

Analysis and study of stability constant for metal Complex with 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone ligand

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ABSTRACT

The electrochemical polarographic analysis of complex of Re (II) complex with the ligand 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone were analyzed and it found that ligand forms 1:2 complex with Re(II) in between pH of alkaline range between 7.4-8.6. The logarithm value of stability constant of 1:2 metalis 14.9 and the entropy and free energy observed at -78.69 and -43.48 respectively.

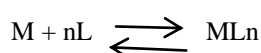
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Introduction

The stability of complex defines in general; the complexes exist under suitable conditions may be stable for long period. However the formation of complexes analyzed in solution, for that two types of stabilities are count 1. Thermodynamic stability and 2. Kinetic stability. In the thermodynamic calculation the equilibrium constants of a reaction is determine with this the heat exchange and entropy change during reaction also determine. It also found that during the reaction the large amount of heat liberated in the reaction which indication of the most stability of reaction products. Secondly, increment in entropy during the reaction is greater the stability of products¹.

The kinetic stability of complexes shows the speed of reaction which given transformation leading to the attainment of equilibrium. In this study we are mainly focus on the thermodynamic stability of the complex compound²⁻³. The determination of stability constant for the complexes in terms of stability is count in two ways thermodynamic stability and kinetic stability, the thermodynamic stability of complex deals with the bond energy (E_{bin}), stability constant (β) and redox potential (EMF), and the kinetic stability count with the rate of the reaction (K).

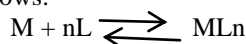
For that the mechanism of reaction focuses to be pointed on formation of intermediate, and activation⁴⁻⁵. The thermodynamic stability of complexes is reveled the extent to which the species will be transformed into other species under the certain conditions, when the equilibrium is occurs than metal ion (M^+) combines with ligand (L) to form complex $[ML_n]$, sofare;



$$K = \frac{[ML_n]}{[M][L]^n}$$

Thus by knowing the value of [M], [L] and $[ML_n]$ the value of K, stability constant of the complex $[ML_n]$ can be count⁶.

For the determination of stability constant is required knowledge of data mining and MAT-LAB in that case we capable to find out computing quantitative analysis with the concentration of free metal ion, ligand and any of its complexes formed in the chemical process, under different conditions of pH. These all type of data must be exclusively employed in the field of analytical chemistry, stereochemistry, bio-inorganic chemistry, non-ferrous and rare metals, ion exchange etc. There are so many methods for the analysis of computational stability constants. Here we working on only two methods are explained known as pH-metric method and spectrophotometric method. For determination of stepwise stability constant of complex by pH-metric method as complexing processes are considered, thus it is possible to analyzed formation of stability constants which refer to the addition of ligands in a stepwise manner as follows:



$$K = \frac{[ML_n]}{[M][L]^n}$$



$$K = \frac{[ML_n]}{[M_{n-1}][L]} \quad [ML_n] = [ML_{n-1}][L]$$

The constants $K_1, K_2, K_3 \dots K_n$ are called stepwise stability constants for the complex formation and it related to the overall stability constant as:

$$\beta_1 = K_1, \beta_2 = K_1.K_2, \beta_3 = K_1.K_2.K_3, \beta_4 = K_1.K_2.K_3.K_4$$

$$\text{Therefore } \beta_n = K_1.K_2.K_3. \dots K_n$$

And the Thermodynamic constants of the reaction and product formation related to the stability constants and the properties such as free energy change (ΔG), enthalpy (ΔH) and entropy change (ΔS).

$$\Delta G = -2.303 RT \log K$$

$$\Delta H = 2.303R \frac{T_2 T_1}{T_2 - T_1} \log_{10} \frac{k_2}{k_1}$$

$$\Delta H = 2.303 R \frac{T_2 T_1}{T_2 - T_1} (\log_{10} \beta_2 - \log_{10} \beta_1)$$

$$\Delta S = \frac{\Delta G - \Delta H}{T}$$

Where, K_2 and K_1 are the stability constants at the absolute temperatures T_2 and T_1 respectively.

In this present study we are utilized Bjerrum's method. In this method Bjerrum suggested the certain formation functions such as A_n, \bar{n}, pL , which used to calculate the stepwise stability constants. The formation function (n) of a metal-ligand (M, L) system can be defined as:

$$n = \sum_{i=0}^n i(n-1)\beta_i [L]^i$$

In this same way for ligand-proton (L, H) system formation function n_A is defined as:

$$n_A = \frac{\sum_{i=0}^n i \beta_i^H [H]^i}{\sum_{i=0}^n \beta_i^H [H]^i}$$

Now formation function n is -

$$\bar{n} = \frac{\text{TCL} - \text{Concentration of L not bonded with metal}}{\text{TCM}}$$

Where $\text{TCL} =$ Total concentration of ligand L and $\text{TCM} =$ Total concentration of metal M

$\bar{n} \text{TCM} = \text{TCL} - \text{Concentration of L not bound to M}$

Concentration of L not bound to $M = \text{TCL} - \bar{n} \text{TCM}$

From the value of n_A , Total concentration of L not bound to $M = [L](1 + \beta_1^H [H] + \beta_2^H [H]^2 + \beta_3^H [H]^3 \dots)$, and $M = [L] \sum_{i=0}^n \beta_i^H [H]^i$

Therefore;

$$[L] = \frac{\text{TCL} - \bar{n} \text{TCM}}{\sum_{i=0}^n \beta_i^H [H]^i}$$

And the along with pH the values of pL is given for the complex is:

$$pL = \log_{10} \frac{\sum_{i=0}^n \beta_i^H [H]^i}{\text{TCL} - \bar{n} \text{TCM}}$$

Some imitations are applicability of computation methods, so few assumptions are made in the formation function viz. Therefore; it required to sets limits to the applicability of computation method described above, in addition of those arising from the particular conditions under which the method is proceed. According to the method the neglected factors also correcting for them, if possible. Rossotti and Rossotti⁷ have suggested that \bar{n} would be independent of TCM in absence of poly-nuclear complex formation. Where only one poly-nuclear complex is formed, determination of \bar{n} at different values of TCM and then extra potation to low values of TCM has been recommended⁸⁻⁹.

Mathematical analysis of computing mononuclear stability constant, even when poly-nuclear species are present, have been determine^{10,11}, but it found only to complexes which arising in metal ion hydrolysis. And the metal ion hydrolysis occurs in the certain pH range of complex formation in solution, which provides us higher

value than the true values of stability constants. Fraiser and his fellows¹² work on hydrolysis of several divalent metal ions in suitable solvents and have shown that, the computations mode working in the pH range of 3 – 6 which given least deviation by metal ion hydrolysis sofare; the use of high ligand-metal ratio has been recommended for the pH range, if it necessary. We are studied the proton ligand stability constants and metal ligand stability constants at $35 \pm 0.2^\circ\text{C}$ temperatures for synthesized metal complexes by the Calvin Bjerrum titration technique¹³.

The stability constant is very useful physical entities, which shows the importance function of various complexes in biological systems.

Experimental

For the Calvin Bjerrum method pH of solutions to determine for the proton ligand stability constants and metal-ligand stability constants were analyzed with an EQUIP-TRONICS instrument, which is well equipped with a combined electrode and magnetic stirrer, pH-meter with a combined glass electrode assembly of pH range 0 to 14. This instrument has been also has temperature sensors covering the range from 0 to 100°C . The instrument was calibrated with buffer solution of known pH before starting the pH titrations.

1. NaCl- 1.0 M.

2. Sodium hydroxide-NaOH 0.5 M & 0.1 M.

3. HCl 0.1 M.

4. Ligand solution 0.1 M.

5. Metal solution (Cu, Ni and Co) 0.1 M HCl, were standardized by titrating with 0.1 N NaOH and 0.05 M succinic acid solution respectively.

Calvin Bjerrum pH titration

For the titration the following sets of solutions were prepared.

1. Set 1 : 0.8 mL 0.1 M HCl + 11.2 mL distilled water + 24.0 mL dioxane + 4.0 mL 1

M NaCl.

2. Set 2 : 0.8 mL 0.1 M HCl + 11.2 mL distilled water + 22.0 mL dioxane + 2.0 mL +0.1 M ligand solution + 4.0 mL 1 M NaCl.

3. Set 3 : 0.8 mL 0.1 M HCl + 10.8 mL distilled water + 22.0 mL dioxane + 2.0 mL +0.1 M ligand solution + 4.0 mL 1 M NaCl + 0.4 mL 0.1 M metal solution.

The total volume (V) of the every set is 25 ml were taken and the drug solutions were prepared in organic solvent (Dioxane) : Water ratio 60 : 40 (V/V). Solutions mentioned above sets were allowed to stand at a 35°C temperature for few minutes then titrated against standard alkali solution (NaOH 0.5 N) under an inert atmosphere of nitrogen.

For pH measurements we used an Elico pH meter with glass and calomel electrodes and fixed at 7.30 ± 0.01 which was adjusted with dilute solutions of HCl or NaOH as required. Electrochemical study were carried out by using Polarographic Analyzer. In this instrument the Polarographic capillary is 5.0 cm. long with diameter 0.06 mm with dropping mercury electrode (DME) with characteristics of $m^{2/3}t^{1/6} = 2.04 \text{ mg}^{2/3} \text{ s}^{-1/2}$. All the data were determine by immersing of pure nitrogen gas before recording the current - voltage data. Potassium dihydrogen phosphate – sodium hydroxide buffer was added with the analyte to stabilize its pH.

And for the next experiment we are count pH and determine stability constant therefore we performed second experiment of pH:

Chemicals

Metal ion solution were prepared by precipitation of metal carbonates from 0.1 M solution of Chlorides of Fe(III), Cu(II) and Re(II) (A.R. grade) with the solution of sodium carbonate. The precipitate is occurs which were thoroughly washed with boiling water and treated with a calculated amount of 1% HClO₄ acid.

Filter Paper Strips

Strips of What-man filter paper for chromatography (30×1) cm² were used and the potential gradient was 6.6 V/cm.

Electro-osmotic indicator

5.0 × 10⁻³ M glucose (BDH A. R. grade) was prepared in water and used as an electro-osmotic indicator for the correction due to electro-osmosis.

Detecting reagent for metal ions

Ammonium thio-cyanate for Fe (III), Re (II) and 0.1% (W/V) solution of 1-(2-pyridylazo)-2-naphthol (PAN) in ethanol for Cu (II) was used.

Background electrolyte

Stock solution of (5.0 M) was prepared by suitable dilution of 70% HClO₄ (SDS A. R. grade). 2.0 M sodium hydroxide (A. R. grade) and 0.5 M stock solutions of the complexing reagent Chloramphenicol (A. R. grade) solutions were prepared. All chemicals were used without further purifications. Each solution was standardized using the appropriate method. The background electrolyte used in the study of binary complexes was 0.1M % HClO₄ and 0.01M ligand solution with the system was maintained at various pH by the addition of sodium hydroxide.

Procedure

The center-point of each Whatman filter paper was marked for the mobility observation of metal ions. Each of the vessels was filled with 100 ml of background electrolyte containing 0.1 M HClO₄ and ligand reagent (1.0×10⁻² M). The paper becomes moistened with the background electrolyte solution, and then the spot of each metal solution was applied at the marked center-point of the strips using micropipette. At least one strip was spotting with glucose solution for electro-osmotic correction. The next paper strips put on insulator and then thermo stated water at 25⁰C. Than after the paper strip was exchanged over the insulator plates at constant temperature. The lid air tight for left to 20 minutes to insure wetting of paper strips.

Subsequently, a direct 180 volts was set in between the electrodes, and after Electrophoresis was carried out for 45 minutes after which these strips were removed from and dried. The metal ions and glucose spots were detected by specific reagents. The edges were analyzed from the center-point and the mean were counted. The distance moved by glucose point was neglected to find out the correct length. Migration of ions towards anode and cathode were denoted by negative and positive signs, respectively.

Electrophoretic analysis for metal ion done at various pH values with the background electrolyte which measured by addition of sodium hydroxide solution, during this process the ionic strength being maintained at 0.1M. The observed mobility of the migrant was calculated by using the following formula.

$$U = \frac{\zeta dx}{4\pi\eta} (d_G - d) \times t$$

After applying the correction factor, the observed mobility is given as Where U = mobility of metal ion/complexion, d = mean of duplicate distances travelled by metal ion/complex ion, d_G = mean of duplicate distances travelled by glucose spots, x = field strength and t = time for electrophoresis.

After the experiment following data are analyzed:

Table 3.1. Proton-ligand stability constants of the ligands at 35° ± 0.2°C.

Ligand	pK H 1	log pK H 2	logβ
Solution - 1	10.66	3.11	13.87
Solution - 2	10.76	3.23	14.01
Solution - 3	10.74	3.22	14.08

Table 3.2. Metal ligand stability constant at 35° ± 0.2°C by Computational Methods.

	a	b	c	d
Fe(III)				
logK H ₁	8.62	8.63	8.6	8.64
logKH ₂	5.73	5.71	5.76	5.72
logβ	14.35	14.34	14.36	14.38
Cu(II)				
logK H ₁	9.02	8.98	8.99	8.96
logKH ₂	4.61	4.62	4.62	4.66
logβ	13.63	13.63	13.61	13.62
Re(II)				
logK H ₁	8.61	8.6	8.61	8.63
logKH ₂	6.35	6.36	6.37	6.36
logβ	14.95	14.96	14.98	14.99

Table 3.3. The pH titration reading of acid, acid + ligand and acid + ligand + metal ions at N° = 0.5, E° = 0.02 M, V° = 40.0 ml, TCL° = 5 × 10⁻³ M, TCM = 1 × 10⁻³ M, t = 30 ± 0.2°C, u° = 0.1 M Solvent = Dioxane : water 60 : 40 (v/v).

Vol. of alkali	added Acid	Acid +ligand	Acid + ligand + metal ions	Fe(III)	Cu(II)	Re(II)
0	1.7	1.7	1.7	1.7	1.7	1.7
0.5	1.8	1.8	1.85	1.85	1.85	1.88
1	1.9	2	2.35	2.45	2.48	2.52
1.5	2	2.3	2.71	2.62	2.68	2.74
2	2.1	2.35	2.9	2.85	2.9	2.96
2.5	2.2	2.5	3.25	3.2	3.4	3.45
3	2.3	2.75	3.75	3.75	3.8	3.86
3.5	2.4	2.82	3.9	3.85	3.9	3.98
4	2.5	2.9	4	3.96	3.98	4.02
4.5	2.6	3.01	4.19	4.07	4.22	4.28
5	2.7	3.1	4.4	4.2	4.46	4.66
5.5	2.8	3.2	4.52	4.25	4.27	4.34
6	2.9	3.55	4.61	4.5	4.56	4.68
6.5	3	4.35	4.75	4.52	4.56	4.58
7	3.1	8.4	5	5.02	5.06	5.1
7.5	3.2	10.25	8.5	5.24	5.16	5.28
8	3.3	11.2	8.98	5.72	5.3	5.38
8.5	3.4	11.75	9.7	6.26	6.3	6.36
9	3.5	12.1	10.3	7.78	7.8	7.88
9.5	3.6	12.25	10.76	8.69	8.78	8.98
10	3.7	12.3	11	8.95	9.09	9.18
10.5	3.8	12.41	11.18	9.04	9.16	9.34
11	3.9	12.5	11.4	9.5	9.55	9.88

Table 3.4. 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone at 35° ± 0.2°C for log pK₂H.

B	V1 – V2	n A 1	log 2-n/n-1	log pK ₂ H
2.5	0.321	1.8042	-0.686	3.1135
2.75	0.279	1.6967	-0.664	3.1113
3	0.226	1.564	-0.088	3.1118
3.25	0.171	1.4252	0.1311	3.1188
3.5	0.116	1.2901	0.1388	3.1113
3.75	0.075	1.1876	0.6366	3.1134
4	0.046	1.1149	0.8865	3.1135
4.25	0.027	1.068	1.1339	3.1161
4.5	0.016	1.0394	1.3877	3.1123
4.75	0.009	1.0226	1.6377	3.1152
5	0.005	1.0128	1.8845	3.1155

Table 3.5. 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone at 35° ± 0.2°C for log pK₁H.

B	V1 – V2	n A 1	log 2-n/n-1	log pK ₁ H
9.25	0.015	0.9626	1.4122	10.6612
9.5	0.026	0.9355	1.1613	10.6013
9.75	0.044	0.8908	0.9111	10.6611
10	0.072	0.8208	0.612	10.6612
10.25	0.112	0.7204	0.4114	10.6614
10.5	0.163	0.592	0.1615	10.6615
10.75	0.221	0.4493	-0.0883	10.6617
11	0.275	0.3142	-0.3398	10.661
11.25	0.318	0.2049	-0.5889	10.6611
11.5	0.35	0.1267	-0.8384	10.6616

Table 3.6. pL value of Fe (III) + 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone.

B	V3	V2	V3-V2	n	pL
4.5	1.602	1.593	0.009	0.0958	11.0146
4.75	1.614	1.6	0.014	0.1749	11.0227
5	1.636	1.618	0.018	0.1957	10.2819
5.25	1.665	1.637	0.028	0.3183	9.5419
5.5	1.678	1.64	0.038	0.4745	8.8043
5.75	1.698	1.643	0.055	0.6868	8.0651
6	1.711	1.647	0.064	0.7992	7.3253
6.25	1.73	1.65	0.08	0.9985	7.3253
6.5	1.751	1.654	0.097	1.2107	5.8486
6.75	1.765	1.66	0.105	1.3106	5.1863
7	1.778	1.663	0.115	1.4352	4.7307
7.25	1.789	1.666	0.123	1.5351	3.6388
7.5	1.8	1.67	0.13	1.6225	2.8988
7.75	1.81	1.673	0.137	1.7096	2.1617
8	1.82	1.682	0.138	1.8145	1.8094
8.25	1.838	1.688	0.15	1.8832	0.4843

Table 3.7. pL value of Cu (II) + 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone.

B	V3	V2	V3-V2	n	pL
4.25	1.595	1.588	0.007	0.0784	12.4071
4.5	1.611	1.593	0.018	0.183	11.765
4.75	1.627	1.6	0.027	0.2859	11.0228
5	1.651	1.618	0.033	0.3784	10.3881
5.25	1.675	1.637	0.038	0.4683	9.5508
5.5	1.696	1.64	0.056	0.6591	8.815
5.75	1.721	1.643	0.078	0.8995	8.0785
6	1.745	1.647	0.098	1.1481	7.3414
6.25	1.765	1.65	0.115	1.3477	6.6034
6.5	1.778	1.654	0.124	1.4725	5.8648
6.75	1.789	1.66	0.129	1.5723	5.1298
7	1.801	1.663	0.138	1.6846	4.3914
7.25	1.813	1.666	0.147	1.7845	3.6541
7.5	1.823	1.67	0.153	1.846	2.9206

Table 3.8. pL value of Re (II) + 1 -{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone.

B	V3	V2	V3-V2	n	pL
4.5	1.601	1.593	0.008	0.0903	12.093
4.75	1.613	1.6	0.013	0.1499	11.353
5	1.637	1.618	0.019	0.1968	10.6161
5.25	1.664	1.637	0.027	0.3205	9.8789
5.5	1.677	1.64	0.037	0.4623	9.1416
5.75	1.688	1.643	0.045	0.5744	8.401
6	1.709	1.647	0.062	0.7866	7.663
6.25	1.724	1.65	0.074	0.9989	6.9238
6.5	1.755	1.654	0.101	1.3081	6.185
6.75	1.771	1.66	0.111	1.4105	5.4498
7	1.781	1.663	0.118	1.511	4.7095
7.25	1.793	1.666	0.127	1.6226	3.97
7.5	1.803	1.67	0.133	1.7096	3.2321
7.75	1.815	1.673	0.142	1.809	2.4984
8	1.833	1.682	0.151	1.8828	1.76

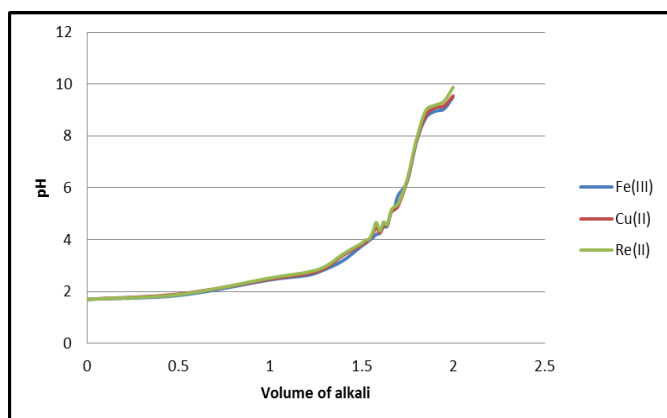


Figure 3.1. pH titration curve with volume of alkali added.

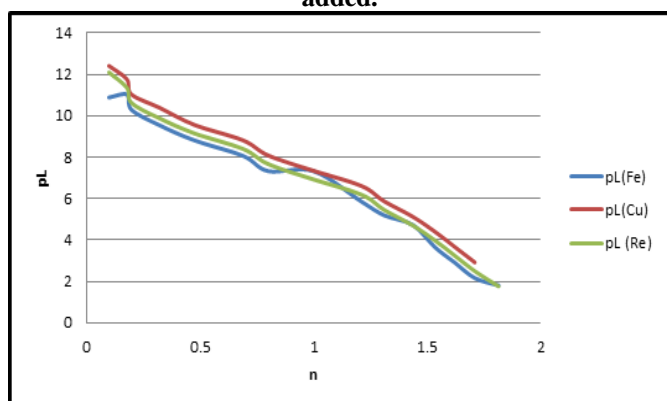


Figure 3.2. Change in pL with value of n.

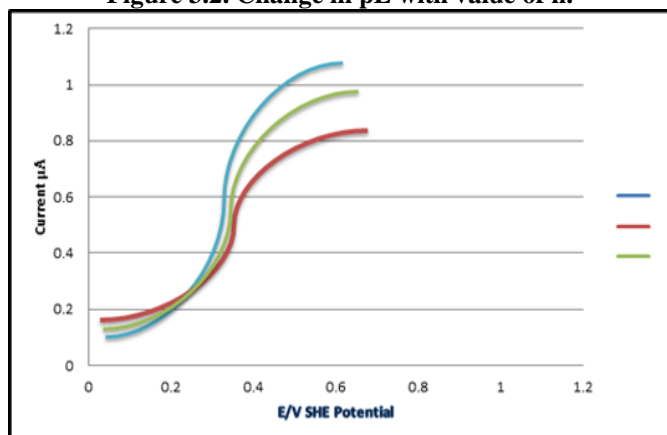


Figure 3.3. Polarogram of Complexes for Fe (III), Cu(II),Re(II).

3.3 Result discussion

Comparison of stability of the binary and ternary complexes:

The value of mixing constant $\log K_m$, which compares the stability of binary and ternary complexes have been calculated by following equation¹⁴⁻¹⁵.

$$\log K_m = \log \beta_{11} - 1/2 [\log \beta_{02} + \log \beta_{20}]$$

The values of $\log K_m$ were -0.275, -0.240, -0.148, for [Fe-1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone], [Cu-1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone], [Re-1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone], complexes respectively. The negative values of $\log K_m$ showed that binary complexes are more stable than their ternary complexes while in case of the positive value indicates that the ternary complex is more stable than their simple binary complexes.

It is clear from the values of stability constants of complexes that 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone ligand is formed it means that the complexes of minimum stability as its complexes showed the lowest values of $E_{1/2}$ in comparison to the other complexes¹⁶. The stability constants of complexes are lesser than other metal drug complexes is due to the presence of two electron withdrawing groups in frame work than caused greater steric hindrance¹⁷. Similar is the case with ligand in which the N^1 -substituted derivatives of formed complexes with metal which having lesser stability constants than sulfonyl complexes, it might be the fact that it has CH_3CO group¹⁸. The highest values of stability constants of 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone complexes amongst all other sulphur containing are due to having the largest shift of $E_{1/2}$ in its complexes¹⁹. The values of stability constants varied from 1.70 to 9.20 confirmed that either 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone in combination or their metal complexes could be effective against metal toxicity²⁰.

The electro kinetic mobility of metal ions of Fe, Cu, and Re point out against the pH which gives so many peaks in the graph. These peaks show the pH range where mobility of ions is practically remains constant. In the region of first peak the metal ions are uncoupled with the ligand. It found at very low pH at this point highly protonated species of ligand is

maximum, thus it concluded that the protonated species of ligand is not given complex. Beyond this pH range of metal ions has decreasing order of mobility; this decrement revealed that the complex is formed. And also found that a mobility of the metal ion species remain constant at some point which also conclude that complex is produced. At this point where we gate 1:2 cationic complex is formed. One ligand anion combines with each metal ion to form $[\text{Fe}(\text{L})_2]^+$ and $[\text{Cu}(\text{L})_2]^{++}$, and $[\text{Re}(\text{L})_2]^{++}$ cationic complexes respectively²¹⁻²⁵. During the analysis it also find out further increment of pH beyond the second peak than after no change occurs it indicates no mobility of metal ion so far no complexation takes place. It is significant that these studies give clear evidence of the binary complex formation of 1:2 compositions. For that calculation of stability constant K, the region between first and second peaks is determine²⁶⁻²⁸.

The system contains using the principle of average mobility of ions, with this principle we determine Stability constant for the complex can be calculated graphical value, which shows that solution containing a mixture of free metal ion and 1 -{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone as 1:2. Using the principle of average mobility accordingly the pH corresponding to the dissociation constant of ligands, the concentration of ionic ligands at this pH is calculated which is reciprocal to the stability constant K of the 1:2 metal-drug complex²⁹.

With the help of dissociation constant of 1-{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone and the metal ions. The concentration of 1 -{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone ligand is determined for the pH, from the stability constant is calculated³¹⁻³⁵.

A single well defined wave was obtained for metal-ligand system between the pH of 7.5-9.5. and diffusion controlled of each wave determine and verified from i_d vs C and i_d vs \sqrt{h} plots where i_d = diffusion current in μA ; C = conc. In m mole lit⁻¹, h = height of mercury column.

Slope of the linear graph of $\log(i/i_d - i)$ vs E_d was determined in the range of 30-32 mV, thereby showing the reversible nature of reduction process. The plot of $E_{1/2}$ vs $\log C_x$ has been straight line showing stable complex. The coordination no. (j), the metal complex is obtained from the slope of this plot, which given as:

$$d(E_{1/2})/d \log C_x = -j.0591/n$$

where n = no. of electrons involved (here $n = 2$). The value of j was found to be 4 for Cu(II) and Re(II) and for Fe(III) it is 6. This shows that composition of the complex is 1:2 (metal: ligand).

The $E_{1/2}$ has a linear correlation with ligand concentration; which shows that there is only one complex formed. The following equation has been used to calculate the stability constant of the complex studied³⁶⁻³⁷.

$$\Delta(E_{1/2}) = 0.0591/n \log \beta + j.0591/n \log C_x$$

Here, $\Delta(E_{1/2})$ = Difference of half wave potentials of simple metal ion and complexed ion, n = number of transferred electron, $\log \beta$ = Stability constant of complex formed, j = Coordination number, C_x = concentration of ligand.

Thus the value of $\log \beta$ has been found to 14.37, 13.62 and 14.97. Polarographic data of metal ligand complex found around 0.32, 0.36 and 0.38 respectively.

3.4 Conclusion

Calvin Bjerrum pH titration for the determination of stability constant suggest that the value of $\log \beta$ vary for Fe, Cu and Re metal ions is 14.37, 13.62 and 14.97 respectively. The highest value of stability is showing the stability of complex. From these values ΔG , ΔH , ΔS values are determine, from these values it conclude that if ΔG is more negative than ΔH is more and more negative and ΔS tend to its positive side, thus complex is stable (Table-3.9)

Table 3.9. Thermodynamic properties for metal and 1 -{3-[2-Amino-5-(5-hydroxy-5H-imidazol-4-ylmethanesulfonyl)-benzyloxy]-4H-pyrazol-4-yl}-ethanone complex.

SN	ION	ΔH kJ/mole	ΔS j/mole/degree	$-T\Delta S$ kJ/mole	ΔG kJ/mole
1	Fe(III)	-64.28	-75.54	22.54	-41.74
2	Cu(II)	-60.93	-71.60	21.37	-39.56
3	Re(II)	-66.97	-78.69	23.49	-43.48

Thus the value of $\log \beta$ has been found to 14.37, 13.62 and 14.97. Polarography analysis of metal ligand complex given $E_{1/2}$ values around 0.32, 0.36 and 0.38 respectively which also revealed that complexes are stable.

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