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Ligand Field Parameters of Some Transition Metal Ion Complexes of Some Substituted Hydrazones and their Antibacterial Activity

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ABSTRACT

Potentiometric studies have been carried out on transition metal complexes of Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2} with hydrazones synthesized from 4-amino benzoic acid hydrazide and 2-hydroxy-1-acetonephthone/2-hydroxy-1-naphthaldehyde. The dissociation constants of ligand and formation constants of its metal complexes have been determined by Calvin-Bjerrum pH titration technique, as adopted by Irving and Rossotti at 27±0.1ºC and at an ionic strength of 0.1M in 60:40 (v/v) dioxane water medium. The order of the stability of complexes is $Cu^{+2} > Ni^{+2} > Co^{+2} > Mn^{+2} > Zn^{+2}$ for both the ligand AHNEH and AHNMH. All the metal complexes screened for their antibacterial activity. The result indicates that the growth of the tested organism was inhibited by most of the compounds.

Key words: Antibacterial activity, Transition metal ion complexes, Substituted Hydrazones.

INTRODUCTION

The interest in the study of hydrazones possessing potential donor sites has been intensively increasing last years because of their pharmacological activity, attributed to their ability to form stable chelates with transition metals present in the vivid cell[1,2]. This process inhibits many vital enzymatic reactions catalyzed by the metal ions. It has been also observed that the biological activity of the hydrazones increases by complexation to metal ions, like copper, nickel, cobalt or iron. Thus, a considerable number of hydrazones and their metal complexes have been reported as tuberculostatic,[3,4] antitumor,[5,6] antibacterial and antifungal[7-9] agents. The thiazole and benzothiazole hydrazones, which have sulphur-nitrogen donor sites, have also been reported to show various pharmacological importance.[10,11] A series of hydrazones obtained by the condensation of 2-hydrazinobenzothiazole with aromatic aldehydes have been demonstrated to possess tuberculostatic and anticonvulsant activity[12-14]. A great number of transition metal complexes with these ligands have been prepared in view of their potential application as antibacterial and antifungal drugs,[15,16] but also for the various bonding and stereo chemical possibilities that they offer.[17,18] Keeping the above

facts in mind and in continuation of our research work[19,20] on the transition metal complexes of hydrazones we report here the results of pH metric study of the formation of metal complexes of above ligands.

EXPERIMENTAL

4-amino benzoic acid hydrazide and 2-hydroxy-1-acetonephthone/2-hydroxy-1-naphthaldehyde were synthesized by reported method[10-11]. The hydroxy hydrazones were synthesized by the equimolar mixture of ethanolic solution of hydrazide and substituted hydroxy ketone/aldehyde were refluxed for three hours. The mixture was poured in cold water and then filtered. The solid product thus obtained was crystallized in ethanol.

We report here the formation constant of transition metal complexes of

1. 1-(4-aminobenzoyl)-2-[1-(2-hydroxy-1-naphthyl)ethylidene]hydrazine [AHNEH]
2. 1-(4-aminobenzoyl)-2-[1-(2-hydroxy-1-naphthyl)methylidene]hydrazine [AHNMH]

The pH metric titrations were carried out against 0.1M KOH solution with a Systronic digital pH meter with glass calomel electrodes to determine the pH. The meter has an accuracy of ±0.01 pH and reproducibility of ±0.02 pH in standard scale operation. The instrument was standardized against 0.05M potassium hydrogen phthalate solution (pH=4) in the beginning of each titration. The metal ion solutions were prepared from the corresponding acetate (BDH, AR) and were standardized by conventional methods[21]. Solutions of ligands were prepared in pure[22] dioxane. Standard carbonate free KOH (E. Merck) solution was prepared by the method of Allen and Low[23] Potassium nitrate and nitric acid were used to maintain constant ionic strength. The buffer solution was kept in a Pyrex flask and a few drops of toluene were added as a preservative. The total volume 50ml and (μ = 0.1M KNO_3) of each system were kept constant in the beginning of each titration. All other chemicals used were also AR grade.

The proton ligand stability constants of Schiff bases and formation constants of their metal complexes were determined using Calvin-Bjerrum technique as modified by Irving and Rossotti[24].

The values of $\bar{n}_H$, $\bar{n}$ and pL were calculated from the plots of pH vs volume of alkali added. Proton ligand formation curves were obtained by plotting pH vs. Proton ligand formation constants were obtained by Bjerrum half integral values (at $\bar{n}_H$=0.5) from the formation curves and were also calculated by Pointwise method. The values determined by two methods are in good agreement with each other. The metal-ligand formation curves were obtained by plotting $\bar{n}$ vs pL. From these curves the metal ligand formation constants ($\log K_1$ and $\log k_2$) were determined by Half Integral, Midpoint slope, Pointwise, Least square, Linear plot and Correction term methods. The values obtained by various methods are in good agreement with each other. The accuracy of the stability constant values is in the order of ±0.02.

RESULTS AND DISSCUSSION

The acid-dissociation constant of the ligand was calculated from the potentiometric titration curve of nitric acid in the presence and in the absence of the ligand. The formation curve for the proton ligand system extended from 0 and 1 in the $\bar{n}_H$ scale, suggest that the ligand has one dissociable proton. It is observed from the titration curve that the ligand curve start deviating from free acid curve at about pH=7.5 and the deviation increased continuously up to pH=10.3. It also indicated that hydroxyl (–OH) group starts to dissociate at about pH= 10.3 to 11[5].

Irving and Rossotti expression is used to calculate proton ligand formation numbers ($\bar{n}_H$). The P^K values were estimated from the formation curve ($\bar{n}_H$ vs pH) by noting the pH at which n_A=0.5. The accurate values of P^K=8.751 and 9.948 were determined by pointwise calculations. Making the use of Bjerrum-pH titration techniques as adopted by Irving and Rossotti, the stability constant of the metal complexes were determined by Half Integral, Midpoint slope, Pointwise, Least square, Linear plot and Correction term methods. The formation of metal complexes between Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2} and ligand was indicated by (1) The significant departure starting from pH 3.30 to 3.45 of metal titration curves from the ligand curve and (2) The

change in colour from light yellow to dark yellow as pH was raised from 3.30 to 9.50. The log K values were directly read from the formation curves ($\bar{n}_H$ vs pH) using half integral method. The most accurate log K values were calculated by pointwise calculation (Table: 1&2). The log K_1 and logK_2 values follow the order as $Cu^{+2} > Ni^{+2} > Co^{+2} > Mn^{+2} > Zn^{+2}$ for both the ligand AHNEH and AHNMH. It can be seen that with both the ligand studied, order of logK1 confirm the well established Irving-Williams order. The values of "log K (log K_1- logK_2) and log K_1/logK_2 are given in Table 1 and 2. The results show that the ratio of log K_1/logK_2 is positive in all cases.

Antibacterial activity

The antibacterial activity of all the synthesized compounds was tested against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* using nutrient agar medium (Hi-Media Laboratories, India) by the method of Tandon *et al*. (2005). The sterilized (autoclaved at 120 °C for 30 min) medium (40~50°C) was

Table 1: Proton-ligand formation constants of transition metal complexes:

Metal ion	Computational method	Ligand: AHNEH Formation constants			Log (K_1/K_2)	Log K_1/log K_2
		Log k_1	Log k_2	Log B		
H^+	Point-wise	08.75	-	08.75	-	-
Mn^{+2}	Half Integral	09.96	08.69	18.65	1.27	1.146
	Midpoint slope	10.23	09.24	19.47	0.99	1.107
	Pointwise	09.66	08.56	18.22	1.10	1.128
	Least square	09.39	08.52	17.91	0.87	1.102
	Linear plot	10.71	09.52	20.23	1.19	1.125
	Correction term	08.91	08.02	16.93	0.89	1.110
Co^{+2}	Half Integral	11.61	10.32	21.93	1.29	1.125
	Midpoint slope	09.01	08.21	17.22	0.80	1.097
	Pointwise	10.07	08.98	19.05	1.09	1.121
	Least square	11.58	10.54	22.12	1.04	1.098
	Linear plot	10.55	09.54	20.09	1.01	1.105
	Correction term	09.04	08.02	17.06	1.02	1.127
Ni^{+2}	Half Integral	11.01	09.95	20.96	1.06	1.106
	Midpoint slope	09.95	08.86	18.81	1.09	1.123
	Pointwise	10.14	09.12	19.26	1.02	1.111
	Least square	10.72	09.42	20.14	1.3	1.138
	Linear plot	11.68	10.73	22.41	0.95	1.088
	Correction term	09.78	08.74	18.52	1.04	1.118
Cu^{+2}	Half Integral	10.69	09.34	20.03	1.35	1.144
	Midpoint slope	09.87	08.80	18.67	1.07	1.121
	Pointwise	10.60	09.52	20.12	1.08	1.113
	Least square	10.99	09.98	20.97	1.01	1.101
	Linear plot	11.87	10.76	22.63	1.11	1.103
	Correction term	11.23	10.18	21.41	1.05	1.103
Zn^{+2}	Half Integral	09.02	07.81	16.83	1.21	1.154
	Midpoint slope	09.72	08.52	18.24	1.20	1.140
	Pointwise	10.25	09.13	19.38	1.12	1.122
	Least square	09.87	08.85	18.72	1.02	1.115
	Linear plot	09.52	08.36	17.88	1.16	1.138
	Correction term	09.37	08.35	17.72	1.02	1.122

inoculated (1 ml/100 ml of medium) with the suspension (105 CFU/ml) of the microorganism (matched to McFarland barium sulphate standard) and poured into a petridish to a depth of 3~4 mm. The paper impregnated with the test compounds (50µg/ml in dimethyl formamide) was placed on the solidified medium. The plates were preincubated for 1 h at room temperature and incubated at 37 °C for 24 h. Neomycin was used as standard for antibacterial activity. The observed zone of inhibition is presented in Table 4. Minimum inhibitory concentration (MIC) of the test compounds was determined by agar streak dilution method. A stock solution of the synthesized compound (50 µg/ml) in dimethyl formamide was prepared and graded quantities of the test compounds were incorporated in specified quantity of molten sterile nutrient agar. A specified quantity of the medium (40~50 °C) containing the compound was poured into a petridish to a depth of 3~4 mm and allowed to solidify.

Table 2: Proton-ligand formation constants of transition metal complexes

Metal ion	Computational method	Ligand: AHNMH Formation constants			Log	Log
		Log k_1	Log k_2	Log B	(K_1/K_2)	K_1/log K_2
H^+	Point-wise	09.94	-	09.94	-	-
Mn^{+2}	Half Integral	10.12	09.45	19.57	0.67	1.070
	Midpoint slope	10.39	09.82	20.21	0.57	1.058
	Pointwise	09.82	09.15	19.07	0.67	1.073
	Least square	09.55	08.96	18.53	0.59	1.065
	Linear plot	10.87	09.98	21.17	0.89	1.089
	Correction term	09.07	08.23	17.57	0.84	1.102
Co^{+2}	Half Integral	11.18	10.59	21.77	0.59	1.055
	Midpoint slope	10.14	09.55	19.69	0.59	1.061
	Pointwise	10.72	10.11	20.83	0.61	1.060
	Least square	10.94	10.03	20.97	0.91	1.090
	Linear plot	10.37	09.90	20.27	0.47	1.047
	Correction term	10.73	10.24	20.97	0.49	1.047
Ni^{+2}	Half Integral	10.67	10.18	20.85	0.49	1.048
	Midpoint slope	10.97	10.07	21.04	0.90	1.089
	Pointwise	10.58	09.58	20.73	0.73	1.074
	Least square	11.21	10.25	20.91	0.96	1.093
	Linear plot	11.85	10.80	23.22	1.05	1.097
	Correction term	09.85	08.96	18.81	0.89	1.099
Cu^{+2}	Half Integral	10.02	09.63	19.65	0.39	1.040
	Midpoint slope	10.01	09.50	19.51	0.51	1.053
	Pointwise	10.95	10.01	21.67	0.94	1.093
	Least square	11.95	11.17	23.12	0.78	1.069
	Linear plot	11.85	10.76	22.61	1.09	1.101
	Correction term	11.38	10.65	22.36	0.73	1.068
Zn^{+2}	Half Integral	09.21	08.24	17.79	0.97	1.117
	Midpoint slope	10.22	09.23	19.81	0.99	1.107
	Pointwise	10.41	09.60	20.19	0.81	1.084
	Least square	09.40	08.65	18.17	0.75	1.086
	Linear plot	10.04	09.35	19.45	0.69	1.073
	Correction term	09.58	08.65	18.53	0.93	1.107

Table 3: Antibacterial activity of the synthesized compounds

Compounds	Zone of inhibition in mm(MIC in µg/ml)		
	E. coli	***B. subtilis***	***S. aureus***
AHNEH	08(30)	09(33)	08(31)
$[Mn(AHNEH)_2]$	12(38)	14(35)	13(37)
$[Co(AHNEH)_2]$	10(41)	12(39)	11(39)
$[Ni(AHNEH)_2]$	11(27)	12(37)	12(30)
$[Cu(AHNEH)_2]$	10(32)	10(41)	13(31)
$[Zn(AHNEH)_2]$	08(21)	09(25)	08(20)
AHNMH	09(32)	08(34)	08(28)
$[Mn(AHNMH)_2]$	14(45)	11(32)	13(39)
$[Co(AHNMH)_2]$	12(35)	14(34)	13(41)
$[Ni(AHNMH)_2]$	13(41)	12(33)	10(26)
$[Cu(AHNMH)_2]$	12(29)	13(31)	09(39)
$[Zn(AHNMH)_2]$	09(32)	08(21)	08(22)
Neomycin(30 µg/disk)	24(0.6)	27(0.8)	29(0.8)

Suspension of the microorganism was prepared to contain approximately 105 CFU/ml and applied to plates with serially diluted compounds in dimethyl formamide to be tested and incubated at 37 °C for 24 h. The MIC was considered to be the lowest concentration of the test substance exhibiting no visible growth of bacteria on the plate. The observed inhibition of growth in mm and MIC in µg/ml are presented in Table: 3.

CONCLUSION

The dissociation constants of ligand and formation constants of its metal complexes have been determined by Calvin-Bjerrum pH titration technique. All the compounds moderately inhibited the growth of Gram positive and Gram negative bacteria. The antibacterial activity was evaluated by measuring the zone of inhibition in mm. In the present study, both ligands were showed moderate effective against the bacteria when metal complexes Mn(II) and Co(II) were found to be most potent.

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REFERENCES

1. Terzioglu G. N. and Otuk G.J., *Med. Chem.*, **32**: 753-757 (1997).
2. Popp F. D., *J. Heterocyclic Chem.*, **21**: 1641-1645 (1984).
3. Singh N. K, Agrawal N. and Agarwal R. C., *Indian J. Chem.*, **23**A**:** 1011-1015 (1984).
4. Kumar Y. and Sethi P. D., *J. Indian Chem. Soc.*, **67**: 796-799(1990).
5. Mohan M, Gupta M. P, Chandra L. and Jha N. K., *Inorg.Chim. Acta*, **151**: 61-68 (1988).
6. Mohan M, Kumar A. and Kumar M., *Inorg. Chim. Acta.*, **136**: 65-74 (1987).
7. Sharma R. C, Ambwani J. and Varshney V. K., *J. Indian Chem. Soc.*, **69**: 770-772 (1992).
8. Singh N. K. and Singh D. K., *Synth. React. Inorg. Met.-Org. Chem.*, **32**: 203-218(2002).
9. Chohan Z. H, Khan K. M. and Supuran C. T., *Appl.Organomet. Chem.*, **18**: 305-310(2004).
10. umalan L, Macarovici D, Neamþu M. and Coman M., *Rev. Roum. Chim.*, **42**: 277-

280(1997).
11. Yilmaz and Çukurovali A., *Polish J. Chem*., **78**: 663-772(2004).
12. Katz L., *J. Amer. Chem. Soc*., **73**: 4007-4010 (1951).
13. Carp E. and Toma A., Analele Univ. ªtiinþ. "Al.I. Cuza",Iaºi, *Sect. Chim.,* **11**c: 67-72 (1965).
14. Gheorghiu C. V. and Carp E., Analele Univ. ªtiinþ. "Al.I. Cuza", Iaºi, Sect. I., **3**: 367-372 (1957).
15. Tiwari G. D, Tripathi Ar., Tripathi An, Kumari O. and Reddy M. V. B., *J. Indian Chem. Soc*., **71**: 755-756 (1994).
16. Kabeer Shaikh, Baseer M. A. and Mote N. A., *Asian J. Chem*., **13**: 496-500 (2001).
17. Hamman A. H, Ibrahim S. A, Abo Elwafa M. H, El-Gahami M. A. and Thabet W., *Synth. React. Inorg. Met.-Org.Chem.,* **22**: 1401-1416 (1992).
18. Girish S. R, Revankar V. K. and Mahale V. B., *Trans. Met.Chem*., **21**: 401-405 (1996).
19. Joshi K. T, Dabhi H. R, Rai R. K, Pancholi A. M. and Rana A. K., *Acta Ciencia Indica.,* **XXV** C(1): 013 (1999).
20. Pancholi A. M, Patel M. A. and Shah K. J., *Indian Journal of Chemical Sciences*, **5**: 39 (1991).
21. Vogel A. I., A Text-book of quantitative inorganic analysts, (Longmans Green & Co, London) (1971).
22. Vogel A. I., A Text-book of Practical Organic Chemistry, (Longmans Green & Co, London) 177(1956).
23. Allen N. and Low G. W., *Ind. Eng. Chem. Analyst Edu*., **5**: 195 (1933).
24. Irving H. and Rossotti H. S., *J. Chem. Soc*., 2904 (1954).