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Solution Studies and Biological Activity of Some Bivalent Metal Complexes with Schiff Bases Derived From 3-Phenyl Salicylaldehyde

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Potentiometric studies have been carried out on metal complexes of Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Cd^{2+} and Mg^{2+} with N-[3-phenyl salicylidene]-4-methoxy aniline, N-[3-phenyl salicylidene]-2,5-dimethoxy aniline, N-[3-phenyl salicylidene]-2,5-dimethoxy-4-nitroaniline. The stability constants of the regents and their bivalent metal ion chelates have been determined by Calvin-Bjerrum pH titration technique as adopted by Irving and Rossotti at 303 K and at an ionic strength of 0.1 M in 75 : 25 (v/v) dioxane-water medium. Since the above reagents investigated by us are good chelating agents they were also screened for their antibacterial and anticoagulant activity.

INTRODUCTION

Most of the common biologically active compounds have structures quite suitable for chelation with metal ions and studies on the chelation tendency of various organic compounds have supported the hypothesis that formation of strain-free chelate rings enhances the biological activity. Schiff bases derived from salicylaldehyde have been screened for various pharmacological activities. In the present investigation various Schiff bases derived from 3-phenyl salicylaldehyde have been used as chelating agents or ligands for the formation of metal complexes with some bivalent metal ions.

The work of Bjerrum[1] and Ido Leden has enhanced the interest in the investigation of equilibria of metal chelates and ionic complexes in solution. It has greatly contributed to our present knowledge of solution chemistry and development of different methods of examining complex equilibria. It is now possible to arrive at more accurate values of stability constants of metal complexes which has resulted in the development of quantitative theories explaining the interaction between metal ions, ligand and the solvent.

It is known that any factor which increases the localisation of negative charge in the coordinating ligands, makes the electron more readily available and thus increases the ability of a base to coordinate. Bearing this fact in mind, it was thought that if a series of ligands are so chosen as to vary the ligand basicity by changing the substituents at one of the coordinating sites, the investigation would prove to be of interest. Such a variation in basicity of ligands was possible in the Schiff bases.

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Thus an attempt has been made to study the effect of substitution on the azomethine group and formation of complexes with different bivalent metal ions.

EXPERIMENTAL

All the metal salts used were of A.R. grade. All the chemicals used except ligands and perchloric acid were of B.D.H. (AR) grade. The perchloric acid used was of E. Merck (GR) grade. A.R. quality 1.4-dioxane was purified by the method of Vogel[2].

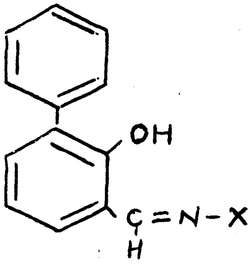
The reagents were synthesised by refluxing equimolar quantities of 3-phenyl salicylaldehyde and the respective amines in the ethanol. The products obtained were repeatedly crystallised to obtain analytically pure samples. The purity was tested by TLC. All the ligands were synthesised for the first time and their structure was confirmed by spectral analysis. The IR-spectra of the ligands were recorded using KBr pellets in the region 4000–400 cm^{-1}. The PMR spectra of the ligands were recorded on Varian FT-80 NMR spectrometer using $CDCl_3$ as solvent and TMS as internal standard.

The stock solutions of metal perchlorates were diluted with 0.16 M perchloric acid to obtain 0.008 M metal solution in 0.16 M $HClO_4$. The titrations were carried out in an inert atmosphere by bubbling oxygen free N_2 gas through the solution. The temperature of the solution was kept constant at 303 K.

The experimental details and computational methods are the same as described in our earlier publications[3].

RESULTS AND DISCUSSION

Potentiometric studies have been carried out for Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Cd^{2+} and Mg^{2+} complexes of the following series of ligands:



where

(B) X-4-methoxy aniline
(C) X-2,5-dimethoxy aniline
(D) X-2,5-dimethoxy-4-nitroaniline

All the above ligands were prepared for the first time and their structures and purity were confirmed by infra-red and PMR spectral analysis.

The dissociation constants of the reagents and formation constants of their metal chelates have been determined by Calvin-Bjerrum pH-titration technique as adopted by Irving and Rossotti at 30 ± 0.1°C and at ionic strength 0.1 M in 75 : 25 (v/v) dioxane-water medium. The reagents were also screened for their biological activities, namely, antibacterial and anticoagulant.

The proton-ligand stability constants of the ligands have been tabulated in Table-1.

TABLE-1
PROTON-LIGAND STABILITY CONSTANT

Name of the Ligand	pK_1^H	pK_2^H
[A] N-[3-phenyl salicylidene]-aniline	10.72	3.03
[B] N-[3-phenyl salicylidene]-4-methoxy aniline	11.20	4.75
[C] N-[3-phenyl salicylidene]-2,5-dmethoxy aniline	10.85	3.00
[D] N-[3-phenyl salicylidene]-2,5-dimethoxy-4-nitroaniline	12.75	2.15

Before taking the discussion on the proton-ligand stability constants of the ligands, it is necessary to discuss the structures of the parent ligand and its substituted derivatives to give a clear understanding regarding its dissociation character. It is already pointed out that the acidic character of the ligands is due to the dissociation of proton from phenolic —OH group. The hydrogen bonding established with the neighbouring nitrogen from azomethine group is the deciding factor for the release of proton. The strength of H-bond mainly governs the release of proton which is affected by the electron environment on the nitrogen atom. With this view in mind, the IR-spectra of the ligands are recorded in KBr pellets and it was observed that the phenolic —OH group and azomethine group (>C═N) are kept undisturbed. These groups form the site for the coordination complex.

Phenolic –OH group goes for H-bonding with nitrogen atom of azomethine group. Thus absorption in the region 3400 cm^{-1} for the ligands may be attributed to ν(O—H). The bond is very broad and weak due to intramolecular hydrogen bonding. This also makes it clear that the variation of acidity of the dissociable —OH group is affected by the substitution of nitrogen. The azomethine (>CH═N—) group is seen to absorb strongly in the region 1590 cm^{-1} to 1620 cm^{-1}. The above series of ligands are selected so as to study the effect of substitution on the basicity of azomethine nitrogen. The pK_1^H values are found to be in good agreement with the change in basicity of the azomethine nitrogen. This may be explained as follows:

Proton-Ligand Stability Constants

The pK_1^H value for ligand 'A' has been reported[4] as 10.72. Considering this as the parent compound substitution in the phenyl ring are carried out by electron withdrawing and electron releasing groups to understand the dissociation character of the hydrogen-bonded phenolic —OH group.

In compound 'B' the substitution of —OCH_3 group at *para* position causes an increase in the elecron density around the azomethine nitrogen as compared to phenyl group in ligand 'A'. This is confirmed by the higher value of pK_1^H value (11.20). At the same time it has also shown considerable increase in the basicity of the nitrogen atom as indicated by its pK_2^H value (4.72). This may be attributed to moderate electron releasing tendency of the methoxy group at *para* position.

The presence of two methoxy groups at *ortho* and *meta* positions has resulted in the lowering of the pK_1^H value to 10.85. In compd. 'C' *meta* position is comparatively weaker and the presence of bulky —OCH_3 group at *ortho* position may cause steric hindrance leaving azomethine nitrogen unaffected by the substitution. Therefore the pK_1^H value is close to that of ligand A (10.72).

The pK_1^H value for compound 'D' is found to be highest in spite of the presence of strong electron withdrawing —NO_2 group at *para* position in the anilino ring. This increase in stability may be probably due to the steric hindrance caused by the bulky —OCH_3 groups. As a result the electron withdrawing effect of —NO_2 group may be delayed and resonance effect may predominate increasing the basicity of azomethine nitrogen.

Metal-Ligand Stability Constants

The above compounds were employed as ligands to study their coordination behaviour with some bivalent metal ions. The formation constants were evaluated by plotting $\bar{n}$ vs B to get formation curves. Metal-ligand stability constants have been tabulated in Table-2.

TABLE-2
METAL-LIGAND STABILITY CONSTANTS

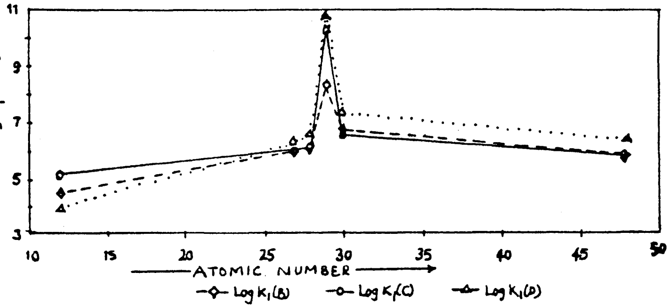
Ligand		Mg^{2+}	Cu^{2+}	Zn^{2+}	Ni^{2+}	Cd^{2+}	Co^{2+}
B	log k_1	4.50	8.32	6.70	6.14	5.78	5.98
	log k_2	–	–	6.18	–	–	5.28
C	log k_1	5.18	10.26	6.55	6.15	5.82	6.05
	log k_2	–	–	–	–	–	–
D	log k_1	3.98	10.76	7.32	6.54	6.38	6.26
	log k_2	–	–	–	–	–	5.92

It is evident from the data that formation curves are incomplete due to precipitation; 1 : 1 complexes however could be evaluated in all the cases. The stability of metal complexes decreases with increasing basicity of the metals. This is apparent from the series of metals selected. The weakly basic copper forms stronger complexes than the strongly basic metals such as Mg^{2+} forming the weakest chelates. This suggests that strength of bonding in these chelates depends on the ability of metals to form homopolar bonds. The metals which form the strongest homopolar bonds form the most stable chelate. In case of ligands B, C, D, the 1 : 2 complexes could not be detected in the solution thereby indicating that these reagents form very strong 1 : 2 complexes. It also suggests that they have fewer donor groups and form less chelated structures.

Since the log K values indicate the strength of bond between metal ion and the ligand, a comparison would give an idea of the relative strengths of the metal-ligand bonds in case of a series of closely related bivalent metal ions.

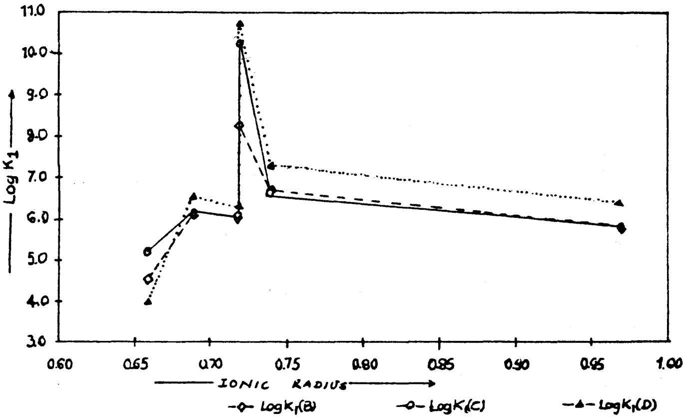
The order of stability constants suggested by Irving-Williams is strictly followed in most of the cases studied here. In order to explore any possible relationship between log K_1 values of metal ligand systems and some of the fundamental properties of metal ions, three types of graphs were drawn.

(i) *log K_1 vs. Atomic Number:* The log K_1 values of the metal-ligand systems were plotted against atomic number of the element. There was monotonic rise to maximum of Cu^{2+}, followed by a lower value of Zn^{2+}. A similar correlation was observed by Irving and Williams[5]. The plots also confimed the observation that the stability seems to decrease with increase in basicity of the metal, *i.e.*, weakly basic metals like Cu^{2+} form stronger chelates and strongly basic metals like Mg^{2+} form weaker chelates. (Graph-3).



Graph 3

(ii) *log* K_1 *vs. ionic radius:* It is observed that log K_1 values increase somewhat uniformly with increase in ionic radii irrespective of the nature of ligand. This could be expected due to predominant electrostatic interaction (Graph 2).

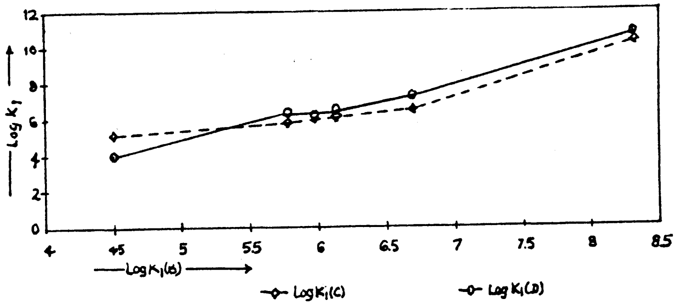


Graph 2

(iii) *log* $K_1(B)$ *vs log* $K_1(C)$ *and log* $K_1(D)$: When the log K_1 values of the various metal complexes of ligands B were plotted against log K_1 values of the same metal complexes of ligand C and D (analogous ligands), a straight line of unit slope was obtained. This is in accordance with the observation of Irving and Rossotii. (Graph-1)

Antibacterial Activity: Reagents B, C, D were screened for antibacterial activity using standard "Ditch plate method"[6]. Results are shown in Table 3-B.

Anticoagulant Activity: The reagents investigated are good chelating agents and they form chelates with Ca^{2+} like EDTA. The activity of these reagents is evaluated by employing Sabraze's technique.[7] The results are shown in Table 3A.



Graph 1

TABLE-3

[A] Anticoagulant Activity

Compound	Clotting Time in Min.	No. of expts.
B	1.80	6
C	1.79	6
D	5.46	6

Normal Clotting time: 1.5 ± 0.5 min.

[B] Antibacterial Testing

Compound	Gram +ve bacteria			
	S. aureus	*S. lutea*	*S. pyogenes*	*H. bacillus*
B	+	+	–	+
C	+	+	+	–
D	+	+	+	+

Compound	Gram –ve bacteria			
	S. paratyphosa	*E. Coli*	*P. Vulgaris*	*S. typhosa*
B	+	–	–	+
C	+	+	+	–
D	–	–	+	+

REFERENCES

1. Bjerrum, Metal-Ammine Formation in Aqueous Solution, Haase and Sons, Copenhagen (1941).
2. A.J. Vogel, A Textbook of Quantitative Inorganic Analysis, 4th Edn., Longmans, p. 302 (1978; reprinted 1985).
3. M.S. Mayadeo, A.M. Chaubal and S.D. Vartak, *J. Indian Chem. Soc.*, **55**, 450 (1978).
4. V.T. Bagwe, H.N. Pande and M.S. Mayadeo, *Acta Ciencia Indica*, **16**, 205 (1990).
5. H. Irving and R.J.P. Williams, *Nature*, **162**, 746 (1948).
6. Kolmer, E.H. Spaulding and H.S. Robinson, Approved Laboratory Technic, 5th ed., Scientific Book Co, Calcutta, p. 110 (1969).
7. F. Kavanagh, Analytical Microbiology, Academic Press, New York, p. 125 (1972).

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