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Spectrophotometric Analysis of Stability Constants of Benzohydroxamic Acid Complexes with Fe(III), Co(II), and Cu(II) at Varying Temperatures

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Abstract: ***This study investigates the stability constants of Fe(III), Co(II), and Cu(II) complexes with benzohydroxamic acid in ethanol at 298.15 K and 318.15 K using the continuous variation method. The results reveal a 1:2 stoichiometric ratio for the Co(II) complex and 1:1 ratios for both Fe(III) and Cu(II) complexes. Calculated stability constants followed the trend Fe > Co > Cu. Thermodynamic parameters suggest that the complexation reactions are endothermic and spontaneous, with large positive entropy changes supporting this interpretation. These findings enhance the understanding of hydroxamic acid coordination with transition metals and their thermodynamic behavior in ethanol media.***

Keywords: benzohydroxamic acid, metal complexes, stability constant, spectrophotometry, thermodynamic analysis

1. Introduction

The chemistry of hydroxamic acid began in1869 separated oxalohydroxamic acid from production of alkyl oxalate and hydroxylamine (1). Ueber die Oxalohydroxamsaure, of general formula RCONHOH, Hydroxamic acids exist in two forms (2) "Acyl derivatives of hydroxylamine VIII, spectroscopic study of tauterism of hydroxamic acids

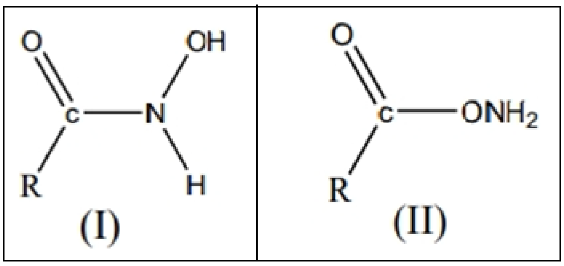


Figure 1: (I) N-acyl derivative and (II) O-acyl derivatived

N-acyl are found in two tautomeric forms, keto-and enolforms (I) and (II) respectively.

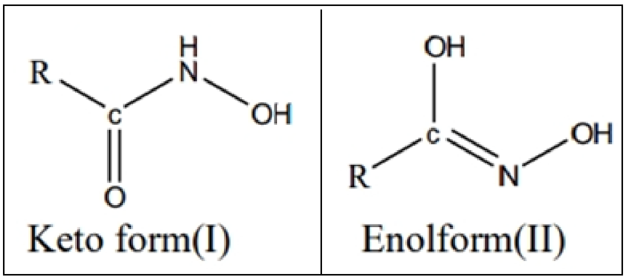


Figure 2: keto-and enol forms of hydroxamic acid

where (I) is hydroxyamide or hydroxamic acid and (II) is hydroxyimine or hydroximic acid. When an acyl group replaces one of the nitrogen bonded hydrogen in hydroxylamine molecule, a monohydroxamic acid, R-CONHOH, is formed and when another hydrogen of hydroxylamine is substituted by an aryl group, the N-arylhydroxamic acid formed. If there is restricted rotation about C -N bond, the Z and E isomers of the keto form exist, as do the enole form

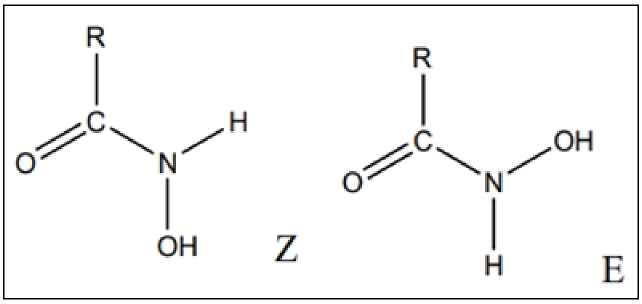


Figure 3: Z and E isomers of hydroxamic acid

represent a very important family of bioligands One of the first roles attributed to hydroxamic acids is their use fulfil a variety of roles in biology and medicine. These compounds possess antibacterial and antifungal properties and are selective inhibitors of enzymes such as peroxidases (3), ureases (4). Matrix metalloproteases which degrade the barriers holding cells in place and are involved in tumour growth. (5). cyclooxygenases (6), lipoxygenases (7), and peptide deformalizes (8). The mentioned biological properties make hydroxamic acids ideal drug candidates. Hydroxamic acids also represent a wide spectrum of bioactive compounds that have a hypotensive (9)., anticancer (10). and anti-tuberculosis (11).

In recent years the preparation, characterization of hydroxamic acid metal complexes had been extensively studied because these compounds possess antibacterial and antifungal properties.

Hydroxamic acids are among the most well studied compounds due to their significance in so many fields (12) ,that can act as O-O donor ligands with high affinities for hard cations such as Fe3+.Other binding modes are possible, including monodentate binding through the deprotonated nitrogen or oxygen atoms, and bidentate binding of two metal ions has also been observed in an an (O,μ-O′)

chelating mode, Metalogic and Metallo proteomic approaches have been employed to investigate the potential antibacterial mechanism of action of Bi against H. pylori for example and strong evidence suggests that Bi interference with metal homeostasis and oxidation reduction processes may be important (13).Hydroxamic acids, RCONHOH, form highly stable complexes with metals in 1:1, 1:2 and 1:3 molar ratios. The stability constants of the complexes were determined through spectrophotometric and potentiometric methods at various pH values and found in agreement. The hydroxamates are of interest due to their ability to form stable transition metal complexes through the formation of a five membered chelate ring (14). Even in acid media iron (III) forms intensely coloured complexes with this ligand which are useful for spectrophotometric analysis. The ability of hydroxamic acids to chelate metal ions has also found pharmaceutical applications (15). Stoichiometry is determined by different methods: mole ratio, slope ratio and continuous variations (job's method). Mole ratio method determines the concentration of metal ion is held fixed, while the concentration of the reagent (ligand) increased stepwise. One the graph of absorbance vs. moles of reagent added, the intersection of the extrapolated linear segments determines the ratio: moles of reagent / moles of metal. In slope ratio method, two series of solutions are prepared. In the first series various amounts of metal ion are added to a large excess of the reagent, while in the second series different quantities of reagent are added to a large excess of metal ion. The absorbance of the solutions in each series is measured and plotted vs. the concentration of the variable component. The discovery of continuous variations method is attributed to Job (13). Who first applied it to complex formation; it is a simple and effective approach to the determination of chemical reaction. In this method, cation and ligand solutions with identical analytical concentrations are mixed in such a way that the total volume and the total moles of reactants in each mixture is constant but the mole ratio of reactants / varies systematically (for example, 9:1, 8:2, 7:3, …, 1:9). The absorbance of each solution is then measured at a suitable wavelength and corrected for any absorbance that the mixture might exhibit if no reaction had occurred. The corrected absorbance is plotted against the volume fraction of one reactant, that is, VM/ (VM+VL), where VM is the volume of cation solution and VL is the volume of the ligand solution. The resulting curve will show a maximum at the mole fraction corresponding to that in the complex. When the curvature is pronounced and the maximum is not apparent, the apex may be obtained by drawing tangents (16). This study aims to analyse the stoichiometry and thermodynamic stability of Fe(III), Co(II), and Cu(II) complexes with benzohydroxamic acid using spectrophotometric methods." The findings contribute to the understanding of coordination behaviour and thermal stability of hydroxamic acid complexes, with potential implications for their use in pharmaceutical and analytical applications."

2. Materials and method

2.1 Materials

All chemicals used were of high purity grade and used without further purification. hydroxylamine hydrochloride was obtained from Fluke Chemical Co. benzoic acid, methanol (MeOH), sulphuric acid, ferric chloride $FeCl_3$, and $Co(NO_3)_2 6H_2O$ cobalt nitrite hex hydrate , $CuCl_2.4H_2O$ copper chloride tetra hydrate, sodium hydroxide pellets (NaOH), sodium hydrogen carbonate ($NaHCO_3$), glacial acetic acid, diethyl ether, were obtained from from Aldrich Chemical Co.

2.2 Methods

2.2.1 Synthesis of Ligand

The ligand was prepared by the drop wise addition of hydroxylamine and methyl benzoate 14 g (0.2mol) of hydroxyl amine was weighed and added to 200cm^3 of 10% sodium hydroxide solution and cooled at room temperature. Then 1.37g (0.1mol) of methyl benzoate was added little with vigorous shaking after each addition to secure complete dissolution. The mixture was allowed to stand for 36 hours. Then it was acidified with 3M hydrochloric acid and cooled. The precipitate was filtered, recrystallized from hot water containing a drop of acetic acid, recorded and filtered, white precipitate collected and weighed, the yield was 12.9g.

2.2.2 Preparation of metals stock solution (0.01M):

1 cm of 1000ppm metals was diluted and, then transferred to 100cm^3volumetric flask 5cm^3 of buffer solution was added to the solution then diluted to the volume mark with distilled water.

2.2.3 Preparation of hydroxamic acid stock solution (0.013M):

0.02g of **hydroxamic acid** was weighed and dissolved in 1.0 cm^3 ethanol, then transferred to 100cm^3 volumetric flask, 5cm^3 of buffer was added (pH =3), the volume was completed up to the mark with distilled water.

2.2.4 Preparation of hydroxamate complex:

A series volumes (0, 1, 2, 3, 4, 5, 6 ,7 ,8, 9cm3) of the metal solutions and (9, 8,7,6, 5, 4,3, 2, 1 and 0cm3) of the ligand were added, the mole fraction and pH were kept constant throughout the experiment." "The absorbance of each solution was measured at the wavelength of maximum absorbance…" of the complex

3. Results

3.1 Result of stoichiometric of benzohydroxamic acid complexes at room tempeture

Table (1) show bellow the results of mole fraction of Iron, cobalt, copper, complexes vs absorption of metals benzo hydroxamate complexes to determine the stoichiometry (mole ratio) of complexes. the stoichiometry ratio of benzo hydroxamate and complexes of, Fe (III), Co (II), Cu (II) were determined by jobs method of continuous variation the mole ratio and found to be in the ratio (M: L) of for Co and1:1 for Fe, and Cu.

3.2 Result of stoichiometric of metals hydroxamic acid complexes at 15C°

Result of stoichiometric of benzohydroxamic acid complexes at 15C° Table (2) show bellow the results of mole fraction of iron, cobalt, and copper benzo hydroxamate, complexes vs absorption of metals benzo hydroxamate complexes to determine the stoichiometry (mole ratio) of complexes ratio and found to be in the ratio (M: L) 1:2for Co and1:1 for Fe, and Cu.

3.3 Calculation of stability Constant for Metal Complexe:

To achieve this objective continuous variation was used to find the ratio of ligand to metal and benefit from it in calculating the stability constant by taking the resulting absorption values of the solutions of mixing the ligand with the metal ion that wanted to perform stability, and therefore it was used (17):

$\underline{M + n L}$
ML_n

$$K=\frac{[ML]}{[M][L]}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

K= Stability constant

n =number of ligand

$$\alpha =\frac{A_m - A_s}{A_m} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

Absorbtion of complexes

A_m = The highest absorbance of complex
As= The less highest absorbance of complex
α =The degree of bonding between the ligand and ion
C= Concentration of complex

Were (n=1) uses this relation;

$$K=\frac{(1-\alpha)}{\alpha 2 .C}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(3)$$

Were (n= 2) uses this relation;

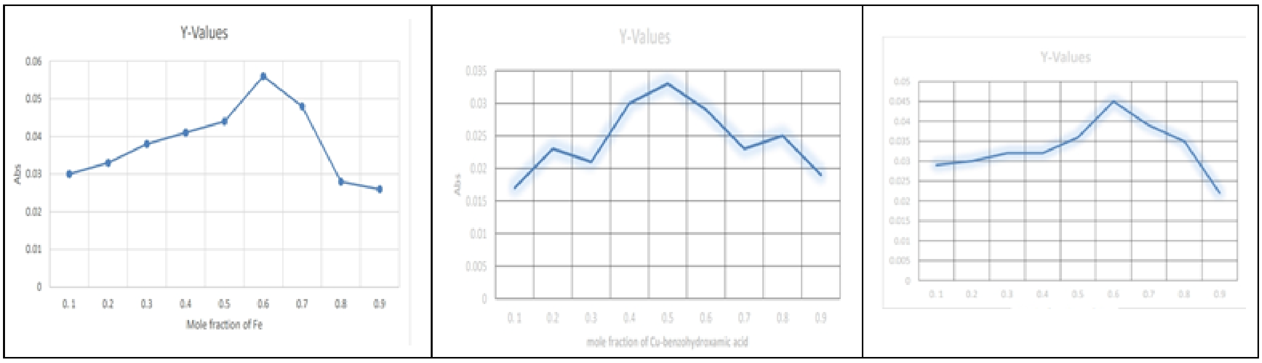
$$K = \frac{(1-\alpha)}{4\alpha^3 C2}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(4)$$

When stability values are found, it is easy to calculate the change in free energy from

□G = - RT Ln K) …………………… (5)

Table 1: The results of mole fraction of Iron, cobalt, copper, complexes vs absorption of metals benzohydroxamate complexes at room temperature

M\ M + L	Fe(III)	Co(II)	Cu(II)
0.1	0.010	0.038	0.022
0.2	0.015	0.062	0.023
0.3	0.011	0.080	0.043
0.4	0.017	0.075	0.045
0.5	0.019	0.051	0.051
0.6	0.021	0.052	0.047
0.7	0.023	0.043	0.040
0.8	0.019	0.040	0.033
0.9	0.017	0.041	0.024
0.00	0.00	0.00	0.00



Mole fraction of Co (II)

Table 2: Stability constant of metal ions complexes of benzohydroxamic acid 25C°

Metal ion complex	A_m	As	*a*	K
Fe(III)	0.037	0.017	0.54	3.7×10^3
Co(II)	0.024	0.016	0.33	2.7×10^3
Cu(II)	0.035	0.012	0.65	59.1

Table 3: Stability constant of metal ions complexes of benzohydroxamic acid 15C°

Metal ion complex	A_m	As	*a*	K
Co(II)	0.045	0.022	0.51	4.7×10^3
Fe(III)	0.056	0.026	0.56	2.7×10^3
Cu(II)	0.033	0.017	0.48	1.6×10^2

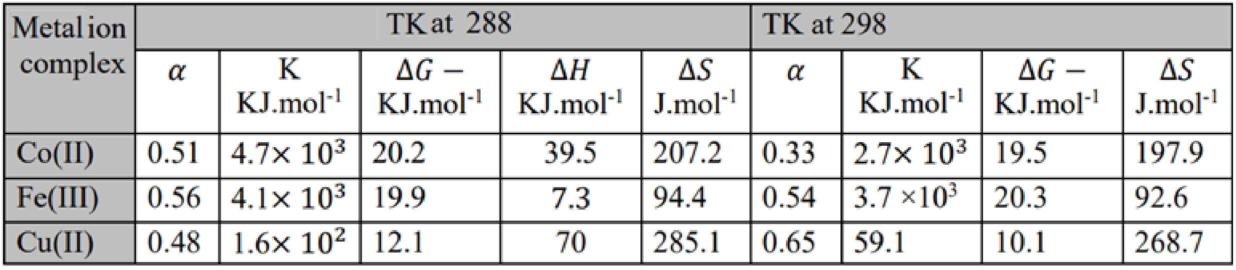
Calculation of thermodynamic perimeter for Metal Complexes The extra stability in the hydroxamic acid complexes can be measured by other parameters such as ΔH^o, ΔS^o and ΔG^o, the thermodynamic parameters for hydroxamic acid complexes evaluated by studying the stability constants at (15- 25C), In both hydroxamic acid complexes, stability constants increased with decreasing in temperature Table (3). and evaluate the enthalpy change (ΔH^o) for this complex by Van't Hoff's from the relation.

$$\mathrm{Ln}K2\ K1 = \Delta H\ R\ (\ 1\ T2 - 1\ T1\ )\ldots\ldots\ldots\ldots\ldots\ldots(6)$$

Values of change the entropy ΔS, were obtained from the relation;

$$\Delta G = \Delta H - T\,\Delta S \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$
$$\Delta S = (\Delta H - \Delta G)/T\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(8)$$

Table 4: Calculation of different parameters of thermodynamics and kinetic



Metal ion complex	TK at 288					TK at 298			
	α	K KJ.mol^{-1}	$\Delta G -$ KJ.mol^{-1}	ΔH KJ.mol^{-1}	ΔS J.mol^{-1}	α	K KJ.mol^{-1}	$\Delta G -$ KJ.mol^{-1}	ΔS J.mol^{-1}
Co(II)	0.51	4.7×10^3	20.2	39.5	207.2	0.33	2.7×10^3	19.5	197.9
Fe(III)	0.56	4.1×10^3	19.9	7.3	94.4	0.54	3.7×10^3	20.3	92.6
Cu(II)	0.48	1.6×10^2	12.1	70	285.1	0.65	59.1	10.1	268.7

4. Discussion

benzohydroxamic acid was prepared by react the ester with hydroxylamine. The acid was recrystallized and identified by M.pt, "complex-colour test, IR spectra, NMR, and mass spectra." Iron benzohydroxate, cobalt benzohydroxate, copper benzohydroxate complexes were prepared in the solution.

Based on complex formation, following continuous variation method; iron shows 1:1 stoichiometric ratio at pH5. cobalt shows 1:2 stoichiometric ratio at pH 5 and copper shows 1 :1 stoichiometric ratio at pH 6. The higher value of K, for this compound can be attributed to resonance, from the benzene rings where there could be delocalization of electrons between the ligand-metal π-bonding there by providing extra stability for the chelates. and also, formed a five member ring - when associated with metallic ion, complexes of iron and cobalt and copper hydroxamate have small size more stable ion but the iron ion more stable than the other metal ions, and this is due to that the extra charge carried by the positive Iron ion gave it high ability to attract uniform ligand. In addition To the size of the metal ion, it plays a role in the stability of the complex state. Thus, they are arranged as follows: Fe > Co> Cu in which low stabilities of Cu – hydroxmate was observed. From the thermodynamic parameters can be pointed out that: (i) a positive value of ΔHo indicates that its reaction of complexation is endothermic. (ii) a negaitive value of ΔGo point that the process is spontantaneous (meaning higher energy loss to obtain more stable compounds). (iii) ΔS values were all large and positive, indicating spontaneous complexation reactions.

5. Conclusion

This study demonstrates that benzohydroxamic acid forms thermodynamically stable complexes with Fe(III), Co(II), and Cu (II), with stability influenced by stoichiometry and temperature. The findings support the endothermic and spontaneous nature of these complexation reactions, highlighting the relevance of hydroxamic acids in metal chelation and coordination chemistry.

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