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## Investigation of Stability Constant of Biologically Active Substituted Acetophenones and Aminothioxazines by Job's Variation Method

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### ABSTRACT

Recently a new series of biologically active 2-hydroxy-5-methyl- $\alpha$ -H/Substituted thiocarbamido-acetophenones and 3-(2-Hydroxy-3-nitro-5-methyl) substituted-1,2,5-amino/ substituted aminothioxazines have been synthesized in our laboratory. The conditional stability constants of metal-ligand complexes of these compounds with Co(II) and Cr(II) have been investigated in polar and non polar solvents by Job's method of continuous variation, spectrophotometrically. The stiochiometry of complex formation was found to be 1:1.

**Keywords:** Thiocarbamidoacetophenones, Aminothioxazine, Job's Method, Spectrophotometry

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## INTRODUCTION

In continuation of our work [1] we have synthesized yet another new series of biologically active thiocarbamidoacetophenones and aminothioxazines and investigated their physical properties. In recent years spectrophotometric method [2,3] have become the most frequently used and important methods of quantitative analysis. They are applicable to many industrial and clinical problems involving the quantitative determination of compounds that are colored or that react to form a colored product. It is widely used to study the progress of reaction and to determine the position of equilibrium. This technique [4] allows scientist to identify substance without having to touch to them. This particularly is useful for the substance that may be dangerous or highly toxic. Spectrophotometry is used to calculate the composition and formula of inorganic complexes. It is one of the important methods to determine the stability constant of complex and the knowledge of stability constant is essential for correct interpretation of its optical as well as kinetic properties. Thus determination of stability constant leads to the important discoveries on structure, reactivity and analytical application of complexes. It is also very useful in planning analytical and separating producers. Spectrophotometry is used in a variety of scientific research projects and bioassays. It is very sensitive and precise and measurements are very simple and easy to carry out. It is an important and versatile tool for the chemist as the knowledge of chemical substances comes from their specific absorption or emission spectra. Every substance absorbs or transmits certain wavelength of radiant energy but not the other wavelengths. Thus the absorption or transmission of specific wavelength is characteristic for a substance and a spectral analysis as a “fingerprint” of the compound. In continuation of our work [5] on spectrophotometric studies we intended to study the same on thiocarbamidoacetophenones, and aminothioxazine.

## EXPERIMENTAL

The 0.01M solutions of 2-hydroxy-3-nitro-5-methyl- $\alpha$ -thiocarbamido-acetophenone (6a), 2-hydroxy-3-nitro-5-methyl- $\alpha$ -phenylthiocarbamidoacetophenone (6d) and 3-(2-Hydroxy-3-nitro-5-methyl) phenyl-6-amino-1,2,5thioxazine (7a) ligands were prepared in two different solvents, ethanol and dioxane. All the solutions of ligands were always used a fresh in the present investigation. The metal ions Co(II) and Cr(II) in the form of their nitrates (to avoid the possibility of complex formation of metal ion with anion) were used to prepare stock solutions of 0.01 M in requisite quantities in distilled water. Carbon dioxide free, double distilled water was used. Extra pure (E. Merck) dioxane and absolute alcohol (AR grade) were purified [6] and used for the preparation of solutions of ligand. The optical densities of the ligand solutions and their metal complexes have been measured by visible spectrophotometer model 106, (Systronic make) with an accuracy  $\pm 0.005$ . Pyrex glass cells of 1.00 cm path length were used for the study of spectra. One of the cells was filled with reference solvents (ethanol/dioxane) and the other with experimental solution, and the absorbance values were noted. The same cells were used for all the measurements. The pH measurements were carried out on EQ-612 pH meter (accuracy  $\pm 0.05$  units) using combined glass electrode. Before use, the electrode was dipped in distilled water for 24 hrs. Weighing was made on Roy CCB-4 digital electronic balance, having an accuracy  $\pm 0.001\text{gm}$

## RESULTS AND DISCUSSION

During study when the ligand solution was mixed with metal ion solution, it was observed that the colour of the solution changed for Co(II)-L complexes, the colour changed from yellow to green whereas, for Cr(II)-L complexes, it changed to faint brown. Also the temperature of reaction mixture increased, which clearly indicates the formation of complex in both the solvents. In the present investigation the Job's method [7] of continuous variation is used for determination of metal-ligand stability constants and for the confirmation of complex formation. Normally the maxima appear in the Job's curves at the mole fraction corresponding to the complex that forms. In most of the curves the maxima at the mole fraction would indicate the formation of 1:1 complex [8].

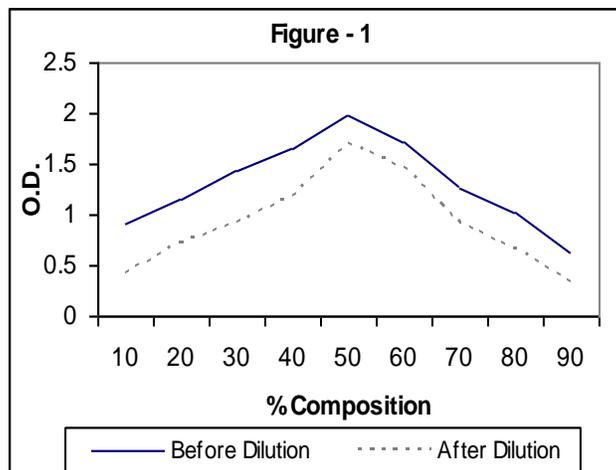
$$[M] / [M] + [L] \cong 0.5$$

It is observed that in general, absorption (optical density) of the metal-ligand complex solution in dioxane solvent is higher than that of in ethanol solvent, probably due to denser solvent dioxane. The conditional stability constants were calculated from the graphs and the values of log K obtained for all the systems are enlisted in Table-2(Fig.2). It is observed that the conditional stability constant values for ligands 2-hydroxy-3-nitro-5-methyl- $\pi$ -thiocarbamido-acetophenone (6a), 2-hydroxy-3-nitro-5-methylphenyl thiocarbamido-acetophenone (6d), 3-(2-Hydroxy-3-nitro-5-methyl)phenyl-6-amino-1, 2, 5 thioxazine (7a) with Co(II) in ethanol as well as in dioxane medium continuously decreased. Similar pattern is observed for Cr(II) ion.

Table 1: System : Co(II) - Ligand (6a)  $\lambda_{\max} = 360 \text{ nm}$       pH = 3.0

% Composition	Before Dilution	After Dilution
10	0.913	0.416
20	1.145	0.717
30	1.43	0.92
40	1.646	1.18
50	1.975	1.702
60	1.723	1.46
70	1.253	0.92
80	1.027	0.66
90	0.626	0.32

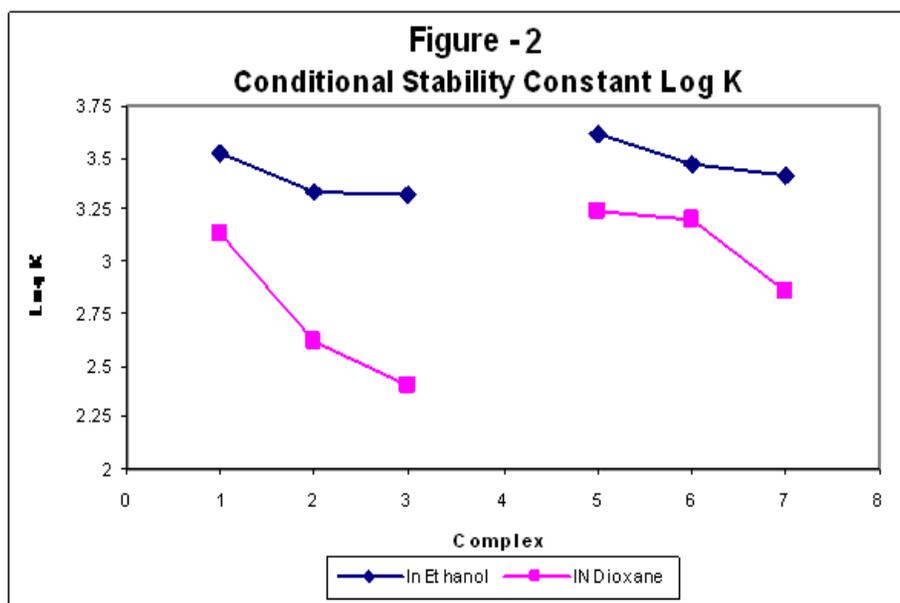
Figure 1: Optical Density, System : Co(II) - Ligand (6a)



It is also observed from Table-2 that the conditional stability constants in alcohol medium for all Co(II)-L complexes are higher than in dioxane medium. This may be attributed to the protic and polar nature and higher dielectric constant (24.6) of ethanol than dioxane (2.2). Similarly, Cr(II)-L complexes have higher conditional stability constants in alcohol medium than in dioxane medium. The atomic number of cobalt is 27 and chromium is 24. The valence shell electronic configuration of chromium is  $4s^13d^5$  while cobalt has  $4s^23d^7$ . The chromium is comparatively stable than that of cobalt due to 4s and 3d half filled orbitals hence atomic radius of Cr is  $1.85 \text{ \AA}$  and atomic radius of Co is  $1.67 \text{ \AA}$ . The  $\text{Cr}^{2+}$  radius is  $0.82 \text{ \AA}$  while  $\text{Cr}^{3+}$  radius is  $0.69 \text{ \AA}$ . The  $\text{Co}^{2+}$  radius is  $0.74 \text{ \AA}$  while  $\text{Co}^{3+}$  radius is  $0.63 \text{ \AA}$ . Higher the charge/radius ratio greater is the stability of complex formed [9-10]. The same trend is found in dioxane solvent (Table-2).

**Table 2: Conditional stability constant log K**

Sr. No.	Complex	In Ethanol	In Dioxane
1	Co (II) - L(6a)	3.52	3.14
2	Co (II) - L(6d)	3.34	2.62
3	Co (II) - L(7a)	3.32	2.40
4	Cr (II) - L(6a)	3.62	3.24
5	Cr (II) - L(6d)	3.47	3.20
6	Cr (II) - L(7a)	3.41	2.85



In general, the metal ion with higher charge and smaller size forms more stable complexes. A smaller but more highly charged cation permits a closer approach of the ligand and larger electrostatic attraction which gives more stability. The inspection and comparison of values in Table-2 reveals that log K values for ligand 2-hydroxy-3-nitro-5-methyl- $\beta$ -thiocarbamidoacetophenone (6a) and with Co(II)/Cr(II) in both ethanol and dioxane media is the highest. The values for ligand 2-hydroxy-3-nitro-5-methylphenylthiocarbamidoacetophenone (6d) and 3-(2-Hydroxy-3-nitro-5-methyl)phenyl-6-amino-1,2,5thioxazine (7a) for each system decrease respectively. The variations in log K values are due to structure, steric hindrance, resonance stabilization and effect of substituents on ligand. The steric hindrance of bigger thiocarbamido and 1,2,5-thioxazino groups will directly affect the approach of metal ion, consequently formation of complex will become difficult as a result of which stability constants will decrease. The electron withdrawing nature of nitro group may destabilize the complex formed and influence the stability constant. Hence, due to more steric hindrance and strong electron withdrawing nature of nitro group the log K values are comparatively lower.

### CONCLUSION

All the above observations clearly showed that the interactions of solvents with metal ions will directly affect the formation of complex. The dielectric constant, polarity of solvent, protic-aprotic nature and hydrogen bonding in solvent will directly interferes the stability and formation of complexes and hence changes in log K values will occur. These properties of solvents are not prime factors for change in log K values or for conditional stability constants and formation of complexes but nature of metal ions and ligands are other two prime factors which are used during study, will also indirectly affect the change in log K values, formation and stability of complexes. It means that in the case metal ions nuclear charge, ionic charge, ionic radius, size of metal ions, oxidation number, effective nuclear charge, electronegativity of metal ions will also make direct interactions for change in log K values, stability of complexes and

conditional stability constants. Third important factor which is responsible for conditional stability constant and complex formation is ligand. When we consider ligand, the size of ligand, electron donating capacity of heteroatom present in ligand with respect to its resonance, total atoms present in ring, the different substituents present in the ring, effect of electron donating and accepting groups, steric hindrance of substituents, resonance stabilization in substituted group must be considered.

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