Metal ion complexes of Sr(II), Cd(II), Pb(II), Zn(II) with substituted pyrazoles, isoxazoles and their antimicrobial activities

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ABSTRACT

The stability constant of some metal ions like Sr(II), Cd(II), Pb(II) and Zn(II) complexes with substituted 1-Carboxamido-3-(2-hydroxy-5-methylphenyl)-5-phenylpyrazole (ligand 1) and 3-(2-hydroxy-5-methylphenyl)-5-phenylisoxazole (ligand 2) have been investigated by pH metric technic at 1×10^{-3} M ionic strength and at 30 ± 0.1^{0} C in 70% alcohol (methanol) water mixture. The Data obtained were used to compare and evaluate the values of proton-ligand stability constant (pK) and metal-ligand stability constant(log k), proton-ligand and metal-ligand stability constant have been determined by Bjerrum method, it is observed that Sr(II), Cd(II), Pb(II) and Zn(II) metal ions forms 1:1 and 1:2 complexes with both ligands. The ligands and their corresponding complexes were also screened for their antimicrobial activities.

Key words: Ligand, stability constant, complexes, antimicrobial activities etc.

INTRODUCTION

The stability of metal complexes with medicinal drugs play a major role in the biological and chemical activities[1,2]. Metal exhibit a preference for particular ligand during interaction like ligands. This has important medicinal implication when one considers that most drugs contains group that can acts as a ligands. Attempts to measure metal ligand selectivity in terms of relative strengths of metal ligand bonds are based on stability constant. Generally metal complexes play a very important role in biological process such as metalloprotines, metalloenzymes, storage, transport, detoxification, etc[3]. In a view of analytical applications it is important to know the physicochemical properties such as stability constant of complexes with metal ions[4].

In the present work the comparative study of metal complexes i.e. the interaction of Sr(II), Cd(II), Pb(II) and Zn(II) with (ligand 1) and (ligand 2) has been investigated pH-metrically in 70% methanol-water mixture in very dilute solution of 1×10^{-3} M ionic strength. The ligands and their corresponding complexes were screened for their antimicrobial activities.

EXPERIMENTAL

Metal nitrates (All B.D.H. AnalaR) were dissolved in perchloric acid and their concentrations were estimated by standard method[5]. 1-Carboxamido-3-(2-hydroxy-5-methylphenyl)-5-phenylpyrazole and 3-(2-hydroxy-5-methylphenyl)-5-phenylisoxazole were synthesized in laboratory, their purity was checked by IR, NMR and m.p. 70%

methanol-water (v/v) was used as a solvent. The other solutions were prepared by using double distilled water. The pH measurements were carried out with 335 Systronic pH meter (accuracy $\pm$ 0.05 unit) using glass and calomel electrodes at 27 ± 0.10 C. The B values (pH water reading in 70% methanol-water mixture)were converted to (H^+) values by applying the corrections by   Van Uitery and Hass[6].

RESULTS AND DISCUSSION

Proton ligand stability constants

Substituted pyrazoles, and isoxazoles may be considered as monobasic acids having only one replaceable H^+ ion –OH group and that –OH group generally dissociates completely above pH 9.0 and can therefore represented   HL   i.e. HL = $H^+ + L^-$.

The overall 0.001 M ionc strength of solution was calculated by the expression $\mu = \frac{1}{2}$ "$c_i z_i^2$ the contribution of the other ions in addition to Na^+ and ClO_4^- were also taken into consideration. The titration data were used to construct the curves between volume of NaOH vs pH . They are called Acid, Ligand and Metal titration curves. It is observed from titration curves for all the system that ligand curves start deviating from the free acid ($HClO_4$) curves at about pH 5.4 and deviated continuously up to pH 12.4.the deviation shows that dissociation of –OH group in substituted pyrazoles, and isoxazoles. The average number of proton associated with the ligand (n-A) was determined from acid and ligand titration curves employing the equation of Irving and Rossotti[7]. The proton ligand formation curves were then obtained by plotting the values of n-A vs pH. From these graphs the values

**Table 1: Determination Proton Ligand Stability Constants (pK) of
some substituted pyrazoles, and isoxazoles at 0.001 M ionc strength**

System	Constant pK	
	Half integral	Pointwise Calculation
1. 1-Carboxamido-3-(2-hydroxy-5-methylphenyl)-5-phenylpyrazole	11.28	11.33 ± 0.04
2. 3-(2-hydroxy-5-methylphenyl)-5-Phenylisoxazole	11.19	11.23 ± 0.05

Table 2: Determination of metal ligand stability constants logk of Sr(II), Cd(II), Pb(II) and Zn(II) complexes with substituted pyrazoles, and isoxazoles at 0.001 M ionic strength

System	Constant	
	log k_1 i.e.PL_1	log k_2 i.e. PL_2
1. Sr(‖) ligand No.1	11.28	6.28
Cd(‖) ligand No.1	10.17	4.04
Pb(‖) ligand No. 1	9.67	6.28
Zn(‖) ligand No. 1	10.79	9.90
2. Sr(‖) ligand No. 2	11.09	6.33
Cd(‖) ligand No.2	9.22	5.33
Pb(‖) ligand No. 2	9.72	5.83
Zn(‖) ligand No. 2	10.72	6.83

Table 3: Metal ligand stability constants at 0.001 M ionic strength

System	Constant	
	log k_1. log k_2	log k_1/ logk_2
1. Sr(‖) ligand No.1	4.98	1.78
Cd(‖) ligand No.1	6.12	2.49
Pb(‖) ligand No. 1	3.28	1.52
Zn(‖) ligand No. 1	3.37	1.15
2. Sr(‖) ligand No.2	4.74	1.72
Cd(‖) ligand No.2	3.83	1.71
Pb(‖) ligand No. 2	3.79	1.65
Zn(‖) ligand No. 2	3.87	1.55

Validity of logk = a pk + b relation

of pK were determined (half integral method) by noting the pH at which n-A = 0.5. The accurate values of pK were estimated by pointwise calculation method which was presented in table 1.

pK values of ligand no. 1 is greater than ligand no.2 This is due to the fact that ligand no. 2 contains phenyl ring which acts as a electron realising roups that results to decrease the proton-ligand stability constants. Theses groups are not present in ligand no.1 which contains ccarboxamido (-$CONH_2$) as an electron withdrawing group which increases proton-ligand stability constant.

Metal-ligand stability constant

Metal-ligand stability constants of Sr(II), Cd(II), Pb(II) and Zn(II) with same substituted pyrazoles, and isoxazoles were determined by employing Bjerrum-Calvin pH titration technique as adopted by Irving and Rossotti. The formation of chelates between Sr(II), Cd(II), Pb(II) and Zn(II) with substituted pyrazoles, and isoxazoles were indicated by

´   The significant departure of some metal lignd staring from pH 3.5.

´   The deviation of some metal ligand titration curve from ligand curve was observed from pH 4.00.

´   The change in colour from light yellow to light brown, from pH 2.5 to 9.00.

Deviation between (acid + ligand + metal) titration curve and (acid + ligand) titration curves started from pH 3.5 which shows the commencement at complex formation it could be seen from Table 2 that log k values follows decreasing trend. This is due to the effect of electron releasing group phenyl and electron withdrawing group (-$CONH_2$), the value of logk (log k_1 - log k_2) and (log k_1/ log k_2) are represented in table 3. It is observed that the smaller differences may be due to trans-structure. The result shows that the ratio (log k_1/ log k_2)   is positive in all cases. This implies that there is little or no steric hindrance to the addition of secondary ligand molecules.

The linear relation of log k = a pk + b relation has been found out by some workers[8] to hold for titration metal complexes of a series of closely related ligands. Similarly plots of log k_1 and log k_2 against pk showed satisfactory linear relation giving slope values 0.948, 0. 898 respectively.

When the change in partial molal free energies of thermal ligand and proton- ligand complex exactly compensate each other, The log k vs pk plot is linear with the slop of unity.

The order of stability constants of complexes are presented as below.

i)For ligand No. 1   Sr(II),> Zn(III) > Cd(II),> Pb(II)
ii) For ligand No. 2   Sr(II),> Zn(II) > Pb(II) > Cd(II)

Antimicrobial activity of compounds and their complexes

The compounds and their complexes were analysed for their antimicrobial activity[9] against six test organisms namely E.coli, S. typhi, A.aerogenes, Ps.aeruginosa, S. aureus at a concentration of 100 µ g/ml by Agarwal technique[10] using DMF as a solvent. The compounds and complexes when tested for their antimicrobial activity against six micro-organisms at a temperature of 37^0 C ($\pm$ 1^0 C) it is observed that most of the complex samples tested showed high microbial activity as compared to their compounds. Carboxamido pyrazoles is more active in complex state than pure state. These activities are due to presences of -$CONH_2$ group, -CH_3 and –OH group.

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