Inter-ligand Stacking Interactions in Ternary Complexes

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The formation constants of the ternary complexes [MA(ATP)] where M = Cu or Ni and A = 5-nitro-1,10-phenanthroline (A1) or 2,2'-dipyridylamine (A2) have been determined potentiometrically in 50% (v/v) aq dioxan at ionic strength = 0.2 mol dm⁻³ [NaClO₄] and temperature = 30°C. It is observed that there is an intramolecular stacking between the heteroaromatic nitrogen bases and the base part of ATP resulting in greater stabilization of the mixed ligand complexes.

The coordination chemistry of the nucleotide, adenosine-5'-triphosphate (ATP) has biochemical significance⁴. In several enzymatic reactions the nucleotide is bound to the metal ion along with another ligand and hence the importance of the study of mixed ligand complexes involving ATP. Formation of mixed ligand complexes [Cu(2',2'-dipyridyl)(ATP)] and [Cu(1,10-phenanthroline)(ATP)] has been studied by Sigel et al.².³ As Cu(II) does not prefer an axial coordination, therefore, ATP can not be expected to act as a tridentate ligand in ternary complexes. Hence, coordination will occur only from the phosphate end and Δlog K = log KMA - log KML is expected to be less positive than that in the case of other bidentate O⁻O⁻ coordinating ligands. However, Δlog K has been found to be more positive.

In addition, in the case of [M(2',2'-dipyridyl)(ATP)] complexes where M = Zn(II), Mn(II) or Ca(II)³, with less significant or no M→A interaction, Δlog K has been found to be positive. The extra stabilization in [M(2',2'-dipyridyl)(ATP)] has been explained by Sigel et al.².³ by considering that in the ternary complex the nucleotide coordinates with Cu(II) from the phosphate end only, but there is also an intramolecular stacking interaction of charge-transfer type between 2,2'-dipyridyl molecule and the base moiety of the nucleotide. Orioli et al.⁴ on the basis of X-ray study of the above ternary complexes observed two types of stacking interactions, inter- and intramolecular, the intramolecular stacking interaction being of the type suggested by Sigel.

Recently it has been shown by us⁵ that inter ligand interaction is dependent on the nature of the tertiary base. In case of [Cu(2-(2'-pyridyl)-benzimidazole)(ATP)] the stacking interaction is more than that observed in case of [Cu(2,2'-dipyridyl)(ATP)] or [Cu(1,10-phenanthroline)(ATP)]. It has also been shown⁶ that the inter ligand interaction is hydrophobic in nature and is less in solvents with lower dielectric constants such as dioxan.

Presently we have studied the ternary complexes of the type [CuA (ATP)] where A = 5-nitro-1,10-phenanthroline (A¹) or 2,2'-dipyridylamine (A²) in order to see the effect of substitution on the ligand (A) on the mixed ligand formation constants.

Materials and Methods

All the reagents were of AR grade. Potentiometric titrations were carried out in 50%(v/v) aq dioxan using digital pH meter (DIGICHEM-8201) having an accuracy of ±0.01. The pH meter readings were corrected for the non-aqueous solvent using the method suggested by Uitert and Haas⁶. The value of proton ligand formation constant of AHz, AH, LHz, LH, L and the formation constants of binary complexes [CuL]+, [CuL₂] and [CuA]+ and [CuA₂]+ were determined in 1:1 (v/v) aq. dioxan at an ionic strength 0.2 mol dm⁻³ [NaClO₄] and temp. 30°C using SCOGS computer program as detailed earlier. The values of Kₐ¹, K₂¹, log Kₐ⁰Cu and log Kₐ⁰M are 7.5 (±0.07), 4.98 (±0.07), 8.22 (±0.02) and 8.57 (±0.05), respectively.

The formation constant of [CuA₂]+ could not be determined pH-metrically in this solvent medium because the formation of the complex [CuA] is complete at very low pH⁸. Solvent extraction method⁹ using chloroform as an extractant could not be used because of the solubility problem. Hence the formation constant, log Kₐ⁰Cu was refined by presuming complete formation of [CuA]²⁺. The value works out to be less than that in aqueous solution. This is expected because Kₐ¹ of ligand A in 50%(v/v) aq dioxan is less than that in aqueous medium. Hence the formation constant, log Kₐ⁰Cu of [CuA]²⁺ was considered to be one log unit less than the value in aqueous solution.

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The values of the formation constants of [CuA], [CuA₂] were not computer-refined. However, reactions in these systems almost occurred in steps.

\[
\text{Cu} + A \rightleftharpoons [\text{CuA}]
\]

\[
[\text{CuA}] + L \rightleftharpoons [\text{CuAL}]
\]

And hence less precise value of the formation constant of the complex [CuA] did not affect the formation constants of the mixed ligand complexes.

The formation constants of the ternary complexes [CuAL]⁺ were determined by titrations of 1:1 (v/v) aqueous dioxan solutions (50 ml) of the reactants ([M]²⁺ : [A] : [L] : 1:1:1 and 1:1:2) against carbonate-free standard alkali and using the computer program SCOGS. Titrations of each set was carried out twice to check the reproducibility of the data. The species present in solution were considered to be LH₂, LH⁻, L²⁻, AH₂⁺, AH⁺, A²⁻, [CuL]⁺, [CuL₂], [CuA]²⁺, [CuA₂]²⁺ and [CuAL]⁺.

The preliminary values of \( K_{\text{CuAL}} \) fed into the computer were obtained by considering the reaction to be of the type [CuA] + L \rightleftharpoons [CuAL] (see ref. 9). The values of the mixed ligand formation constants obtained using the two titration data are almost identical (see Table I).

**Results and Discussion**

The formation constants of the mixed ligand complexes obtained by the computer calculation are nearly in agreement with the preliminary values fed into the computer, considering the reaction to be taking place in steps.

The analysis of representative species distribution curves (Fig. 1), shows that in the pH range 1-3, Cu(II) and [CuA] are the major species and in the pH range 4-7 the species [CuA] and [CuAL] are predominant. Formation of [CuA₂], [CuL] and [CuL₂] is very less. This shows that the reaction takes place in steps.

The stability of [MA₃L] is found to be much greater than that of [M(1,10-phenanthroline)(L)] because of the presence of the electron withdrawing group in the ligand A¹. This depletes the electron density over the ring, making it a stronger \( \pi \)-acid than 1,10-phenanthroline and hence stabilizes the ternary complex.

The ligand, 2,2'-dipyridylamine (DPA) forms a six-membered ring on coordination to the metal ion. Moreover, an electron donating imino group (-NH group) in between two pyridine moieties enhances the electron density on the ring due to the presence of a lone-pair of electrons on the nitrogen atom. This should reduce M→A \( \pi \)-interaction resulting in lower value of the mixed ligand formation constant. However, delocalization of electron density in DPA is over a larger area than in 2,2'-dipyridyl. Hence the formation constants of ternary complexes are close for [Cu(2,2'-dipyridyl)(ATP)] and [CuA²L].

As in the case of [Cu(2,2'-dipyridyl)(ATP)] complexes, in the complexes of [CuA¹ ATP] or [CuA² ATP], \( \Delta \log K \) values are positive. This is evidently due to stacking interaction between the adenine base of ATP molecule and the tertiary amine. Further, \( \Delta \log K \) value in case of [CuA² ATP] is as much as in case of [Cu(2,2'-dipyridyl)(ATP)] indicating that the extent of stacking interaction is the same in both the cases.

In the case of [CuA¹ ATP], \( \Delta \log K \) is more positive than that for [Cu(1,10-phenanthroline)(ATP)]. Moreover, \( \Delta \log K \) is also more positive for [CuA¹ catecholate] complex than that for [Cu(1,10-phenanthroline)(catecholate)] complex due to greater M→A \( \pi \)-interaction. This shows that more positive value of \( \Delta \log K \) for [CuA¹ ATP] complex is because of

**Table I — STACKING CONSTANTS OF TERNARY COMPLEXES [MA(ATP)] AND \( \Delta \log K \) VALUES**

<table>
<thead>
<tr>
<th>Ligand</th>
<th>( \log K_{\text{CuAL}} )</th>
<th>( \Delta \log K )</th>
<th>( \log K_{\text{CuAL}} )</th>
<th>( \Delta \log K )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A¹</td>
<td>8.53</td>
<td>+0.31</td>
<td>5.86</td>
<td>-2.71</td>
</tr>
<tr>
<td>A²</td>
<td>7.9</td>
<td>-0.32</td>
<td>5.62</td>
<td>-2.95</td>
</tr>
</tbody>
</table>

Fig. 1 — Species distribution curves during the formation of [CuA¹ ATP]
increase in M→A π-interaction. The extent of stacking interaction in [CuA₁ATP] is of the same order of magnitude as for [Cu(1,10-phenanthroline) (ATP)]. There is no significant effect of the nitro group on the stacking interaction. This may be because the intramolecular stacking is due to interaction between one of the pyridine rings and purine base of ATP. Since there is nitro group in one of the rings, it may not hinder the interaction. The present study reveals that inter-ligand interactions affect the stabilities of the ternary complexes.

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References