CHAPTER - I

INTRODUCTION.

Life and its appearences are connected with specific and distinct madroscopic structures. It has been proved beyond doubt that these structures are the result of a molecular order and the information stored in molecules. Obviously then the reactions occuring on the molecular level must be highly specific. This specificity is partly due to qualities of enzymes-the biological catalysts. Approximately 50% of them contain either fixed metal ion or need metal ions to be catalytically active.[1,2] Mixed chelation occurs commonly in biological fluids as millions of potential ligands are likely to compete for metal ions found invivo i.e. sodium, potassium, magnesium, calcium, manganese, iron, cobalt, copper, zinc and molybedenum.[3] Such complexes, where metal ion is bound to two or more different kinds of ligands, are called mixed-ligand complexes. Mixed-ligand complex formation occurs

during the transition state of metal ion catalyzed reactions.[4] They can be regarded as models for metalloenzyme substrate complexes.[5,6] The metal ions help to bring the two ligands closer in the mixed ligand complexes. The extent to which the formation of the mixed ligand complex is probable, will depend upon the formation constant of the mixed ligand complex in question.

In a system containing one metal ion (M^{n+}) and two bidentate ligands AH_2 & LH_2, with significant difference in complexing tendencies, simple complex (MA) is formed by the combination of the more complexing ligand (A) and the metal ion. The other ligand remains unbound in solution. However, if the complexing tendencies of the two ligands are similar, the formation of the mixed ligand complex could be shown as[7]:

$$M + A + L \rightleftharpoons MAL \quad (1)$$

The charges on the ligands have been omitted for convenience. The coordination number of the metal ion has been presumed to be four. However, the above framed equation is an over simplification of the equilibrium which may proceed in two ways:

$$M + A \rightleftharpoons MA \qquad MA + L \rightleftharpoons MAL \quad (2 \ \& \ 3)$$

$$M + L \rightleftharpoons ML \qquad ML + A \rightleftharpoons MLA \quad (4 \ \& \ 5)$$

It was suggested by watters[8] and later by kida[9] that the tendency of mixed legand complex formation is determined by the reproportionation constant and from statistical consideration

it should have a value 4. Under purely statistical consideration when there is no interaction between MAL, MA_2 & ML_2, there is possibility of 50% formation of MAL, while binary complexes MA_2 & ML_2 are formed 25% each.

$$K_{reprop.} = \frac{(MAL)^2}{(MA_2)(ML_2)} = \frac{(\frac{1}{2})^2}{(\frac{1}{4})(\frac{1}{4})} = 4$$

$$\log K_{reprop.} = 0.6$$

This equation has been further rearranged by Bonnett and Paris[10] to show that

$$\log K_{reprop.} = 2 \log K^M_{MAL} - \log (K^M_{MA_2} + \log K^M_{ML_2})$$

$$= (\log K^M_{MAL} - \log K^M_{MA_2}) + (\log K^M_{MAL} - \log K^M_{ML_2})$$

Thus, in a mixed system the probability of formation of mixed-ligand complex is more than the binary complexes. According to Schaap and Mcmasters[11] from statistical considerations, formation of mixed-ligand complex MAL, should be preferred over simple complexes MA_2 & ML_2, whenever the concentrations of the ligands involved are such that the products of the formation constants for the simple complexes and the concentrations of the ligands raised to the appropriate power are approximately equal i.e.

$$K^M_{MA_2} (A)^2 = K^M_{ML_2} (L)^2$$

Sharma and Schubert[12] have given a general treatment of statistical factors in the formation and stability of ternary complexes and have pointed that these favour the formation of mixed complexes rather than complexes containing one type of ligand.

However, the values of formation constants for mixed ligand complexes are observed to be higher or lower than expected from statistical considerations. As proposed by Bjeerum,[13] in case of binary complexes this may be because of electrostatic effect or reset effect, the latter constituting all contribution to the formation constant which cannot be explained either statistically or electrostatistically.

Another way of showing that the formation of mixed ligand complexes is favoured, is to compare the difference in the formation constants K^{MA}_{MAL} & K^{M}_{ML} and also K^{MA}_{MAL} & $K^{ML}_{ML_2}$. With greater contribution from nonstatistical factors log (K_1) = log K^{M}_{ML} - log K^{MA}_{MAL} is less and log (K_2) = log K^{MA}_{MAL} - log $K^{ML}_{ML_2}$ is more.

It can be seen that out of the two ways the consideration of log $K_{reprop.}$ has statistical basis, while log K calculation implies, that the corrosponding binary (1:1) complexes contribute to the formation of MLA i.e. MA+L $\rightleftharpoons$ MAL & ML+A $\rightleftharpoons$ MLA.

In the cases of systems containing same or lesser amounts of ligands than the metal ions, consideration of log K may be preferred. However, in the systems containing excess of L and A, log $K_{reprop.}$ should be preferably used.

It was observed by Watters and coworkers[14,15] that the value of log $K_{reprop.}$ is more than the expected value of 0.4.0.The formation of the mixed ligand complex is, thus, dependent on the factors other than the statistical. They observed that in the mixed ligand complex MAL, where A = ethylenediamine(en) and L = Oxalate ion, K^{MA}_{MAL} is lower than K^{M}_{ML}. This is expected because en molecule has greater

bonding tendency than water molecule and thus increases the concentration of electrons around the metal ions and hence the tendency of the oxalate ion to get bound with $(Men)^{2+}$ is less than its tendency to get bound with aquated metal ion.

It was, however, observed that the mixed ligand formation constant K^{MA}_{MAL} is significantly larger than would be expected from stastical considerations alone. $K^{Men}_{Men.ox.}$ has much higher value than $K^{Mox}_{Mox_2}$. This can be explained by consideration of electrostatic factor, which affects the enthalpy change and also the entropy factor. In the formation of (Cu.en.ox) there is no coulombic repulsion between the neutral en molecule and the oxalate ion. However, in the formation of $(Cu.ox_2)^{2-}$ from (Cu.ox), the incoming second ox^{2-} ion is repelled by existing ox^{2-}. In other words $(Cu.en)^{2+}$ has more attraction for ox^{2-}, than that of neutral (Cu.ox).

The enthalpy change in the formation of (Cu.en.ox) is more negative, than in the formation of $Cu.(ox)_2^{2-}$. Further, since the molecule (Cu.en.ox) is neutral, there is no solvation of the molecule and thus the solvation entropy is more positive, than in the formation of negatively charged $(Cu.ox_2)^{2-}$. Thus both the entropy and enthalpy changes favour the formation of (Cu.en.ox), resulting in higher value of $K^{Cu.en}_{Cu.en.ox}$. This explains why $K^{Cu.en}_{Cu.en.ox} > K^{Cu.ox}_{Cu.ox_2}$.

Schaap and Mcmaster[11] also observed that the tendency of the neutral en molecule to combine as second ligand with Cu.(ox) and $Cu.(en)^{2+}$. The values observed for $K^{Cu.ox}_{Cu.ox.en}$ and $K^{Cu.en}_{Cu.en_2}$ were 9.7

and 9.5 in agreement with the prediction based on statistical factor alone. This is because there is no additional electrostatic repulsion or charge neutralization effect involved in the formation of (Cu.ox.en) or ($Cu.en_2$).

They, however, observed the value of the constants for disproportionation reaction to be - 1.3, much less than expected from statistical considerations. Thus, they argued that the mixed ligand complex does not undergo significant disproportionation. The reason could be explained by considering that the contribution from enthalpy and entropy factors make neutral (Cu.en.ox) less susceptible to disproportionation than $\left[Cu.(en)_2\right]^{2+}$ and $\left[Cu.(ox)_2\right]^{2-}$.

Noji and Kidani[16] studied the complexes CuLen, where L = dibasic acids. They found the order to be the same as in binary complexes. Fridman and coworkers[17] used the solubility method for the determination of the formation constants of M.en.ox.complexes. They observed the mixed ligand complexes to be more stable in solution than the simple complexes. The order of increasing values in the mixed complexes is

$$NiC_2O_4.en < Cu.C_2O_4.en < CdC_2O_4.en < AgC_2O_4.en$$

They observed a greater similarity between the formation constants of the complexes of the type $M(C_2O_4)$ en and $M(glycine)_2$, probably because of the fact that the five membered rings are formed in both with equal numbers of amine and carboxylic groups

attached to the metal ion. The slight difference in the values of $K_{M \cdot C_2O_4.en}$ and $K_{M(gly)_2}$ can be because of the asymmetry in the force field in the mixed ligand complex due to unlike ligands.

Steric factors also affact the formation of the mixed ligand complexes. In the system Cu.(en)N-N ethylenediamine (et_2en), it has been observed that in the formation of the binary complex $Cu.(et_2en)_2^{2+}$, the steric hindrance is more than in the formation of the mixed ligand complex Cu.(en) et_2en and hence the value of $K^{Cu.en}_{Cu.en.et_2en}$ is much higher than $K^{Cu.et_2en}_{Cu.en.et_2en}$.[18]

Steric effect has also been observed in the formation of Cu.en. iminodiacetate[19]. Sigel and coworkers[20,21] observed that sizes of chelate rings also affect the formation of the mixed ligand complex. They have formulated a tentative rule that the order of mixed ligand formation constants in ternary complexes containing two chelate rings is, one five membered ring and one six membered ring $\rangle$ two six membered rings $\rangle$ two five membered rings.

Sorago and coworkers[22] showed that in Cu.diamine-diamine or Cu.diamine-glycine complexes, the stability constants are higher than the statistically expected values. Lim[23] has studied the complexes Pd.en.L where L = aspargine or glutamine. Chung and Huang[24] have carried out interesting study of the coordination of monodentate ligand with Cu.macrosyclic tetra-amine complexes.

Martell and coworkers[25] studied the ternary complexes employing, a series of primary ligands like 2,2' -bipyridyl,

1-10 phenanthroline, N-OH.ethylenediamine (HEN) and N-N-N'-N' tetramethylenediamine (TMEN). The series of secondary ligands used were hydroxy derivatives of benzene and naphthalene. They observed that HEN and TMEN that form more stable 1:1 metal chelates, are secondary ligands to combine with the metal ion in the mixed ligand complex, while the aromatic amines that form less stable chelates are primary ligands to combine first in mixed ligand complexes. They explained the reversal in terms of lower basicities of aromatic amines,which result in higher concentration of aromatic amine in solution than the aliphatic amine. They also observed that,when the primary ligand attached to the metal ion is a neutral aliphatic amine (A), $K^{MA}_{MAL} < K^{M}_{ML}$ and the relative order of affinities of the secondary ligands (L), is same as in binary complexes. However, when the primary ligand is an aromatic tertiary diamine (A), the affinity of the secondary ligand L for MA does not decrease i.e. $K^{MA}_{MAL} \approx K^{M}_{ML}$. In fact there was a slight increase in the value of K^{MA}_{MAL} than K^{M}_{ML} as observed in the case of Cu.dipy.catechol system.

The explanation extended by Sone and coworkers[26] was that the positive value of log $K^{Cu.dipy}_{Cu.dipy.cat.}$ - log $K^{Cu.}_{Cu.cat}$ (Δ log K) may be because of steric factor. However, it is not possible to explain why the coordination of pyrocatecholate-dianion to the hydrated $Cu.^{2+}$ ion should be sterically more hindered, than the coordination of the same ligand to Cu.dipy. 1:1 complex. If at all any steric effect should be operative, it should be more in the ternary complex.

Sigel and coworkers[27,28] observed in the systems M.dipy.L where M = Co^{2+}, Ni^{2+}, $Cu.^{2+}$ and Zn^{2+} and L = Y picoline, methyl αpicolyl sulphonate and 2 acetyl hydroxy thiophene, the ternary complexes are more stable than expected from statistical reason. They also studied the systems Cu.dipy.L. where L = en, glycine, malonic acid and pyrocatechol. It was observed that the formation constant K^{MA}_{MAL} where A = dipy.or o-phen is only slightly lower than K^{M}_{ML} and is much higher than $K^{ML}_{ML_2}$. K^{MA}_{MAL} was even higher than K^{M}_{ML} where L = Catechol, as observed by Martell and coworkers.[43]

Perrin and coworkers tried to interpret the various values of the mixed ligand formation constants studied by them,[29,30] in terms of static, electrostatic, steric and electronic effects. But they have not been able to explain higher values of $K^{M.dipy}_{M.dipy.L}$ in M.dipy.L complexes.

An explanation was extended by Sigel and coworkers[28] and Bhattacharya and coworkers,[31] almost simultaneously, attributing lower negative or positive values of Δlog K to the special behaviour of dipyridyl or O-phenanthroline molecules. These ligands are bound to metal ion by N$\longrightarrow$M σ bond as in case of primary diamines. However, besides that, there is also M$\longrightarrow$N π bond formation by the back donation of electrons from the metal $d\pi$ orbitals to the vacant delocalized π orbitals over the ligand.

The $d\pi - p_\pi$ interaction does not allow the concentration of electrons on the metal ions to increase significantly. In other words, the positive charge on the metal ion or its electronegativity in $\left[M(dipy)\right]^{2+}$ is almost same as in $(Maq)^{2+}$ complexes.

The enthalpy change in the coordination of L^{2+} with $\left[M(aq)\right]^{2+}$ or $\left[M(dipy)\right]^{2+}$ is almost same. Since both the species (M.aq.L.) and (M.dipy.L.) are neutral, the entropy change in the formation of both should be equal. This explains why $K^{M.dipy.}_{M.dipy.L} \approx K^{M}_{ML}$. $K^{M.dipy.}_{M.dipy.L.}$ has a much higher value than $K^{ML}_{ML_2}$, as will be expected from difference in π bonding, electrostatic repulsion and charge neutralization, in the formation of M.dipy.L. and ML_2.

It has been observed by Sigel and coworkers[32-36] and also by Bhattacharya and coworkers[37-42] that the difference $K^{M}_{ML} - K^{M.dipy}_{M.dipy.L}$ is more negative, when in the secondary ligand coordination is from two nitrogen atoms (aliphatic diamines). The difference is less negative, when the secondary ligand atoms are one oxygen and one nitrogen (aminoacids) and is least negative when the secondary ligand has two oxygen atoms (catechol, oxalic acid, salicylic acid).

Sigel[28] has put forth two explanations for the higher values of log $K^{M.dipy.}_{M.dipy.Cat.}$ in M.dipy.Catecholate system. The π system of the oxygen containing secondary ligand may have some effect on increasing K^{MA}_{MAL} value. There may be an interaction between dπ orbitals, π orbitals over dipyridyl molecule and delocalized π electron cloud over the catecholate ion, resulting in high value of K^{MA}_{MAL}. The aliphatic diamines (N,N.donars) and amino acids (N,O donars) do not have π electron clouds and hence π delocalization in the complex molecule is restricted. This does not allow the value of K^{MA}_{MAL} to go up and log K is more negative.

Another explanation extended by them is in terms of Pearson's "hard and soft" acid and base rules. As a result of back donation of electrons from metal d orbitals to dipyridyl the metal ion

becomes a harder acid. This favours coordination with oxygen rather than with nitrogen containing ligands.

To explain the positive value of log K in Cu.dipy.catecholate complex, Sigel[28] considered Jahn-Teller effect as an additional factor. According to him the distorted octahedron $Cu.(H_2O)6$ is somewhat more strongly distorted towards a square planar structure by the coordination of strongly binding 2,2' bipyridyl molecules. This creates the right geometry for the coordination of the secondary ligand. This associated with $d\pi$ delocalization effect makes $K^{Cu.dipy.}_{Cu.dipy.Cat.} > K^{Cu.}_{Cu.Cat}$.

Thus the above mixed ligand complex studies point to the possibility of $M \longrightarrow L$ π interaction in transition-metal complexes of oxygen containing aromatic ligands. A similar $M \longrightarrow L$ π intraction can be envisaged in transition metal complexes of ortho-hydroxy aromatic aldehydes and ketones. The experimental work in the next chapter supports this point.

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