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Complexes of Aminophosphonates.
II. Transition Metal Complexes of Aminophosphonic Acid Analogues of Aspartic Acid and Glutamic Acid

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Abstract

The stoichiometries and stability constants of the proton, cobalt(II), nickel(II), copper(II) and zinc(II) complexes of 2-amino-3-phosphonopropionic acid (β-P-Asp), 3-amino-3-phosphonopropionic acid (α-P-Asp) and 2-amino-4-phosphonobutanoic acid (γ-P-Glu) have been determined pH-metrically at 25 °C and at an ionic strength of 0.2 mol dm^{-3} (KCl).

From the stability data and the spectral parameters of the complexes, it has been established that, similarly as for the aminocarboxylate analogues, the metal ion bonding mode is basically bidentate with P-Glu and tridentate with P-Asp. However, the more basic character of the $-PO_3^{2-}$ group than that of the $-COO^-$ group leads to an enhanced formation of various protonated complexes. PO_3^{2-}/COO^- substitution in the α-position results in a more marked ambidentate character of P-Asp in the copper(II) complexes than does that in the β-position.

Introduction

As analogues of natural amino acids, aminophosphonic acids are of considerable interest because of their occurrence in many living organisms and because of their biological activity.

We have recently reported results on complexes of simple aminophosphonic acids with several 3d transition metal ions [1]. The differences between the complex-forming properties of aminophosphonates and their aminocarboxylate analogues were explained in terms of the differences in basicity, charge and size of the $-PO_3^{2-}$ and $-COO^-$ groups. In the present work, the study has been extended to more complex, potentially tridentate ligands containing both $-PO_3^{2-}$ and $-COO^-$ groups besides an amino group: 2-amino-3-phosphonopropionic acid (β-P-Asp), 3-amino-3-phosphonopropionic acid (α-P-Asp) and 2-amino-4-phosphonobutanoic acid (γ-P-Glu).

These ligands are formal analogues of aspartic acid (Asp) and glutamic acid (Glu), which form a variety of complexes with transition metal ions [2]. From potentiometric and spectral studies with transition metal ions, it is clear that Asp readily forms complexes involving a tridentate bonding mode, while Glu coordinates to metal ions only in a bidentate way, via the amino and α-carboxylate groups [2].

The aim of the present work was to establish the stoichiometries, stability constants and bonding modes of the species formed in the systems containing cobalt(II), nickel(II), copper(II) and zinc(II) with the following tridentate aminophosphonocarboxylic acids: α-P-Asp, β-P-Asp and γ-P-Glu. In this way we can achieve a better comparison of the complex-forming properties of aminophosphonates and aminocarboxylates, for in these ligands all three donor groups are present in the same molecule.

Experimental

The aminophosphonic acids were obtained by the method described in ref. 3. In the case of 4-amino-4-phosphonobutanoic acid (α-P-Glu), considerable pyroglutamization took place and the pure compound could not be isolated either by recrystallization or by other purification methods. Hence, its complex-formation reactions were not studied. The purities and the exact concentrations of the solutions of the other aminophosphonates were determined pH-metrically by the method of Gran [4]. The concentrations of the metal chloride stock solutions were measured gravimetrically via precipitation of the oxinates.

The stability constants of the proton and the metal complexes of the ligands were determined by pH-metric titration of 5 cm^3 samples. The concentration of the ligand in the samples was 4×10^{-3} mol

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dm^{-3} and the metal ion:ligand ratio was 1:1, 1:2, 1:4 or 1:6. The ionic strength was adjusted to 0.2 mol dm^{-3} with KCl in each case. The titrations were performed over the pH range 3–11 with a KOH solution of known concentration (*ca.* 0.2 mol dm^{-3}).

pH was measured with a Radiometer pHM 64 instrument with G2040B glass and K4040 calomel electrodes, using a TTA 80 titration unit. The electrode system was calibrated by the method of Irving *et al.* [5], so that the pH-meter readings could be converted into hydrogen ion concentrations. In all cases the temperarure was 25.0 ± 0.1 °C.

To establish the bonding modes in the complexes formed, visible spectra were recorded for the nickel(II) and copper(II) complexes of the ligand with a Beckman Acta MIV double-beam recording spectrophotometer. ESR spectra were obtained on a JEOL JMN-3X spectrometer at 9.15 GHz and 120 K.

The stability constants $\beta_{pqr} = [M_pA_qH_r]/[M]^p[A]^q[H]^r$ were calculated with the aid of the PSEQUAD computer program [6]. For the sake of clarity charges of the complexes are omitted in the text and in the Figures. It has to be mentioned, however, that the fully deprotonated form of the ligand is A^{2-} for the aminocarboxylates and A^{3-} for the aminophosphonates.

TABLE 1. Dissociation Constants of some Aminophosphonic Acids and their Aminocarboxylic Acid Analogues at 25 °C and I = 0.20 mol dm^{-3} (KCl)

Ligand	$pK_{NH_3^+}$	$pK_{\beta\text{-H}}$	$pK_{\alpha\text{-H}}$
Asp[a]	9.63	3.68	1.95
α-P-Asp	10.07 ± 0.01	3.44 ± 0.01	5.52 ± 0.01
α-Ala-P[b]	10.11	–	5.55
β-Ala[c]	10.14	3.42	–
β-P-Asp	10.79 ± 0.01	6.07 ± 0.01	2.40 ± 0.01
β-P-Asp[d]	10.68	6.05	2.34
β-Ala-P[b]	10.92	6.21	–
α-Ala[c]	9.68	–	2.35
	$pK_{NH_3^+}$	$pK_{\gamma\text{-H}}$	$pK_{\alpha\text{-H}}$
Glu[a]	9.51	4.11	2.11
γ-P-Glu	10.21 ± 0.01	6.90 ± 0.01	2.51 ± 0.01
Gaba-P[e]	11.07	6.87	–
Gaba[d]	10.30	3.99	–
Aaba[a]	9.61	–	2.34

[a] Ref. 9, Aaba = α-aminobutyric acid. [b] Ref. 1. [c] Ref. 10. [d] Ref. 11, Gaba = γ-aminobutyric acid (t = 25 °C, I = 0.10 mol dm^{-3}). [e] Ref. 7, Gaba-P = 3-aminopropanephosphonic acid (t = 25 °C, I = 0.10 mol dm^{-3}).

Results and Discussion

The pH-metrically determined dissociation constants of the ligands, together with those of some simple aminocarboxylic and aminophosphonic acids as references, are given in Table 1. The p*K* characteristic of the dissociation of $-PO_3H_2$ in aminophosphonic acids is $\lesssim 1.0$ [7, 8], and thus this group is fully deprotonated in the pH range studied (pH 2.5–11).

When the p*K* values in Table 1 are compared with the acidity constants* of Asp ($pK_{NH_3^+} = 9.63$, $pK_{\beta\text{-COOH}} = 3.68$ and $pK_{\alpha\text{-COOH}} = 1.95$) [9] and Glu ($pK_{NH_3^+} = 9.51$, $pK_{\gamma\text{-COOH}} = 4.11$ and $pK_{\alpha\text{-COOH}} = 2.12$) [9], it can be seen that because of the strong electron-releasing effect of the phosphonate and hydrogenphosphonate groups, the acidities of both $-NH_3^+$ and $-COOH$ are higher than those in the aminocarboxylates. It is noteworthy that, in spite of the close proximity of the acidic groups, the p*K* values of the phosphonic acid analogues of Asp and Glu are in fairly good agreement with those of the corresponding reference compounds. It can be seen from Table 1 that the presence of an extra carboxylate group in the P-Asp or P-Glu molecule has only a slight effect on the phosphonic acid moiety, and similarly the phosphonic acid moiety has hardly any effect on the acidity of the –COOH group.

The stability constants obtained for the metal(II) complexes of the ligands, together with those for the corresponding aminocarboxylate analogues, are listed in Tables 2 and 3. Taking into account the different ionic strength (1.00 mol dm^{-3}), and regarding the major species, our data are in fairly good agreement with the only data in the literature for the zinc(II)–α-P-Asp system [12].

As an illustration, the concentration distribution curves for the complexes formed in the copper(II)–Asp, copper(II)–α-P-Asp, copper(II)–β-P-Asp, as well as in the copper(II)–Glu and copper(II)–γ-P-Glu systems are depicted in Figs. 1 and 2.

Metal Complexes of γ-P-Glu

In most cases, glutamic acid coordinates to metal ions in a bidentate manner, as the third donor group (in the γ-position) is too far away to form a stable chelate ring [2, 9]. The similarity of the stability data in Table 2 and the visible spectral parameters for the copper(II) and nickel(II) complexes (see Table 4) suggests that substitution of the carboxylate in the γ-position by a phosphonate group does not basically change the complex-forming capability of the molecule. The d–d transition energies found for the copper(II)–Glu and copper(II)–γ-P-Glu systems at different metal ion:ligand ratios agree with each

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*Although the complete dissociation scheme of Asp or Glu is described by 12 microscopic constants, the sequential proton losses occur to a good approximation from the α-COOH, the side-chain –COOH, and finally the ammonium group [2].

TABLE 2. Stability and Derived Equilibrium Constants of the Metal Complexes of Glu and its Phosphonic Acid Analogues at 25 °C and I = 0.20 mol dm^{-3} (KCl)

Ligand		log β values			
		Co(II)	Ni(II)	Cu(II)	Zn(II)
Glu[a]	MAH			12.39	
	MA	4.46	5.52	8.27	4.69
	MA_2	7.74	9.87	14.83	8.55
	MA_3	10.29	12.51		
γ-P-Glu	MAH		13.04 ± 0.04	15.59 ± 0.02	13.18 ± 0.08
	MA	5.44 ± 0.03	6.41 ± 0.01	9.19 ± 0.03	6.55 ± 0.08
	MA_2H_2			29.40 ± 0.06	
	MA_2H			22.45 ± 0.08	
	MA_2	8.69 ± 0.06	10.47 ± 0.02	14.95 ± 0.05	10.72 ± 0.07
	MA_3		12.01 ± 0.09		

		Co(II)	Ni(II)	Cu(II)	Zn(II)
Glu[a]	$\log(K_1/K_2)$	1.18	1.17	1.71	0.83
γ-P-Glu		2.19	2.35	3.43	2.38
Glu[a]	$\log K_1 - pK_{NH_3^+} - pK_{\alpha\text{-H}}$	−7.17	−6.11	−3.36	−6.94
γ-P-Glu		−7.28	−6.31	−3.53	−6.17
Glu[a]	$\log K_2 - pK_{NH_3^+} - pK_{\alpha\text{-H}}$	−8.35	−7.28	−5.07	−7.77
γ-P-Glu		−9.47	−8.66	−6.96	−8.55

[a] Ref. 9.

TABLE 3. Stability and Derived Equilibrium Constants of the Metal Complexes of Asp and its Phosphonic Acid Analogues at 25 °C and I = 0.20 mol dm^{-3} (KCl)

Ligand		log β values			
		Co(II)	Ni(II)	Cu(II)	Zn(II)
Asp[a]	MAH		11.19	12.48	
	MA	5.95	7.14	8.80	5.73
	MA_2	10.21	12.43	15.76	10.20
α-P-Asp	MAH_2	18.06 ± 0.05	17.99 ± 0.04	18.01 ± 0.06	17.92 ± 0.03
	MAH	13.18 ± 0.04	13.20 ± 0.03	14.20 ± 0.03	13.03 ± 0.02
	MA	6.56 ± 0.03	7.23 ± 0.02	9.34 ± 0.03	6.62 ± 0.02
	MA_2	10.69 ± 0.06	11.83 ± 0.04	16.15 ± 0.05	10.82 ± 0.06
β-P-Asp	MAH		13.3 ± 0.2	15.51 ± 0.02	13.1 ± 0.2
	MA	6.22 ± 0.04	7.38 ± 0.03	9.60 ± 0.03	7.15 ± 0.08
	MA_2H_2			29.1 ± 0.1	
	MA_2H			22.4 ± 0.1	
	MA_2	10.30 ± 0.06	12.14 ± 0.05	15.49 ± 0.05	12.16 ± 0.06

		Co(II)	Ni(II)	Cu(II)	Zn(II)
Asp[a]	$\log(K_1/K_2)$	1.69	1.85	1.84	1.26
α-P-Asp		2.43	2.63	2.53	2.42
β-P-Asp		2.13	2.62	3.71	−2.14
Asp[a]	$\log K_1 - pK_{NH_3^+} - pK_{\alpha\text{-H}}$	−5.63	−4.44	−2.78	−5.85
α-P-Asp		−9.03	−8.36	−6.25	−8.97
β-P-Asp		−6.97	−4.81	−3.59	−6.04

(continued)

TABLE 3. *(continued)*

Ligand		log β values			
		Co(II)	Ni(II)	Cu(II)	Zn(II)
Asp[a]	$\log K_2 - pK_{NH_3^+} - pK_{\alpha\text{-H}}$	−7.32	−6.29	−4.62	−7.11
α-P-Asp		−11.46	−10.99	−8.78	−11.39
β-P-Asp		−9.10	−7.43	−7.30	−8.18

[a] Ref. 9.

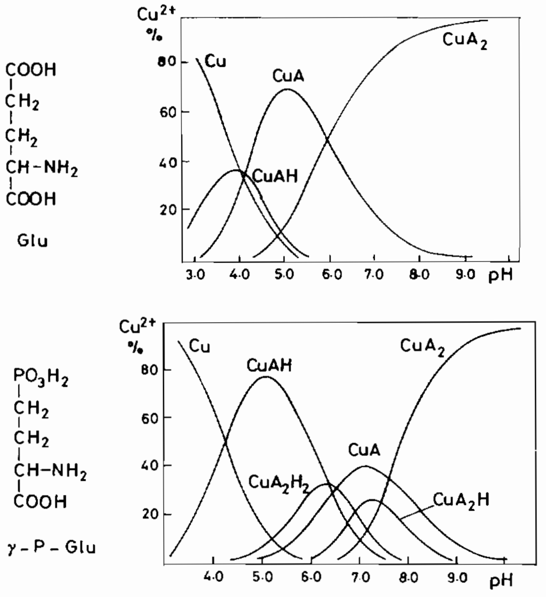


Fig. 1. Concentration distribution of the complexes formed in the copper(II)–Glu and copper(II)–P-Glu systems as a function of pH. $c_{Cu} = 0.002$, $c_{ligand} = 0.004$ mol dm^{-3}.

other. The ESR parameters $g_{\parallel} = 2.244$ and $A_{\parallel} = 160$ for Cu(Glu)$_2$ and $g_{\parallel} = 2.264$ and $A_{\parallel} = 169$ for Cu(γ-P-Glu)$_2$ also indicate two nitrogens in the coordination sphere.

In the nickel(II)–γ-P-Glu system, similarly as for nickel(II)–Glu, a tris complex too is formed in measurable concentration (see Table 2). This fact is strongly supported by the differences in the spectral parameters obtained at metal ion:ligand ratios of 1:2 and 1:4 at high pH (see Table 4).

Although both Glu and its γ-phosphonic acid derivative are bound in a bidentate manner to the metal ions, via the $-NH_2$ and $-COO^-$ groups the PO_3^{2-}/COO^- substitution in the molecule makes slight differences in the complex-forming properties.

(1) Because of the more basic character of the $-PO_3^{2-}$ group, the metal complex formation processes and the deprotonation of the non-coordinated γ-PO_3H^- groups more or less overlap each other (to extents depending on the metal ions), and thus the formation of protonated (1:1 and partly 1:2) complexes is more pronounced (see Table 2 and Fig. 1).

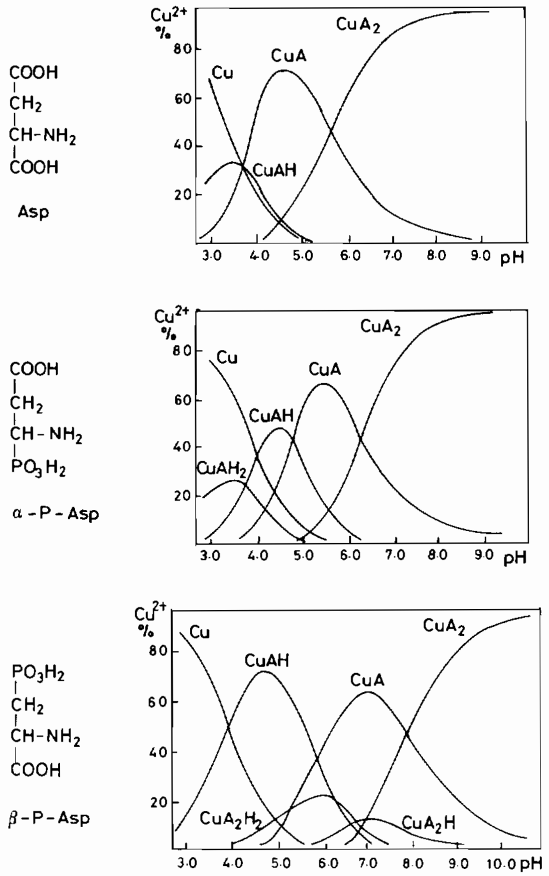


Fig. 2. Concentration distribution of the complexes formed in the copper(II)–Asp, copper(II)–α-P-Asp and copper(II)–β-P-Asp systems as a function of pH. Details as in Fig. 1.

(2) The p*K* values of the MAH complexes correspond to $pK_{\gamma\text{-}PO_3H^-}$ (see Table 1), again suggesting aminocarboxylate-type coordination. Similarly, in the copper(II)–γ-P-Glu system, where 1:2 protonated complexes are also formed, the p*K* values of the species Cu(AH)$_2$ can be ascribed to the stepwise deprotonation of the side-chain $-PO_3H^-$ groups. The difference between $pK_{Cu(AH)_2}$ and pK_{CuA_2H} is 0.55, which corresponds fairly well to the statistical case for the dissociation of two donor groups with the same acidity.

TABLE 4. Spectral Data for the Copper(II) and Nickel(II) Complexes

System	Ratio	pH	λ_{max} (nm)	ϵ ($dm^3\ mol^{-1}\ cm^{-1}$)
Cu(II)–Glu–OH^-	1:1:2	6.4	695	36
Cu(II)–γ-P-Glu–OH^-	1:1:3	6.3	685	44
Cu(II)–Glu–OH^-	1:1:4	9.3	615	60
Cu(II)–γ-P-Glu–OH^-	1:2:6	9.4	619	60
Ni(II)–Glu–OH^-	1:2:4.5	10.7	615	8
			365	14
	1:4:8	10.5	602	9
			360	16
Ni(II)–γ-P-Glu–OH^-	1:2:6	10.2	635	9
			365	16
	1:4:12	10.7	617	9
			350s[a]	
Cu(II)–Asp–OH^-	1:1:2	6.5	700	34
Cu(II)–α-P-Asp–OH^-	1:1:3	6.9	690	41
Cu(II)–β-P-Asp–OH^-	1:1:3	7.3	690	44
Cu(II)–Asp–OH^-	1:2:4	9.5	626	53
Cu(II)–α-P-Asp–OH^-	1:2:6	9.7	650	59
Cu(II)–β-P-Asp–OH^-	1:2:6	10.2	640	62
Ni(II)–Asp–OH^-	1:2:5	11.2	600	6
	1:4:10	11.3	600	5
			360	8
Ni(II)–α-P-Asp–OH^-	1:2:6	10.2	630	6
			375	10
	1:4:12	10.7	628	6
			372	10
Ni(II)–β-P-Asp–OH^-	1:2:6	10.5	625	7
			363	12
	1:4:12	10.7	620	8
			360s[a]	

[a] s = shoulder.

(3) It can be seen from Table 2 that, for steric and mainly electrostatic reasons, PO_3^{2-}/COO^- substitution significantly hinders the binding of the second ligand; this is manifested in the much larger $\log(K_1/K_2)$ values (which express the ratio of the stepwise stability constants). Similarly, as concerns the equilibrium constants for the processes $M + H_2A \rightleftharpoons MA + 2H^+$ and $MA + H_2A \rightleftharpoons MA_2 + 2H^+$, which take into account the difference in acidity of the coordinating $-NH_2$ and α-COO^- donor groups of the aminophosphonate and aminocarboxylate (see Table 2), only the latter constants show a significant decrease as compared to those of Glu. This electrostatic and steric hindrance might be the reason why, in spite of the octahedral coordination, 1:3 complexes are not formed with either cobalt(II) or zinc(II) ions.

Metal Complexes of α-P-Asp and β-P-Asp

Aspartic acid, unlike glutamic acid, is generally tridentate towards metal ions, forming five and six-membered joined chelate rings [2, 9]. Hence, only 1:1 and 1:2 complexes are formed with metal ions of octahedral geometry, such as cobalt(II), nickel(II) and zinc(II), where both ligands coordinate in a tridentate way, whereas in the case of the copper(II) complexes the coordination number is five, with the tridentate binding of only one of the ligands [2]. It should be mentioned that, on the basis of a NMR relaxation study, Khazaeli and Viola [13] recently concluded that the coordination of Asp in its copper(II) complexes is bidentate, through the amino and β-carboxylate groups.

As can be seen from Table 3 and the concentration distribution curves in Fig. 2, PO_3^{2-}/COO^- substitution in either the α- or the β-position enhances the possibility of formation of protonated complexes. In the complex MAH_2, which is formed only with the α-phosphonic acid derivative, the ligand can bind in a monodentate manner via either the β-carboxylate or the α-phosphonate, and the other two donor groups remain protonated. Deprotonation of the complex MAH_2 may take place with structural rearrangement, and the bonding mode can be α-P-Ala-like or β-Ala-like. The former, however, is hardly likely, since the pK_{MAH} values characteristic for the next deprotonation step (4.86 for CuAH, 5.97 for NiAH, 6.62 for CoAH and 6.41 for ZnAH) seem to be much higher than the p*K* for the β-COOH group (although the exact acidity constants of the individual groups are not known because of the microscopic dissociation processes [2]).

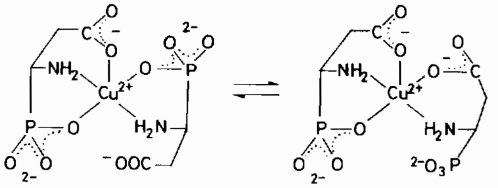
The complex MAH is formed with β-P-Asp too. In these complexes (similarly to the complexes of γ-P-Glu with the same composition) the bonding mode is presumably α-Ala-like and the β-phosphonic acid group is protonated. The pK_{MAH} values (5.91 for CuAH, 5.88 for NiAH and 5.94 for ZnAH) also correspond to the dissociation constant of the non-coordinated $-PO_3H^-$ group.

For both α-P-Asp and β-P-Asp, deprotonation of the complex MAH leads to a species MA in which the ligand is bound in a tridentate way. This is clearly reflected in the equilibrium constant $\log K_1 - pK_{NH_3^+} - pK_{\alpha\text{-}H}$ (taking into account the difference in basicity of the coordinating donor groups), which is 0.5–2 orders of magnitude larger than those for α-Ala [1] or γ-P-Glu (see Table 2) and α-P-Ala [1] coordinated only in a bidentate manner. This relative stability increase, however, is somewhat smaller than for complexes of the aminocarboxylate Asp, since charge neutralization favours formation of the complex MA for the aminocarboxylate, but not for aminophosphonates.

For steric and electrostatic reasons, PO_3^{2-}/COO^- substitution in either the α- or the β-position hinders the coordination of the second ligand molecule. This is the reason why the $\log (K_1/K_2)$ values are larger for the aminophosphonate complexes than for the aminocarboxylate ones. The derived equilibrium constants $\log K_2 - pK_{NH_3^+} - pK_{\alpha\text{-}H}$ for the metal complexes with octahedral geometry, however, are larger again than those for α-Ala [1] or γ-P-Glu (see Table 2) and α-P-Ala [1], which suggests the tridentate or at least partly tridentate coordination of the second ligand too. This appears quite clearly for the nickel(II) systems, where 1:3 complexes are not formed with either Asp or its phosphonic acid derivatives. It is strongly supported by the spectral parameters, which (in contrast with those for Glu and γ-P-Glu) show no changes at different ligand excesses (at 1:2 and 1:4 metal ion:ligand ratios) (see Table 4).

For the copper(II) complexes, PO_3^{2-}/COO^- substitution in the β-position hinders coordination of the second ligand to a larger extent than does that in the α-position. This may suggest that the chelate rings are not purely five-membered in the equatorial plane, *i.e.* the bonding mode is not purely (NH_2, PO_3^{2-}) for the α-phosphonic acid derivative and (NH_2, COO^-) for the β-phosphonic acid derivative, as (for electrostatic reasons) binding of the second molecule in this case would be more hindered for the α-phosphonic acid derivative.

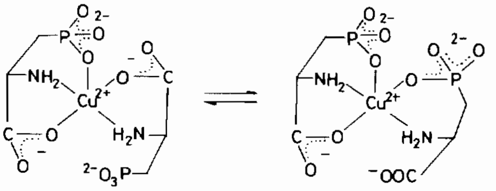
In our previous work on simple bidentate aminophosphonates [1], it was found that the relative stability sequence (which takes into account the differences in basicity of the donor groups) for aminocarboxylates and aminophosphonates forming five or six-membered chelate rings is as follows: 5(NH_2, COO^-) > 6(NH_2, COO^-) > 5(NH_2, PO_3^{2-}) > 6(NH_2, PO_3^{2-}). Accordingly, it is quite obvious to assume that one of the ligands coordinates at least partly β-Ala-like in the 1:2 complex of copper(II)–α-P-Asp. Thus, the equilibrium given in Scheme 1 may exist in solution.



Scheme 1.

The bonding mode on the right-hand side of the equilibrium should be further favoured by the stability increase due to the simultaneous presence of five and six-membered chelate rings in the same molecule [14]. The possibility of this equilibrium between the two bonding modes is supported by the spectral behaviour of the complex. The axial coordination of a donor group generally causes a red shift (20–40 nm) of the d–d absorption band [15], while β-Ala-like coordination causes a blue shift relative to λ_{max} for copper(II)–α-P-Ala [1]. As a result of these two opposite effects, a 5 nm shift to lower energies occurs in λ_{max} as compared to that for copper(II)–α-P-Ala, and a shift of 24 nm to lower energies as compared to that for copper(II)–Asp (see Table 4).

A similar equilibrium (Scheme 2) between different bonding arrangements cannot be entirely excluded for the 1:2 complex of copper(II)–β-P-Asp.



Scheme 2.

The existence of this equilibrium is suggested mainly by the 20 nm red shift of the 1:2 complex in comparison with the absorption band of copper(II)–γ-P-Glu or copper(II)–α-Ala [1]. Since the similarity of the derived equilibrium data on copper(II)–(β-P-Asp)$_2$ with those on copper(II)–(γ-P-Glu)$_2$ (where axial coordination is negligible due to the low stability of a seven-membered chelate ring) suggests a lower extent of axial coordination for β-P-Asp too, the spectral change is highly indicative of some extent of β-P-Ala-like coordination in the equatorial plane. This bonding mode, however, is rather unfavoured (see the stability sequence above), and thus the equilibrium is presumably shifted mainly in the direction of the upper arrow. It is worth mentioning that Khazaeli and Viola [13] suggested a similar bonding mode for O-phosphono-L-serine (which is the β-phosphoric acid derivative of Asp) with copper(II).

The stepwise deprotonation processes of complex $Cu(HA)_2$ of β-P-Asp overlap each other considerably ($pK_{Cu(HA)_2} = 6.7$, $pK_{CuA_2H} = 6.9$) and differ from the $pK_{PO_3H^-}$ of the free ligand, which likewise suggests, that these deprotonation processes are accompanied by a structural rearrangement of the coordination sphere of the metal complex.

Conclusions

The differences in basicity, charge, electron-releasing effect and size of the phosphonate and carboxylate groups result in the following differences in the complex-forming properties of Asp and Glu and their phosphonic acid analogues.

(1) The more basic character of the $-PO_3^{2-}$ group leads to the formation of various protonated 1:1 and 1:2 complexes, partly involving monodentate coordination of the ligand via the phosphonate group or aminocarboxylate-like coordination with protonated $-PO_3H^-$ group(s).

(2) For glutamic acid, PO_3^{2-}/COO^- substitution in the γ-position does not significantly change the binding ability of the ligand. The bonding mode remains bidentate, of (NH_2, COO^-) type, although coordination of the second or the third ligand [in the case of nickel(II)] is less favoured for electrostatic reasons.

(3) For aspartic acid, the PO_3^{2-}/COO^- substitution in any position does not generally change the tridentate (NH_2, COO^-, PO_3^{2-}) coordination of the ligands, although the electrostatic and steric effects hinder the coordination of the second ligand with all metal ions.

(4) For the copper(II) complexes, similarly as with the aminocarboxylate Asp, axial coordination occurs with the phosphonate derivatives, although its extent seems to be less for the complexes of β-P-Asp.

(5) There is a possibility of ambidentate (aminocarboxylate or aminophosphonate) coordination of the ligands, which results in the co-existence of species with the same stoichiometric composition, but with different bonding modes. This is more marked when PO_3^{2-}/COO^- substitution is in the α-position.

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