Formation Constants of Complexes of Tyrosine

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The formation constants of the complexes of L-tyrosine (H_2L) with H^+, Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} are reported at 25 °C and I = 0.10 mol dm^{-3} ($K[NO_3]$). The tyrosine bonds glycine-like, forming complexes of general formula $[M(HL)_n]$ and $[ML_n]$.

TYROSINE (Tyr), 2-amino-3-(4-hydroxyphenyl)propanoic acid, H_2L, is an essential amino-acid similar to phenylalanine but with, in addition, a *p*-phenolic group on the benzene ring. Since the proton of this group ionizes at about pH 10, the neutral ligand must be regarded as a dibasic acid (H_2L) with three potential co-ordination centres.

A review of the literature on tyrosine suggests that the phenolic oxygen does not participate in co-ordination reactions to metal ions with the result that formation constants are close to those of phenylalanine itself. However, this oxygen does appear to co-ordinate to Cu^{II} in some dipeptide complexes [1] and an *X*-ray analysis of $[Cu(\text{L-TyrO})_2]$ [L-TyrO = L-tyrosinate(1−)] shows an abnormally short Cu–phenyl ring distance.[2] Although tyrosine is an important amino-acid, reliable values for the formation constants of proton and metal complexes under closely controlled conditions are few. In fact, there are no results available at 25 °C with an ionic background of 0.1—0.2 mol dm^{-3}, determined with electrodes calibrated in terms of concentrations. We have therefore measured the more important formation constants in 0.1 mol dm^{-3} $K[NO_3]$ so that they can be used for direct comparison with formation constants of complexes of other amino-acids, determined under the same conditions. Since complexes of tyrosine do not appear to form stereoselectively,[3] L-tyrosine was used throughout.

EXPERIMENTAL

L-Tyrosine was obtained from Sigma Chemical Co. (SIGMA grade). Complex formation constants were calculated from potentiometric titration curves obtained as described previously.[4] The glass electrode was calibrated in terms of hydrogen ion concentrations and titrations were carried out at 25 °C with an ionic background of 0.10 mol dm^{-3} ($K[NO_3]$). Calculations were made with the aid of the MINIQUAD computer program.[5] Concentration ratios covered the range of ligand : metal ratios 1 : 1 to 8 : 1.

RESULTS AND DISCUSSION

Calculated formation constants for proton and metal ion (Co^{II}, Cu^{II}, Ni^{II}, and Zn^{II}) complexes are given in the Table. The only comparable results were measured with an ionic background of 0.05 mol dm^{-3} (KCl) [6] or 0.2 mol dm^{-3} (KCl).[7] The proton complex formation constants are close to these values and demonstrate clearly that protonation of the phenolic oxygen overlaps markedly with protonation of the amine nitrogen. In fact, spectroscopic studies have shown that the microconstant for protonation of the phenolic oxygen (log K = 9.63) is a little larger than that of the amine nitrogen (log K = 9.28).[8] Hence the major contribution to the highest constant (log K_{HL} = 10.14) will be protonation of the phenolic oxygen and the second constant (log K_{H_2L} = 9.03) will be mainly protonation of the amine nitrogen. It is interesting to note that this order is reversed in L-3,4-dihydroxyphenylalanine.[9] It is clear that large errors will be introduced if ionization of the phenolic proton is ignored.[10]

The metal complex formation constants given in the Table show that tyrosine can co-ordinate to the transition-metal ions studied as either the monoprotonated form of the ligand (HL^-) with the phenolic oxygen protonated, or as the fully ionized ligand (L^{2-}), depending on the pH. With Co^{II} and Ni^{II}, tris complexes are formed. Both of these observations are typical of bidentate ligands. With Cu^{II}, the $[M(HL)_n]$ species begin to form around pH 3. In general, the formation constants of these complexes are very close to the analogous complexes of phenylalanine, *e.g.* for $[Cu(HTyrO)]^+$, log K = 7.85 while for $[Cu(PhAlaO)]^+$ [PhAlaO = phenylalaninate(1−)] log K = 7.93,[11] and it is reasonable to assume that the bonding is similar, *i.e.* glycine-like.

As the pH is raised further, the stepwise formation of the $[M(HL)_n]$ complexes is followed by stepwise deprotonation of the co-ordinated ligands. The protonation constants for these reactions are given in the Table. With Co^{II} and Ni^{II}, the protonation constants for the reaction $ML + H^+ \longrightarrow [MHL]^+$ are close to the microconstant for the protonation of the amine nitrogen (log K = 9.28) suggesting strongly that this is the protonation centre in the metal complexes also. Similarly, the other protonation constants for Co^{II} and Ni^{II} complexes can be assumed to represent protonation of amine nitrogens, although they are generally slightly larger in magnitude as a result of the increasing negative charge of the

Formation constants of complexes of L-tyrosine at 25 °C and $I = 0.10$ mol dm^{-3} (K[NO$_3$])

Proton complexes
$\log K_{HL} = 10.142(1)$
$\log K_{H_2L} = 9.028(1)$
$\log K_{H_3L} = 1.881(5)$

Metal complexes $[M_xL_yH_z]$

Metal	*xyz*	log β [a]	log *K′* [b]
Co^{II}	110	4.88(2)	
	111	14.17(1)	4.03
	120	8.31(3)	
	121	18.10(4)	
	122	27.52(3)	7.24
	130	11.0(5)	
	131	21.3(3)	
	132	31.2(1)	
	133	40.8(1)	10.4
Cu^{II}	110	10.64(2)	
	111	17.99(1)	7.85
	120	15.36(3)	
	121	25.47(3)	
	122	34.90(3)	14.62
Ni^{II}	110	5.79(1)	
	111	15.14(1)	5.00
	120	10.23(1)	
	121	20.01(2)	
	122	29.55(1)	9.27
	130	13.09(3)	
	131	23.51(3)	
	132	33.57(2)	
	133	42.84(3)	12.41
Zn^{II}	110	6.2(1)	
	111	14.37(5)	4.23
	120	10.11(8)	
	121	19.65(9)	
	122	28.59(3)	8.31

Metal complex protonation reactions

	log *K*			
Reaction	Co	Cu	Ni	Zn
$H + [ML] \longrightarrow [MHL]$	9.29	7.35	9.35	8.2
$H + [MHL_2] \longrightarrow [MH_2L_2]$	9.42	9.43	9.54	9.54
$H + [ML_2] \longrightarrow [MHL_2]$	9.79	10.11	9.78	8.94
$H + [MH_2L_3] \longrightarrow [MH_3L_3]$	9.6		9.27	
$H + [MHL_3] \longrightarrow [MH_2L_3]$	9.9		10.06	
$H + [ML_3] \longrightarrow [MHL_3]$	10.3		10.42	

[a] $\log \beta = [M_xL_yH_z]/[M]^x[L]^y[H]^z$. [b] $K' = [M(HL)_n]/[M][HL]^n$.

complex anion. The protonated metal complexes lose a proton more readily than does the protonated amine group of tyrosine itself. Hence, neglecting the formation of complexes with ionized phenolic protons may contribute to the large errors quoted in some determinations of the formation constants of tyrosine complexes.[3]

The complex species $[Cu(HL)]^+$, $[Zn(HL)]^+$, and $[ZnL(HL)]^-$ are significantly more acidic than the other protonated complex ions, with p*K* values of 7.35, 8.2, and 8.9 respectively. This suggests that the phenolic protons do not ionize first in these species. The ionization of a co-ordinated water molecule is an alternative source of labile hydrogen ions. With Cu^{II}, co-ordinated water has a p*K* value of 6.8 while with Zn^{II} the value is 8.7;[12] these are values comparable to the proton ionization constants of $[Cu(HL)]^+$, $[Zn(HL)]^+$, and $[ZnL(HL)]^-$. It is probable, therefore, that the constants refer to hydrolysis reactions of co-ordinated water.

The metal ions studied all form fully deprotonated mono and bis complexes, [ML] and $[ML_2]^{2-}$, which are more stable than the analogous protonated species, $[MHL]^+$ and $[M(HL)_2]$. Cobalt(II) and Ni^{II} both form deprotonated tris complexes, $[ML_3]^{4-}$. These complexes are less stable than the $[M(HL)_3]^-$ species. This is not unexpected considering the high negative charge of the fully ionized species.

Careful analysis of the experimental data failed to provide evidence of polynuclear complex formation which would indicate the existence of phenol–metal interactions. Examination of the formation constants in the Table similarly failed to provide evidence of any enhanced stability compared to comparable amino-acid complexes.

[1/1201 *Received*, 28*th July*, 1981]

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