Stability Constants of Some Biologically Important Pyrazoles and Their Ni^{2+} Complexes in Different Dielectric Constant of Medium

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Abstract: The proton-ligand stability constants of some biologically important new pyrazoles and formation constants of their complexes with Ni(II) were determined at 0.1 mol dm⁻³ ionic strength and at 303.15 K in different dielectric constant of dioxane-water mixture by potentiometric method. The Calvin-Bjerrum's pH-titration technique as used by Irving and Rossotti was used for determination of stability constants. The results enabled to study the electrostatic forces of attraction between metal ion and ligand with changes in dielectric constant of the medium.

Keywords: Stability constants, Dielectric constant, Substituted pyrazoles.

Introduction

The dielectric constant is one of the characteristics of liquid. The dissociation of ligand and stability constants of metal complexes is strongly affected by dielectric constant of the medium because of the fact that at least one of the constituents is charged and the other is either charged or has a dipole. Specific variations in relative strengths of acids and bases with changing solvents should be a function of the charge, the radius of the ions and the dielectric constants of the medium.

Substituted pyrazoles fall in the class of aromatic heterocyclic compounds involving two nitrogen atoms in a five member ring, which make them interesting ligands. They act as good chelating agents. The pyrazoles used in this investigation are good complexing agents because they contain donor atoms like nitrogen and oxygen. Certain substituted 4-aryl pyrazoles have antipyretic, analgesic anti-inflammatory, muscle-relaxant, sedative hypolipemic and plant growth regulating effect. The 3, 5-Dimethyl and 3, 5-diphenyl pyrazoles have a stimulating action on plant¹. In 3, 4, 5-trisubstituted pyrazoles having substituent like phenyl, substituted phenyl, and thienyl, substituent modify the activity of pyrazole nucleus

and therefore pyrazoles gained importance due to analgesic, antipyretic and anti-inflammatory and other activities².

The proton-ligand and metal-ligand stability constants have been studied using potentiometric method³⁻⁵. Effect of ionic strength [6] and dielectric constants of medium on dissociation and complex equilibria of different organic weak acids have been studied by many workers⁷⁻¹¹. The determination of pK and logK of these biologically important pyrazoles in varying dielectric constant of medium was lacking, therefore, the present work is undertaken to make a systematic study of the role played by dielectric constant of solvent medium on stability constants of these pyrazoles. Energy minimized form of one of the pyrazoles (Figure 1) and general structures of all the pyrazoles used are shown in Figure (2).

Figure 1. Energy minimized form of [5-(2-hydroxyphenyl)-3-(3-nitrophenyl)-(4-benzoyl)]-pyrazol and its deprotonated species.

Figure 2. Structures of pyrazoles used in present investigation.

Experimental

All the glassware's used in present study were of borosil make. The metal ion solutions ($c = 0.002 \text{ mol dm}^{-3}$) were prepared from Analar metal nitrates and standardized with EDTA¹². The pyrazoles were recrystallized before use. The ligand solutions ($c = 0.002 \text{ mol dm}^{-3}$) were prepared by dissolving their accurate mass in dioxane-water. Solution of 0.01 mol dm^{-3} HCl and 1 mol dm^{-3} stock solution of KNO_3 were prepared in doubly distilled water. A carbonate free 0.12 mol dm^{-3} sodium hydroxide solution was used as titrant and it was standardized against oxalic acid (Analar).

The potentiometric titrations were carried out using EQUIP-TRONIC pH meter (accuracy ± 0.05 units) with a combined glass and Calomel electrode assembly. The electrode system was calibrated every day with buffer solutions at pH 4.00 and 9.2. The experimental procedure involved the titration of following solutions.

- 1) Free acid titration (0.01 M HCl)
- 2) Ligand titration (0.01 M HCl + 0.002M ligand) and

- 3) Metal titration (0.01 M HCl + 0.002M ligand + 0.002 M metal ion) with standard sodium hydroxide solution. The total volume of each mixture was adjusted to 50 ml by required amount of solutions and solvents. The ionic strength of solutions was maintained constant at 0.1 mol dm⁻³ by adding appropriate amount of stock solution of KNO₃. The pH meter reading in dioxane was corrected by the method of Van-Uitert and Hass¹³. Metal solutions used were very dilute hence; there was no possibility of formation of polynuclear complexes¹⁴.

Results and Discussion

The titration curves of pH versus volume of sodium hydroxide solution for ligand titration were displaced to right-hand side of the free acid curve, which indicated the release of proton from ligand at particular pH. Also metal titration curves were displaced to right-hand side of ligand titration curves along volume axis, indicating release of proton upon complex formation of ligand with the metal ion. The large decrease in pH of metal titration curves relative to ligand titration curves indicated the formation of strong complexes¹⁵. The pK and logK were determined by pointwise method considering the average number of proton ligand and metal ligand formation numbers. The proton-ligand and metal-ligand stability constants were determined by Calvin-Bjerrum's pH titration technique as used by Irving and Rossotti¹⁶⁻¹⁷.

It can be seen from this Table (1) that, both proton-ligand and Ni(II) metal-ligand stability constants increase with increase in the percentage of dioxane in the medium *i.e.* increase with decrease in the dielectric constant of the medium. The plots of variations in pK and logK with inverse of dielectric constant of the medium for two representative systems are shown in to (3-5). The difference between log K₁ and log K₂ was calculated and reported in Table 1. It could be seen from this table that the difference continuously increases with the increase in the dioxane percentage.

Table 1. The proton-ligand (pK) and metal-ligand (logK) stability constants of pyrazoles and their Ni(II) complexes.

% dioxane	pK	logK ₁	logK ₂	logK ₁ -logK ₂
[5-(2-hydroxyphenyl)-3-(pyridin-3-yl)-4-(benzoyl)]-pyrazol (HPPBP)				
60	5.03	4.94	4.67	0.27
65	5.12	5.08	4.76	0.32
70	5.23	5.24	4.83	0.41
75	5.34	5.51	5.02	0.49
5-(2-hydroxyphenyl)-3-(3-nitrophenyl)-4-(3-pyridinoyl)]-pyrazol (HPNPPP)				
60	4.71	4.95	4.38	0.57
65	4.86	5.24	4.53	0.71
70	5.04	5.48	4.68	0.80
75	5.31	5.79	4.81	0.98
[5-(2hydroxyphenyl)-3-(3-nitrophenyl)-(4-benzoyl)]-pyrazol (HPNPBP)				
60	4.50	5.09	4.56	0.53
65	4.85	5.23	4.61	0.62
70	5.29	5.39	4.72	0.67
75	5.41	5.64	4.86	0.78
[5-(2-hydroxyphenyl)-3 (phenyl)-4-(3-pyridinoyl)]-pyrazol (HPPPP)				
60	5.72	4.98	4.39	0.59
65	5.89	5.16	4.61	0.55
70	6.01	5.34	4.72	0.62
75	6.29	5.69	4.94	0.75

[5-(2-hydroxyphenyl)-3-(3-nitrophenyl)-4-(2-furoyl) pyrazol (HPNPFP)				
60	5.03	4.32	3.37	0.95
65	5.18	4.53	3.56	0.97
70	5.32	4.86	3.71	1.15
75	5.46	5.07	3.84	1.23

Figure 3. Variation of pK with $1/\epsilon$.

Figure 4-5. Variation of $\log K_1$ and $\log K_2$ with $1/\epsilon$.

The lowering of dielectric constant of medium would increase the electrostatic forces of attraction between metal ion and negatively charged ligand to form complex. Therefore, it can be concluded that, the increasing percentages of dioxane which will decrease the dielectric constant of medium and favour the formation of complex, hence increase in $\log K_1$

and $\log K_2$. Such increase in stability constants with decrease in the dielectric constant of medium was observed by Naik *et al*¹⁸ and Sondawale *et al*¹⁹.

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