Studies on Schiff base complexes: Formation constants of Cu(II), Ni(II) and Zn(II) complexes on N-salicylidene-L-valinate, L-phenylalaninate and L-tryptophanate systems

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Abstract. The computer-based analysis of pH titration data obtained for the determination of the stability constants of M–A–B [M = Ni(II), Cu(II) or Zn(II), A = salicylaldehyde(Sal) and B = L-valine (Val), L-phenylalanine (Phe) and L-tryptophan (Trp) and AB the corresponding Schiff base] indicates preference for the formation of Schiff base complexes rather than the ligands binding as such to the metal ions without fusion of rings. The presence of aliphatic or aromatic side chains in the amino acids has no effect on the basicities of the coordinating sites of the Schiff bases. This is shown by the similarity of stability constant values for different Schiff base complex species.

Keywords. Schiff base complexes; stability constants; salicylaldehyde; L-valine; L-phenylalanine; L-tryptophan.

1. Introduction

The formation of Schiff base intermediates in reactions of biological importance, transamination, racemization and decarboxylation, is well documented (Braunschtein and Shemyakin 1953; Metzler et al 1954; Sigel 1971–1983; Srinivasalu and Reddy 1984; Makela et al 1988). Studies on Schiff bases derived from salicylaldehyde (Sal) and L-valine (Val), L-phenylalanine (Phe) or L-tryptophan (Trp) and their metal complexes serve as useful models in understanding the more complicated pyridoxal systems. The scope of the present study, therefore, has been oriented towards carrying out a systematic investigation of Schiff base complex equilibria and evaluating the factors affecting the distribution of binary and ternary Schiff base complex species in solution.

2. Experimental

Nitrates of copper(II), nickel(II) and zinc(II) and amino acids used in this study were of BDH (AR) and Fluka puris grade respectively. Salicylaldehyde (E Merck) was purified by distilling twice under vacuum and used. pH titrations were carried out at a temperature of $30 \pm 0.1°C$ with ionic strength 0.1 maintained by KNO_3. Dissociation

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constants of ligands used in this study were determined by a standard procedure (Albert and Serjeant 1971). The protonation and deprotonation constants of Schiff bases were determined by spectroscopic methods and the formation constants of binary complexes and ternary complexes were determined by reported methods (Chaberek and Martell 1952; Sivasankar 1980).

3. Results and discussion

3.1 *Binary systems*

With Ni(II), both MA and MA_2 were formed but the concentration of MA_2 was very low, whereas in the Cu(II)–Sal(A) system, the value of both MA and MA_2 species could be determined easily because of the presence of appreciable concentrations of both the species. In the case of Zn(II), the plot of n vs pL was found to be a straight line, parallel to the horizontal axis, indicating the absence of the MA_2 species even when the ratio of metal to ligand was kept at 1:6. L-valine, L-phenylalanine and L-tryptophan are found to function as bidentate ligands involving the carboxyl and the amino groups. Stability constants follow the Irving–Williams order Cu(II) > Ni(II) > Zn(II).

3.2 *Ternary systems*

3.2a *Nickel(II)-Sal(A)-Val, Phe and Trp(B) system:* For the Ni(II)-Sal-Val(B) system, trial runs indicated the optimum pH for complexation to be in the range 6·0 to 9·0. The best fit of computed and experimental curves could be achieved by considering the presence of three ternary species MAB, MAB_2, and MA_2B_2, and their overall formation constants K_{11}, K_{12} and K_{22} were found to be 10·42, 13·50 and 17·35 log units respectively. The magnitudes of the values clearly indicate the favoured formation of these ternary species. The relative stabilities of the species and the magnitudes of interactions involved can be understood by comparing the stepwise formation constants as shown below.
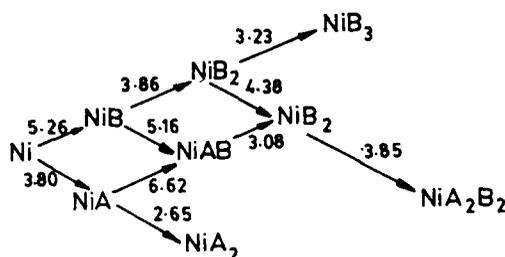
It is clear that the binary valinate complexes are more stable than the corresponding salicylaldehyde complexes which can be attributed to two factors: (i) the five-membered chelate ring in the valinate complexes is sterically more favoured than the six-membered ring in salicylaldehyde complexes and (ii) the ligands containing hetero donor atoms are preferred to those with identical donor sites. The successive stability constants of the binary complexes decrease in accordance with statistical expectation.

In contrast, in ternary complexes, the presence of a ligand of one kind favours the

addition of a ligand of another kind, i.e., the presence of salicylaldehyde in the metal coordination sphere favours the addition of valinate and vice versa. Hence, the preference to form ternary Schiff base complex species may be attributed to the strong inter-ligand attraction. It may be pointed out that the enhanced stability should be attributed in part to the fusion of the two independent ring systems. Multi-ring formation by fusing two chelate rings leads to greater stability than chelation by two independent bidentate ligands due to enhanced entropy.

The log K value for the addition of the second molecule of valinate to MAB is 3·08 and is comparable to that of the successive formation of the *tris*-valinate (MB$_3$) species (log $K_{03} = 3·23$) indicating that the second molecule of valinate in MAB$_2$ is coordinate to the metal ion independently. Thus MAB$_2$ is a mixed ligand species involving the Schiff base AB and the amino acid B and a more appropriate formulation for the complex would be M(AB)B.

The formation of the highly stable MA$_2$B$_2$ species with a log K_{22} value of 17·35 in the Sal(A)-Val(B) system is of interest because of its composition. MA$_2$B$_2$ is obviously a Schiff base complex M(AB)$_2$ containing 2 molecules each of A and B. The *bis*(tridentate AB) complex would involve a coordination number of 6 while independent chelation by four bidentate ligands lead to a coordination number of 8 which is not favoured by 3d metal ions.

The concentration profiles and species distribution diagram of the various species in the Ni(II)-Sal(A)-Val(B) system are shown in figure 1, from which it is clear that the Schiff base complexes are the predominant species and their stability reflects
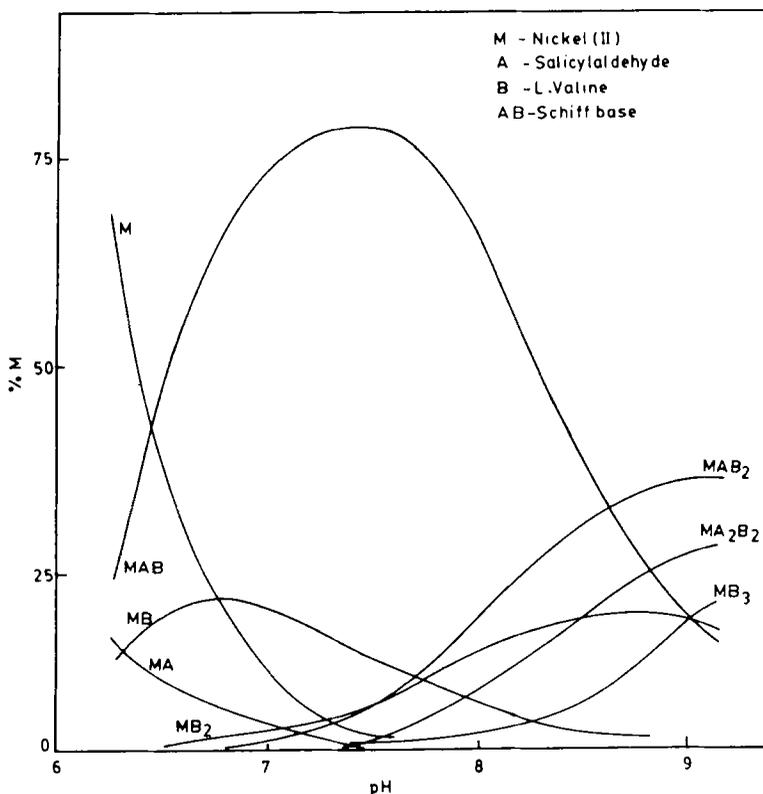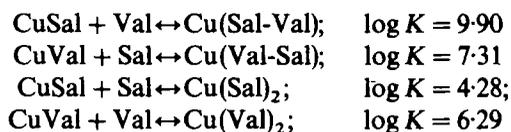

Figure 1. Species distribution for Ni complexes as a function of pH (M:A = 1:1).

their favoured formation as compared to the binary species. Though the value of K_{20} for MA_2 in the Ni(II)-Sal(A) system is 2·66, the species is totally absent in ternary systems. Thus the formation of the ternary species MA_2B_2 would also be negligible. The behaviour exhibited by Ni(II)-Sal(A)-Phe and Trp(B) is found to be the same as that of Ni(II)-Sal(A)-Val(B) indicating that the phenyl and indole groups of the respective Sal(A)-Phe and Trp(B) Schiff bases have no effect on the basicities of the coordinating sites of their corresponding Schiff bases.

3.2b   *Copper(II)-Sal(A)-Val, Phe and Trp(B) systems*:   Cu(II) tends to be 4-coordinate in aqueous solution and hence forms only one ternary species MAB where AB is the tridentate Sal-Val Schiff base. The experimental points were found to fit the computed curve only when the metal to salicylaldehyde ratio was maintained at values higher than 1:1. In equimolar systems, the buffer region is quite steep and extends over a narrow pH range making the computed curve coincide with the experimental curve only over a narrow region, whereas in the case of 1:2, the buffer region is slightly wider making the computation easier and accurate. The buffer region in the Cu(II) systems extends between 2·5 and 3·5 and in this region the predominant species is the Schiff base complex MAB. The fact that MAB is formed even at such low pH values indicates the stabilization of the Schiff base towards hydrolysis and its dissociation in the presence of metal ions.

Under these conditions the protonated and deprotonated forms of the uncomplexed Schiff bases are found to be of the order of 0·001% of the total salicylaldehyde available (table 1). The stability constant of MAB was found to be 15·40 log units and this large value indicates the tridentate coordination. The preference for the formation of the Schiff base species over the binary species is clearly seen from the following equilibrium reactions and their corresponding constants.

$$CuSal + Val \leftrightarrow Cu(Sal\text{-}Val); \quad \log K = 9·90$$
$$CuVal + Sal \leftrightarrow Cu(Val\text{-}Sal); \quad \log K = 7·31$$
$$CuSal + Sal \leftrightarrow Cu(Sal)_2; \quad \log K = 4·28;$$
$$CuVal + Val \leftrightarrow Cu(Val)_2; \quad \log K = 6·29$$

The behaviour of Cu(II)-Sal(A)-Phe and Trp(B) systems are found to be the same as that of the Cu(II)-Sal(A)-Val(B) system indicating that the phenyl and indole groups of Schiff bases have no effect on the basicities of the coordinating sites of the respective Schiff bases.

Table 1. Dissociation constants of ligands, formation constants of protonated (K_{HAB}) and deprotonated (K_{AB}) Schiff bases and stability constants of binary complexes (MA and MB).

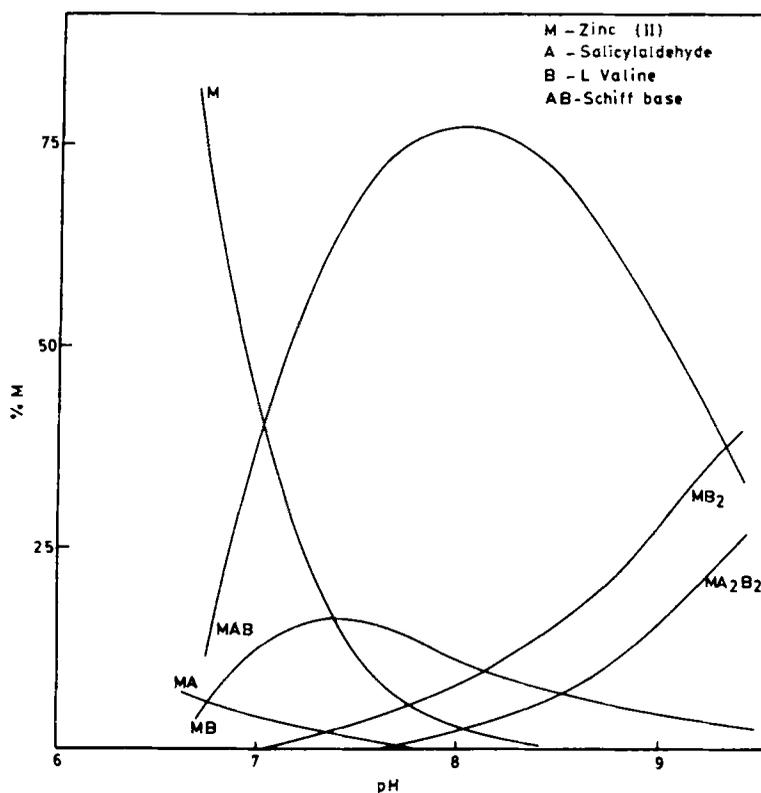| Legends | Dissociation constant | | Formation constant | | Overall stability constant | | | | | | | |
| | pK1 | pK2 | K_{HAB} | K_{AB} | Nickel | | | Copper | | Zinc | | |
					K_1	K_2	K_3	K_1	K_2	K_1	K_2	K_3
Salicylaldehyde	8·20	—	—	—	3·80	6·45	—	5·50	9·78	2·93	—	—
L-Valine	2·24	9·65	3·15	0·40	5·26	9·12	12·35	8·09	14·38	4·75	8·65	—
L-Phenylalanine	2·23	9·15	2·95	0·35	5·15	9·50	12·05	8·05	14·45	4·35	8·28	—
L-Tryptophan	2·20	9·55	3·05	0·25	5·05	9·10	12·10	7·98	14·36	4·30	8·30	—

Figure 2. Species distribution for Zn complexes as a function of pH (M:A = 1:1).

3.2c *Zinc(II)-Sal(A)-Val, Phe and Trp(B) systems*: Zn(II) complexes of Sal-Val have been investigated in the pH region 6·7 to 9·0. The stability constants of MAB and MA$_2$B$_2$ species were computed and the values of log K_{11} and log K_{22} are 9·25 and 15·10 log units respectively. The distribution of various species as a function of pH is shown in figure 2.

Here again, the behaviour of all the three systems of zinc is found to be same because the ligands are identical in complexation, except the phenyl and indole rings of the Schiff bases of Sal-Phe and Sal-Trp which in no way influence the nature of the coordination of the Schiff bases.

4. Conclusions

The preference exhibited in the formation of Schiff base complexes rather than the ligands binding as such to the metal ions without fusion of rings is clearly brought out by considering the stepwise formation constants. The overall formation constants of the mixed-ligands complexes (K_{11}^*) can be derived from binary stability constants,

$$K_{11}^* = K_{10}K_{02} \text{ or } K_{01}K_{20}.$$

The difference in the overall formation constant of Schiff base (K_{11}) and mixed

Table 2. Stability constants of binary and ternary complexes.

Ligand (Schiff base)	Nickel (II)			Copper (II)				Zinc (II)			
	K_{11}	K_{12}	K_{22}	$K_{11}-K_{11}^*$	K_{11}	K_{12}	K_{22}	$K_{11}-K_{11}^*$	K_{11}	K_{22}	$K_{11}-K_{11}^*$
Sal-Val	10·42	13·50	17·35	2·76	15·40	—	—	3·61	9·25	15·10	2·42
Sal-Phe	10·25	13·30	17·10	2·10	15·25	—	—	3·35	9·15	15·05	2·29
Sal-TrP	10·15	13·15	17·10	2·30	15·15	—	—	3·27	9·15	15·10	2·22
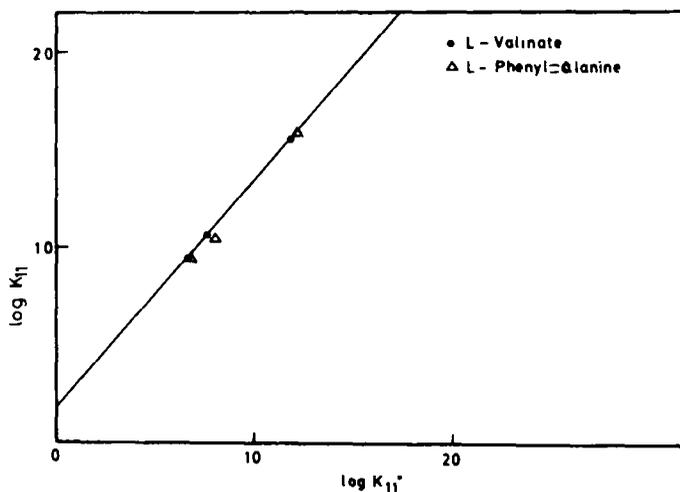
Figure 3. Plot of $\log K_{11}$ vs $\log K_{11}^*$.

ligand species is an indication of the favoured nature of Schiff base species. The $K_{11} - K_{11}^*$ values for the systems investigated in the present study, given in table 2, range between 2 and 4 log units, clearly indicating the preference for the formation of Schiff base complexes.

The plot of $\log K_{11}^*$ vs $\log K_{11}$ as shown in figure 3 was found to be a straight line with a slope equal to unity and an intercept equal to two, irrespective of the metal or the Schiff bases involved. This observation confirms that the enhanced stability of the Schiff base species is mainly due to the entropy factor rather than to mere inter-ligand attractive forces. The latter plays a relatively minor role, in the right direction, in enhancing the stabilities of the Schiff base species over mixed ligand complexes.

Acknowledgement

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