Stereoselective Effects in the Formation of Ternary Complexes of Simple Amino-acids with Copper(II)

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Summary Stereoselectivity is present in the formation of ternary complexes of Cu^{2+} with histidine and some simple amino-acids containing aromatic substituents.

METAL ions can form three *bis*-complexes with optically active amino acids (aa): M(D-aa)$_2$, M(L-aa)$_2$, and M(D-aa)-(L-aa). The first two will have identical stabilities while the last complex, containing ligands with opposite chiralities, is diastereoisomeric to them. Stereoselectivity is the preferential formation of one complex species before another and may be expressed quantitatively as

$$\Delta \log \beta = \log \beta[\text{M(D-aa)(L-aa)}] - \log \beta[\text{M(L/D-aa)}_2]$$

Very few cases of stereoselectivity in the formation of binary copper complexes of simple amino-acids have been reported. With Ni^{2+}, Co^{2+}, and Zn^{2+} and histidine (hist) stereoselectivity has been observed [1,2] but with Cu^{2+} the effect is negligible or very small, and, with the exception of binary histidine complexes, the experimental evidence to date suggests that stereoselectivity is very rare, or non-existent, in the copper–simple amino-acid systems.[2-4] Significant stereoselectivity has, however, been detected with *N*-substituted amino-acids such as *N*-carboxymethyl-L-valine with Cu^{2+}.[3,5]

We report the results of a potentiometric study of the ternary systems: (D- and L-histidine)–Cu/Ni–(L-amino-acid) and (Im-benzyl-L-histidine)–Cu/Ni–(D and L-amino-acid), with the amino-acids proline, serine, threonine, tryptophan, phenylalanine, valine, leucine, and methionine. To minimise errors in comparison the binary metal–amino-acid systems were studied under identical conditions to those used for the ternary system. The experimental data were treated using the 'Miniquad' computer program.[6] A selection of calculated formation constants is given in the Table.

The ternary Cu^{2+} systems resolved into two categories: (a) those with the stability order of Cu(D-hist)(L-aa) > Cu(L-hist)(L-aa) and Cu(Im-benzyl-L-hist)(D-aa) > Cu(Im-benzyl-L-hist)(L-aa), with a large stereoselectivity ($\Delta \log \beta > 0{\cdot}1$ log units); (b) those with the reverse stability order,

e.g. Cu(L-hist)(L-aa) ⩾ Cu(D-hist)(L-aa), with a small or negligible stereoselectivity ($\Delta \log \beta < 0{\cdot}1$). The amino-acids tryptophan and phenylalanine belong to category (a). Both contain aromatic rings in the side chain and neither of them show any stereoselectivity in the formation of binary bis-complexes. The differences in stability are large, $\Delta \log \beta_{1110}$ being 0·48 and 0·20 log units respectively. Valine, proline, serine, threonine, methionine, and leucine all contain aliphatic side-chains and belong to category (b), stereoselective effects being small (maximum of 0·06 log units) or negligible. For all the ternary complexes studied the stabilities with copper were much greater than expected on purely statistical grounds. This appears to be a characteristic of the histidine ligand.

No stereoselective effects whatsoever were found for the ternary complexes of Ni^{2+} and the stabilities of the mixed species were generally of the order expected statistically. The standard deviations quoted in the Table are, in our opinion, realistic for comparison purposes and consistent results were found when cross-checking with different titrations and different optical hands of some of the ligands.

We have also studied a number of other ternary systems containing simple amino-acids other than histidine. In most cases stereoselective effects were small or negligible but were surprisingly large with Cu(L-proline)(D- and L-tryptophan) where the values for log β_{1110} for the formation of the species Cu(L-proline)(L-tryptophan) and Cu(L-proline)(D-tryptophan) were 16·404(6) and 16·148(5) respectively, *i.e.* $\Delta \log \beta = -0{\cdot}26$ log units.

TABLE

Metal complex formation constants for the species $[M_w(D/L\text{-hist})_x(L\text{-aa})_yH_z]$ and $[M_w(\text{benzyl-L-Hist})_x(D/L\text{-aa})_yH_z]$ at 25° and $I = 0{\cdot}10$M. (log β_{wxyz} values, standard deviations in parentheses).

		log β_{wxyz}							
		Histidine			Im-benzyl-L-histidine				
		Cu			Ni	Cu			Ni
Amino-acid (aa)	Species	D-hist	L-hist	$\Delta \log \beta$	(D and L)	D-aa	L-aa	$\Delta \log \beta$	(D and L)
Tryptophan	1110	18·475(4)	18·003(4)	0·47	13·115(7)	18·672(4)	18·178(10)	0·49	13·418(7)
Phenylalanine	1111	21·449(10)	21·436(10)	0		21·460(10)	21·307(20)	0·1	
	1110	17·699(8)	17·504(1)	0·20	13·100(10)	18·033(1)	17·716(1)	0·32	13·326(50)
Valine	1110	17·546(3)	17·603(3)	−0·06	13·006(10)	17·630(3)	17·689(6)	−0·06	13·325(10)
Proline	1110	18·105(6)	Same	0	13·484(10)				
Methionine	1110	17·271(4)	Same	0	12·80(8)				
Leucine	1111	22·220(20)	22·191(20)	0					
	1110	17·662(4)	17·692(4)	−0·03					

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