemicarbazide[6,7] have been synthesized in the laboratory by known methods. Other chemicals used were of analytical grade. Systronics-105 spectrophotometer was employed with proper calibration of wave length for each complex system (Table I). The various metal-ligand systems were studied at respective wave lengths for 1:2 metal-ligand ratio. pH was maintained with aqueous KOH (1.0 M) at 31°C ± 1°C (Table III).

Mole ratio method[8-11] has been employed for computing the stability constants. 2 ml of metal solution in total volume of 10 ml (aqueous-ethanolic medium 70:30) v/v) was titrated spectrophotometrically with equimolar ligand solution (aqueous-ethanolic 70:30 v/v). The use of organic solvents in such systems has increased rapidly and ideal solvents are those which possess a high dielectric constant and high dipole moment, so that the ionic compounds dissociate into free ions and not as ion pairs. As the problem of low solubilities in aqueous medium is experienced when water alone was used as a solvent in organic moieties,

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Table I
Computation of stability constants (By mole ratio method)

Complex	Conc. M/L	λ_{max} (nm)	E_m	E_s	$K^{M}_{L_2} X\ 10^7$
$(4\text{-mMPhTSC})_2$ Ni	0.75×10^{-3}	520	0.370	0.270	01.64
$(4\text{-mMPhTSC})_2$ Co	0.75×10^{-3}	460	0.550	0.460	06.05
$(4\text{-mMPhTSC})_2$ Cu	0.75×10^{-3}	460	0.400	0.340	11.19
$(4\text{-pEPhTSC})_2$ Ni	0.75×10^{-3}	400	0.750	0.640	12.04
$(4\text{-pEPhTSC})_2$ Co	0.75×10^{-3}	460	0.520	0.390	02.13
$(4\text{-pEPhTSC})_2$ Cu	0.75×10^{-3}	480	0.280	0.250	18.17

Table II
Composition of the complexes of 4-mMPhTSC and 4-pEPhTSC by dilution method

Concentration of metal and ligand solution = 0.0075 M
Medium = Aqueous-ethanol (70:30 v/v)
Temperature = 31°C ± 1°C

Sl. No.	4-mMPhTSC									4-pEPhTSC								
	Nickel			Cobalt			Copper			Nickel			Cobalt			Copper		
	O.D.	a_1%	a_2%	O.D.	a_1%	a_2%	O.D.	a_1%	a_2%	O.D.	a_1%	a_2%	O.D.	a_1%	a_2%	O.D.	a_1%	a_2%
1.	0.80	100	30	1.70	100	52	1.30	100	69	1.35	100	65	1.80	100	53	1.40	100	75
2.	0.85	90	34	1.75	95	54	1.35	96	71	1.40	95	70	1.85	92	57	1.42	96	76
3.	0.90	80	37	1.80	90	57	1.40	90	74	1.45	90	73	1.90	84	60	1.44	92	77
4.	0.95	74	40	1.85	82	59	1.42	88	75	1.47	86	76	1.95	77	64	1.46	90	78
5.	1.00	66	46	1.90	80	62	1.45	85	77	1.50	83	78	2.00	72	68	1.48	86	79
6.	1.02	63	48	1.95	75	65	—	—	—	—	—	—	—	—	—	—	—	—
7.	—	—		1.97	73	67	—	—	—	—	—	—	—	—	—	—	—	—

a mixture of ethanol-water was preferred[12]. In the present study, the solvent 70:30 v/v aqueous-ethanol will therefore not affect the stability constant.

The stability constants (Table II) have also been evaluated by the method of Turner and Anderson[13]. (Stability constants can also be determined by assuming that in solutions containing large excess of ligand association is complete. A value for the extinction coefficient can then be calculated. From these values one can calculate the concentration of complex in various mixtures and thus K can be determined by the following equation

$$K = \frac{X}{(a-x)\,(b-x)} \tag{i}$$

Table III
Characteristics of chelates

Sl. No.	Characteristics	4-mMPhTSC			4-pEPhTSC		
		Ni^{2+}	Co^{2+}	Cu^{2+}	Ni^{2+}	Co^{2+}	Cu^{2+}
1.	λ_{max} (nm)	520	460	460	400	460	480
2.	pH range	7-8.5	8.5-10	8-9	7-8	8-9	7.5-8.5
3.	Composition	1:2	1:2	1:2	1:2	1:2	1:2
4.	Degree of dissociation	0.2702	0.1818	0.1500	0.1466	0.2500	0.1071
5.	Log stability constants (By Mole ratio method)	7.216	7.782	8.049	8.080	7.329	8.259
6.	Log stability constants (By Dilution method)	6.945	7.442	8.290	7.767	7.219	8.549

where X is the concentration of the complex, a and b are the initial concentrations of metal and ligand.

For 1:2 complex:

$$K = \frac{X}{(a-x)(b-x)^2} \tag{ii}$$

The above equation is used for computing K values). Both the values are comparable.

Beer's law is followed in the concentration range of solutions under study and the results are reproducible. Order of mixing the reagents has no effect.

3. Results and discussion

1:2 Composition of the complexes was determined by Job's method. This is also indicated by the mole ratio curves (fig. 1).

The apparent stability of the chelates formed was calculated from the absorbance data (mole ratio-method).

The dissociation of the complex ML_2 may be represented as:

$$\begin{array}{lll} ML_2 & \rightleftharpoons & M + 2L \\ C & & O \quad O \text{ (initial concentration)} \\ C(1-\alpha) & & \alpha C \; 2\alpha C \text{ (final concentration)} \end{array}$$

where C is the total concentration of the complex in moles/litres assuming no dissociation, and α is the degree of dissociation. The value of K, the stability constant, was calculated by knowing the value of α from the mole-ratio curve (fig. 1), equation (I)

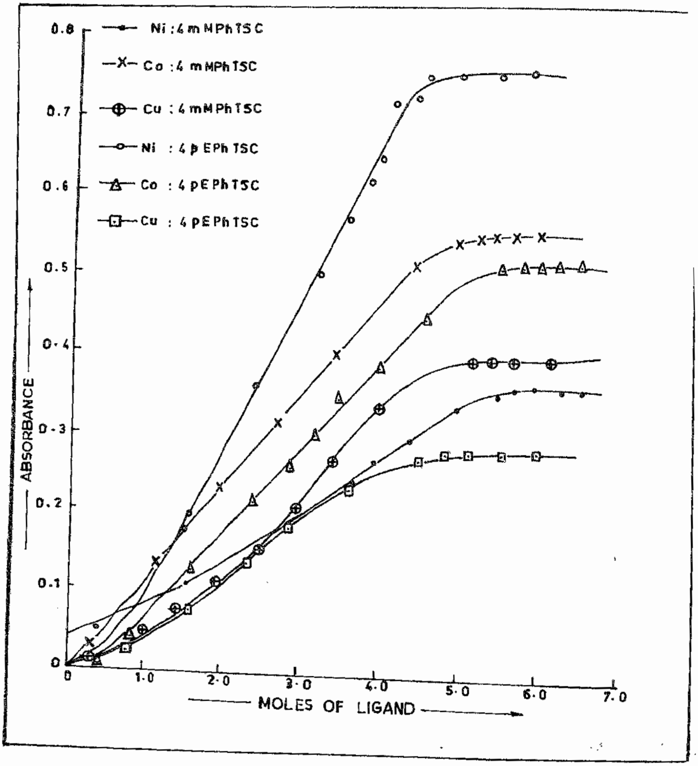

FIG. 1. Composition of the complexes by mole ratio method.

$$\alpha = \frac{E_m - E_s}{E_m} \tag{1}$$

$$K = \frac{(1 - \alpha)}{4\alpha^3 C^2} \tag{2}$$

E_m is the maximum extinction obtained from the horizontal portion of the curve indicating that the whole of the metal ion is present in the form of a complex, E_s is the extinction of the stoichiometric molar-ratio of the ligand to the metal in the complex. To countercheck the results, stability constants have also been evaluated by the method of Turner and Anderson[13]. The values obtained by both the methods are comparable.

The chelate of 4-pEPhTSC with the bivalent metal ions Ni^{2+}, Co^{2+} and Cu^{2+} follow the well-known Mellor and Maley[14] order

$$Cu^{2+} > Ni^{2+} > Co^{2+}.$$

While studying the complexing behaviour of many biological ligands, many workers[15-18] found that with bivalent metal ions the stability order could be either $Ni^{2+} > Co^{2+}$ or $Co^{2+} > Ni^{2+}$; hence the stability order of the above metal ions with 4-mMPhTSC is in agreement with the above finding,

$$Cu^{2+} > Co^{2+} > Ni^{2+}$$

This is also supported by the pK_1^H and pK_2^H for 4-mMPhTSC and 4-pEPhTSC. They are:

$\mu = 0.10$ M, $t = 31°C \pm 1°C$

	pK_1^H	pK_2^H
4-mMPhTSC	11.35 b	10.80 b
	(11.41) (a)	(10.50) (a)
4-pEPhTSC	11.35 b	07.95 b
	(11.41) (a)	(07.90) (a)

b - Interpolation at various $\bar{n}$ values.
(a) - Interpolation at $1/2\ \bar{n}$ values.

Thiosemicarbazides could chelate the metal ions at two points[19]:

(i) The terminal $-NH_2$ group and
(ii) the $-SH$ group (enolic).

Presence of one benzene ring in the thiosemicarbazide molecule does not affect basicity of the terminal $-NH_2$ group. Electron density on the S atom of $-SH$ group in thiol form decreases owing to the presence of benzene ring. It helps the ionization of $-SH$ group.

Substitution of methoxy group at meta position in the benzene ring has a negligible inductive effect on the ionization of $-SH$ group; however + I effect due to substitution of methoxy group at meta position does hinder the ionization of $-SH$ group as they form a conjugated system and affect the stability constants.

In the case of substitution of ethoxy group at para position there is no inductive effect and hence the ionization of $-SH$ group remains unchanged.

Therefore, it is expected that para-ethoxy thiosemicarbazide would form a more stable chelate than the meta-methoxy thiosemicarbazide and our results are in agreement with the above discussion.

4-pEPhTSC > 4-mMPhTSC

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References

1. Buu-Hoi, Ng. Ph., Xuong, Ng. D., Gazave, J.M., Schembri, L., Nam, Ng. H. and Long, C.T. — *Chem. Abstr.*, 1956, **50**, 13916b.
2. Runti, C. and Collino, F. — *Chem. Abstr.* 1962, **57**, 7137 f.
3. Furst, A. — *Chemistry of chelation in cancer* edited by Thomas, C.C., Spring Field, Illinois, U.S.A., 1963.
4. Zsolnai, T. — *Biochem. Pharmacol.*, 1962, **11**, 271-97; *Chem. Abstr.*, 1962, **57**, 6431 d.
5. Joseph, K. and Behnisch, R. — *Ger. Pat.*, 1952, 832, 891, *Chem. Abstr.*, 1953, **47**, 3342 i.
6. Buu-Hoi, Ng. Ph., Xuong, Ng. D. and Nam, Ng. H. — *J. Chem. Soc.*, 1956, **65**, 2160.
7. Tisler, M. — *Croat. Chem. Acta*, 1956, **28**, 147; *Chem. Abstr.*, 1957, **51**, 12016 i.
8. Yoe, J.H. and Jones, A.L. — *Ind. Engng. Chem. Anal. Ed.*, 1944, **16**, 111.
9. Yoe, J.H and Harvey, A.E. — *J. Am. Chem. Soc.*, 1948, **70**, 648.
10. Siddhanta, S.K. — *J. Indian Chem. Soc.*, 1948, **25**, 584.
11. Meyer, A.S. and Ayres, G.H. — *J. Am. Chem. Soc.*, 1957, **79**, 49.
12. Maryott, A.A. — *J. Res. Natn. Bur. Stand.*, 1947, **38**, 527.
13. Turner, S.E. and Anderson, R.C. — *J. Am. Chem. Soc.*, 1949, **71**, 912.
14. Mellor, D.P. and Maley, L. — *Nature*, 1947, **159**, 370; 1948, **161**, 436.
15. Irving, H. and Williams, R.J.P. — *Nature*, 1948, **162**, 746.

16. Srivastava, P.C., Adhya, S.K. and Banerjee, B.K. *J. Indian Chem. Soc.*, 1980, **57**, 985.

17. Pfeiffer, P., Breith, E., Inbee, E. and Tsumaki, T., *Ann. Chem.*, 1953, **84**, 503.

18. Johnston, W.D. and Freiser, H. *J. Am. Chem. Soc.*, 1952, **74**, 5239.

19. Campbell, M.J.M. *Coordination Chem. Rev.*, 1975, **15**, 279.