Thermodynamic and Spectrophotometric Investigation of Complex Formation between Hydrogen, Cobalt(II), Nickel(II), and Copper(II) Ions and 2-Amino-*N*-hydroxypropanamide in Aqueous Solution

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The overall formation constants of the complexes formed between H^+, Co^{2+}, Ni^{2+}, and Cu^{2+}, and 2-amino-*N*-hydroxypropanamide (ahpr) have been measured at 25 °C and $I = 0.5$ mol dm^{-3} (KCl) using potentiometric and spectrophotometric techniques. Complexes of monoaminohydroxamic acids and Cu^{II}, Ni^{II}, and Co^{II} are shown to involve chelation *via* the hydroxamate moiety NHO^- and the amino group NH_2, which are pH sensitive. The protonaton constants of the ligand and the formation constants of several metal complexes have been calculated from potentiometric and spectrophotometric data with the aid of the programs SUPERQUAD and SQUAD, respectively. The complexes $[CuL]^+$, $[Cu_2(OH)L_2]^+$, $[CuL_2]$, $[Cu(OH)L_2]^-$, $[NiL]^+$, $[NiL_2]$, $[Ni(OH)L_2]^-$, and $[CoL]^+$, $[CoL_2]$, $[Co(OH)L_2]^-$, and $[Co_2L]^{3+}$ are formed where $L^- = CH_3CH(NH_2)CONHO^-$. The solution electronic spectra are reported. The u.v.–visible investigations provide important evidence for the formation of different metal(II) complexes with 2-amino-*N*-hydroxypropanamide, depending on the pH; moreover they can be used to estimate the co-ordination sphere around the metal ions and to observe the equilibria between different complexes. The experimental curves $[\varepsilon = f(\lambda)]$ for some complexes, obtained from refinement of absorbance data with the program SQUAD, have been resolved into precisely positioned absorption bands by Gaussian analysis using a non-linear least-squares computer program NLIN. The best data resulting for the metal(II)–ahpr systems have been employed in a weak tetragonal $[Cu(OH)L_2, CuL_2]$ or a square-planar (NiL_2) ligand-field model to calculate as far as possible ligand-field parameters. The specific tendencies of aminohydroxamic acids towards different metal ions have been tested as models for substratum–metal bonding in biological reactions, and the probable structures and stabilities of the chelated compounds formed in aqueous solution are discussed in terms of their biological importance and potential usefulness as therapeutic agents.

In recent years there has been increasing interest in the chemistry of aminohydroxamic acids, due mainly to the biological importance of their metal(II) complexes.[1–6] Following research on the protonation and complex-formation equilibria of aminohydroxamic acids, I have made a potentiometric and spectrophotometric study of 2-amino-*N*-hydroxypropanamide(ahpr). Aminohydroxamic acids and their metal chelates were found to play an important role in biological systems as therapeutic substances in the treatment of urolithiasis[7] and of hepatic coma,[8] constituents of antibiotics, urease activity, and tumour inhibitors. In particular the inhibitory effects of hydroxamic acid derivatives of naturally occurring amino acids on urease of jack bean and the rat alimentary tract were investigated by various authors.[9] The series phenylalanyl, serine, alanyl, glycyl, histidyl, threonyl, leucyl, and arginyl hydroxamic acids are listed in order of decreasing inhibitory power. The inhibition effects (I_{50} values) of α-aminoacyl hydroxamic acids were found to be almost equal to those of the corresponding fatty acyl hydroxamic acids.

This fact shows that the α-amino group does not affect the inhibitory power. However, aspartyl β-, lysyl, and glutamyl γ-hydroxamic acids, in descending order, were much less inhibitory, probably due to the presence of a CO_2H or ω-NH_2 group. Furthermore, the pH optimum of the inhibition shifts to lower values in the presence of a CO_2H group, and to higher values in the presence of an NH_2 group. This fact suggests that the dissociation of an acidic or a basic group reduces the inhibitory power of the hydroxamic acid. At the same time hydroxamic acids reveal a number of pharmacodynamic actions including anti-inflammatory, antimycobacterial, antileucaemic, antifungal, and antineoplastic activities,[10–14] and are used in the therapy of *hyperammonemia*;[10] their action as an inhibitor of *Aeromonas aminopeptidase*, a metalloenzyme that contains zinc,[15] inhibitory effect on DNA synthesis,[1] and also of iron(III) hydroxamates as metallo-therapeutics or new iron-chelating drugs in the treatment of iron overload is intimately connected with iron transport phenomena in the metabolism of micro-organisms.[16] Additional studies on structure–activity relations of metal(II) hydroxamates have recently shown that a great many hydroxamic acids can be employed as indicators of biological activity, the eventual purpose being to design metal(II) chelates as suitable sources of various trace elements which are essential in animal nutrition.

One interesting question concerning the metal complexes of this ligand is which atom of the hydroxamate moiety (CONHOH), the nitrogen or the oxygen, is involved in co-ordination to the metal ion. The hydroxamic acid moiety as a typical bidentate ligand co-ordinates through the carbonyl oxygen and the oxygen atom of the NHOH group.[17,18] However, when the hydroxamic acid contains another donor group, such as the amino group in the present case, the co-ordination to the metal could involve this group and the nitrogen or the oxygen atom of the hydroxamate moiety (NHO^-), forming either five- or six-membered chelate rings, respectively. Additional evidence for this type of co-ordination, already found in the *X*-ray crystal structures of two complexes of Ni^{II} [19,20] and one of Cu^{II} [21] containing two glycinehydroxamate molecules, which persists in solution, was provided by potentiometric and spectrophotometric investigations on nickel(II) and copper(II) complexes.[22–25] A comparison between the stability constants of the ML and ML_2 species and those of the corresponding α-amino acids with the same metal ions is used to clarify the participation of the nitrogen atom of the hydroxamate moiety (NHO^-) in the co-ordination sphere. However, in the field of analytical chemistry aminohydroxamic acids have found widespread use as analytical reagents for a variety of metal ions.[26] Yet in spite of their extensive analytical and biological applications, few detailed potentiometric and spectrophotometric studies have been performed on the metal complexes that are formed. In this paper I report results on the potentiometric and spectrophotometric behaviour of bidentate 2-amino-*N*-hydroxypropanamide (ahpr), alone and in the presence of Cu^{II}, Ni^{II}, and Co^{II} in aqueous solution.

Experimental

Reagents.—DL-Alaninehydroxamic acid (HL) was obtained from Sigma (St. Louis) and its purity was checked by potentiometric titrations. Doubly distilled and deionized water was used throughout and all potentiometric and spectrophotometric experiments were carried out under an atmosphere of damp and purified nitrogen. Potassium hydroxide solution (*ca.* 0.408 mol dm^{-3}) employed for e.m.f. measurements was prepared with carbonate-free doubly distilled water and was standardized by potentiometric dynamic titrations of a known amount (*ca.* 2.0 cm^3) of hydrochloric acid (0.421 mol dm^{-3}) according to Gran's method as previously described.[27,28] All titration solutions were prepared as a total volume of 25.0 cm^3 and thermostatted at 25.0 ± 0.1 °C using a Paratherm electronic (Julabo) circulating constant-temperature water-bath. The ionic strength was kept at 0.5 mol dm^{-3} with KCl. The starting solutions for each potentiometric experiment were prepared by adding successively to the titration vessel a known volume of ahpr (3.0—4.5 cm^3), and an exact volume of metal chloride (5—20 cm^3); then the required quantities of potassium chloride (Merck), employed as supporting electrolyte, and a sufficient amount of doubly distilled water were added to make up the total volume V_0, which was 25.0 ± 0.01 cm^3.

Potentiometric Measurements.—Potentiometric titrations were carried out using a Metrohm E 636 Titroprocessor and an electrode arrangement consisting of an H 268 glass electrode (Schott-Jena glass) and a B 343 Talamid reference electrode (Schott-Jena glass). The potentiometric titrations (dynamic and monotonous)[24–28] were carried out at 25 ± 0.1 °C and $I = 0.5$ mol dm^{-3} (KCl) as previously reported[27,28] for solutions of binary systems containing protons, copper(II), nickel(II), cobalt(II), and ahpr at different molar ratios. The system was calibrated in terms of hydrogen-ion concentrations before and after two series of measurements by titrations of hydrochloric acid solution at 25 ± 0.1 °C and $I = 0.5$ mol dm^{-3} KCl with standard carbonate-free potassium hydroxide solution, according to Gran's method[29] using the computer programs MAGEC[30] and NBAR[31] as previously described.[27,28] The temperature was maintained at 25 ± 0.1 °C inside the reaction cell and the solution was shaken by means of a mechanical stirrer. A thermostatted nitrogen atmosphere, presaturated with water vapour, was maintained in the vessel throughout all titrations by blowing over the surface of the solution.

Spectrophotometric Measurements.—Absorption spectra in the ranges 410—700 ± 0.3 nm for the Co^{2+}-ahpr, 400—795 ± 0.3 nm for the Cu^{2+}-ahpr, and 360—700 ± 0.3 nm for the Ni^{2+}-ahpr systems were recorded on a Hitachi U-3200 spectrophotometer to the fourth decimal place with a stepping of 5.0 nm, obtaining 59, 80, and 69 absorbance values for each solution, respectively. Solutions containing ligand and metal ion (Cu^{2+}, Ni^{2+}), prepared and maintained under purified nitrogen with $I = 0.5$ mol dm^{-3} (KCl), were scanned at a series of pH from 3.639 to 9.650 at 25 °C using a 10-mm cell. Potential measurements for the different solutions in order to obtain the pH values were made with the system used in the potentiometric titrations, calibrated in the same way.

Calculations.—Careful attention was paid to the calculation and critical evaluation of some parameters (E°, A_j, B_j, N, K_w, RT/F) relating to potentiometric calibration graphs, using different mathematical methods as previously described.[24,27,28] In particular, from the results reported in Table 1 it is possible to see the good agreement between the parameters [E°, v_e, N (in acidic and basic solution)] obtained from the two computer programs, even when it is well known that the standard potential of a glass membrane tends to vary from day to day (owing to asymmetry effects) and that liquid junction potentials are not easily reproduced, as can be seen from the calculations performed with the program NBAR. A factor that critically affects the refinement by the program MAGEC of the titrant concentrations in the final stage is the value used for the dissociation constant of water, K_w. This parameter is very sensitive to correlations with the concentration of alkali in the burette. In other words, either the base titrant concentration or K_w (but not both) can be determined by finding the value that yields the best least-squares slope (2.303 RT/F). Owing to relatively small errors in the concentration of titrant (KOH) and titrand (HCl), the least-squares straight line does not normally possess a Nernstian slope. In those situations when K_w is uncertain, the subprogram CALIBT permits the user systematically to vary the estimate of K_w. For other important features of MAGEC and NBAR see refs. 30 and 31 respectively.

The overall stability constants (β_{pqr}), which are defined by equation (1) (charges are omitted for simplicity), were refined by

$$pM + qH + rL \rightleftharpoons M_pH_qL_r$$
$$\beta_{pqr} = [M_pH_qL_r]/[M]^p[H]^q[L]^r \qquad (1)$$

the method of rigorous least squares using the computer program SUPERQUAD;[32] initial estimates of protonation and formation constants and the stoicheiometries of possible complexes were obtained, in the case of binary systems, from the features of the protonation and formation curves ($\bar{n}$ against pH or pL, where pH = $-\log[H^+]$ and pL = $-\log[L^-]$ by using the programs GAUSS Z[33] and NBAR.[31] The adequacy of a mathematical model to reproduce the experimental data was determined by considering the lowest value of the standard deviations of the parameters, the agreement factor (σ^2) between experimental and calculated titration curves, the goodness of fit statistic (χ^2), and the chemical significance of the species selected. All the calculations were carried out on the CRAY X-MP/48 and IBM 4341/10 computers of the Consorzio per la Gestione del Centro di Calcolo Elettronico Interuniversitario dell'Italia Nord Orientale, Casalecchio di Reno, with financial support from University of Parma. The compositions of the starting solutions for all potentiometric titrations are reported in Table 2, the concentrations and the experimental pH of the different solutions used in the spectrophotometric experiments in Table 3. Listings of all experimental data and final computations from SUPERQUAD, GAUSS Z, and SQUAD[34] are available from the author.

Results and Discussion

Protonation Equilibria.—Starting from sets of potentiometric data, first the cumulative protonation constants of the ligand

Table 1. Evaluation of the equivalence point, v_e/cm^3, N/mol dm^{-3} (normality of KOH), K_w (ionic product of water), $E^\ominus$/mV[a] (standard potential), A_j/mV [a] (junction potential in acid solution), B_j/mV[a] (junction potential in basic solution), and 2.303 RT/F (Nernstian slope)[a] from eight potentiometric titrations of HCl (0.409 86 mol dm^{-3}) with KOH at 25 °C and I = 0.5 mol dm^{-3} (KCl) using the computer programs NBAR and MAGEC

	MAGEC				NBAR[b]				
Run	$E^\ominus$	2.303 RT/F	$10^{14}K_w$	v_e	$E^\ominus$	A_j	B_j	v_e	N
1	1 162.90(7)[c]	59.16(3)[c]	1.8535	2.003	1 163.15(9)[d]	4.54(5.34)[d]		2.010[d]	0.407 75[d]
	1 162.40(24)[e]	58.91(6)[e]			1 162.82(5)[f]		−7.56(2.82)[f]	2.008[f]	0.408 14[f]
2	1 163.30(9)	59.17(4)	1.8664	2.009	1 163.10(7)	0.77(5.72)		2.009	0.408 08
	1 163.00(16)	59.09(2)			1 162.96(5)		−15.27(4.19)	2.007	0.408 39
3	1 160.90(10)	59.16(5)	1.8578	2.004	1 160.86(9)	−1.62(4.00)		2.009	0.407 93
	1 160.70(12)	59.16(1)			1 160.59(6)		−13.12(3.39)	2.007	0.408 45
4	1 159.80(8)	59.17(4)	1.8408	2.010	1 159.68(7)	3.92(3.51)		2.009	0.407 94
	1 159.82(14)	59.11(2)			1 159.36(4)		0.86(1.81)	2.008	0.408 18
5	1 159.70(10)	59.16(7)	1.8365	2.005	1 159.50(9)	23.56(4.20)		2.010	0.407 75
	1 159.30(19)	59.20(10)			1 159.02(9)		24.26(5.38)	2.010	0.407 79
6	1 158.90(15)	59.16(7)	1.8197	2.005	1 158.47(8)	18.21(6.83)		2.009	0.408 10
	1 158.80(17)	59.32(2)			1 158.70(5)		0.53(3.41)	2.007	0.408 39
7[g]	1 156.60(11)	59.18(5)	1.8707	2.011	1 156.32(6)	6.17(2.78)		2.019	0.408 00
	1 156.30(13)	59.01(2)			1 157.24(10)		22.09(5.53)	2.017	0.408 51
8	1 152.45(12)	59.17(7)	1.8621	2.010	1 152.24(13)	60.32(9.64)		2.013	0.407 28
	1 152.82(11)	59.11(8)			1 152.67(16)		96.78(8.35)	2.012	0.407 38

[a] Standard deviations in $E^\ominus$, 2.303RT/F, A_j, and B_j are given in parentheses. [b] In the calculations, K_w was kept constant (1.7614 × 10^{-14} mol^2 dm^{-6}). [c] Using the data before the end-point. [d] Parameters calculated following the principles of Gran by using the experimental data in acidic solution. [e] Using all the buffered data. [f] Parameters calculated following the principles of Gran by using the experimental data in alkaline solution. [g] Initial amount of hydrochloric acid was 2.01 cm^3, for all the others 2.0 cm^3.

Table 2. Determination of protonation and complex-formation constants. Initial amounts of the reagents* for the alkalimetric titrations of 2-amino-*N*-hydroxypropanamide (ahpr) with bivalent metal ions at 25 °C and I = 0.5 mol dm^{-3} (KCl)

Run	System	T_L	T_M	T_H	pH
1	H$^+$–ahpr	0.380 220		0.760 440	6.003—9.803
2		0.332 692		0.665 385	5.978—10.424
3		0.304 176		0.608 332	5.934—10.010
4		0.389 725		0.779 451	6.364—10.937
5		0.361 209		0.722 418	5.938—10.095
6		0.323 187		0.646 374	5.987—10.107
7	Cu^{II}–ahpr	0.375 412	0.183 287	0.762 461	2.949—6.911
8		0.375 412	0.122 191	0.762 461	3.018—8.980
9		0.328 486	0.050 913	0.667 153	3.191—9.209
10		0.328 486	0.091 643	0.667 153	3.081—9.488
11		0.281 559	0.101 826	0.571 846	3.118—9.199
12		0.337 871	0.132 374	0.686 215	3.022—8.741
13	Ni^{II}–ahpr	0.375 412	0.147 010	0.762 461	5.014—7.412
14		0.281 559	0.147 010	0.571 846	4.659—8.614
15		0.375 412	0.073 505	0.762 461	4.158—8.618
16		0.328 486	0.066 155	0.667 153	3.612—8.859
17		0.281 559	0.073 505	0.571 846	3.757—9.303
18		0.309 715	0.095 557	0.629 030	3.630—8.582
19	Co^{II}–ahpr	0.375 412	0.142 265	0.762 461	3.532—8.364
20		0.375 412	0.113 812	0.762 461	3.516—8.758
21		0.375 412	0.085 359	0.762 461	3.545—8.625
22		0.281 559	0.142 265	0.571 846	3.657—8.844
23		0.328 486	0.113 812	0.667 153	3.531—8.358
24		0.300 329	0.113 812	0.609 969	3.534—8.590

* T_L = mmol of ligand, T_M = mmol of metal, T_H = mmol of hydrogen ion in the titration vessel.

and the initial amounts of reagents (T_L, T_H/mmol) were refined simultaneously by using SUPERQUAD. Since the liquid-junction potentials of the cell used in the measurements are fairly small and not prominent in the calculations of the equilibria (pH interval used 3.018—10.937) they have been neglected in the present calculations. After the refinement procedure, the variance as regards the initial amounts of the reagents (T_L, T_H) was 2.35092 × 10^{-5} and 3.932 24 × 10^{-5} mmol^2, respectively. GAUSS Z was also applied to refine the parameters (log β_{0q1}) starting from the same potentiometric data. The cumulative and stepwise protonation and complex-formation constants (log β_{pqr} and log K) of ahpr are quoted in Table 4. In the normal aqueous titration range, DL-alaninehydroxamic acid (ahpr) $[H_2L]^+$ can liberate two protons, one from the protonated amino group (NH_3^+) and one from the OH group of the hydroxamic acid moiety (NHOH). These show two distinct buffering zones: in the pH range 5.93—8.20 corresponding to protonation of the oxygen group [log $K^H{}_2$ = 7.44(1)], and in the pH range 8.20—10.0 corresponding to protonation of the α-amino group [log $K^H{}_1$ = 9.18(1)]. All the protonation constants calculated by both computer programs (Table 4) agree closely. The values for the protonation equilibria

Table 3. Initial concentrations (c/mol dm^{-3}), standard deviation of absorbance data* and the measured pH of the solutions, employed in the spectrophotometric experiments

Run	System	$10^2\ c_L$	$10^3\ c_M$	pH	$\sigma(A)$
1	Cu^{2+}–ahpr	1.3632	6.6553	5.446	2.829×10^{-2}
2		1.3525	6.6035	4.774	1.365×10^{-2}
3		1.3473	6.5779	4.157	1.660×10^{-2}
4		1.4034	4.5679	8.922	3.696×10^{-2}
5		1.3895	4.5227	7.446	4.638×10^{-2}
6		1.3786	4.4871	6.194	2.149×10^{-2}
7		1.3705	4.4608	5.539	1.448×10^{-2}
8		1.3625	4.4348	5.191	2.209×10^{-2}
9		1.3546	4.4092	4.476	8.661×10^{-3}
10		1.3468	4.3838	3.922	1.447×10^{-2}
11		1.2337	3.4420	9.380	1.968×10^{-2}
12		1.2215	3.4079	8.237	6.150×10^{-3}
13		1.2096	3.3745	6.506	8.556×10^{-3}
14		1.2025	3.3548	5.573	8.361×10^{-3}
15		1.1950	3.3340	5.142	1.915×10^{-2}
16		1.1886	3.3140	4.248	9.543×10^{-3}
17		1.1813	3.2957	3.856	2.350×10^{-2}
18		1.0615	3.8389	9.650	1.289×10^{-2}
19		1.0489	3.7934	7.424	1.099×10^{-2}
20		1.0407	3.7636	5.712	1.004×10^{-2}
21		1.0246	3.7055	3.984	1.318×10^{-2}
22		1.0129	3.6630	3.639	3.206×10^{-2}
23	Ni^{2+}–ahpr	1.3891	5.4398	9.045	1.205×10^{-2}
24		1.3727	5.3753	7.683	8.675×10^{-3}
25		1.3619	5.3331	6.613	1.371×10^{-2}
26		1.3513	5.2916	6.197	2.196×10^{-2}
27		1.3409	5.2508	5.977	8.148×10^{-3}
28		1.0482	5.4732	8.158	2.718×10^{-2}
29		1.0420	5.4407	6.915	1.464×10^{-2}
30		1.0359	5.4086	6.412	7.537×10^{-3}
31		1.0278	5.3665	6.096	7.205×10^{-3}
32		1.0218	5.3353	5.957	4.746×10^{-3}
33		1.4140	2.7686	8.700	5.996×10^{-3}
34		1.4028	2.7466	8.094	7.308×10^{-3}
35		1.3917	2.7249	7.458	8.823×10^{-3}
36		1.3808	2.7037	6.668	9.919×10^{-3}
37		1.3701	2.6827	6.089	3.826×10^{-3}

* $\left\{\sum_{k=1}^{N_w}[A_o(K) - A_c(K)]^2 w_k/(N_w - N_c)\right\}^{\frac{1}{2}}$ where $A_o(K)$ and $A_c(K)$ are the observed and calculated absorbances at the Kth wavelength, N_w = number of wavelengths and N_c = number of constants to be refined; w_k = is the weighting factor.

(Table 4) for the ahpr base are not the same as obtained previously.[35] Kurzak *et al.*[35] reported values of log β_{011} = 9.15(1), log β_{021} = 16.34(2) at I = 0.1 mol dm^{-3} ($NaClO_4$) at 25 °C. In particular, the greatest differences, as regards the data reported in the literature, occur for log K^H_2. This might be caused by the influence of the ionic strength on the protonation constant with changes in a manner similar to that of glycine[36] or acetic acid.[37]

The influence of the α-amino group in aminohydroxamic acids on the acidic character of the OH group [log K^H_2 = 7.44(1)] for DL-alaninehydroxamic acid (ahpr) in comparison with the corresponding alkyl hydroxamic acid is similar to that found for all the aminohydroxamic acid examined.[28,38,39] Likewise the substitution of a NHOH group for the carboxyl OH group in aminohydroxamic acids lowers slightly the protonation constant of the α-amino group [log K^H_1 = 9.18(1)] compared to the analogous protonation constant of the corresponding α-amino acids due to the electron-withdrawing effect of the NHOH group. All these aspects (the variation of log K^H_1 and log K^H_2, protonation constant of NH_2 and NHO^- groups, respectively; against log K^H_1, protonation constant of the α-amino group of the corresponding amino acids) for all the aminohydroxamic acids examined are shown in Figure 1.

Metal(II) *Complex Equilibria*.—Titration data obtained at different ligand-to-metal ratios were processed initially by the program NBAR to obtain formation curves ($\bar{n}$ *versus* pL). Initial estimates of formation constants and the stoicheiometries of possible complexes were obtained, in the case of the binary systems, from the features of the formation curves. This strategy facilitated the search for not only mononuclear binary complexes but also polynuclear species, particularly in the copper(II)–ahpr system. Plots of $\bar{n}$ against $-\log [L^-]$ from some experimental potentiometric titrations (runs 7—9, Table 2) of copper(II)–ahpr mixtures are shown in Figure 2. That the formation curves are not superimposable indicates the presence of polynuclear species. On the other hand, the formation curves are not parallel with a spacing, $\Delta\log[L^-]$, proportional to $\Delta\log[Cu^{2+}]_T$, so the system does not contain predominantly a 'core-plus-links' series of metal complexes.[40] A decrease in spacing between the curves obtained under different experimental conditions as the metal ion concentration is reduced suggests that mononuclear complexes are the major species in more dilute solutions and that the curves are converging towards Biedermann and Sillen's 'mononuclear wall'.[41] The formation curves (Figure 2) intersect at the point n = 1.26 and $\log[L^-]$ = 9.76. Following our usual approach, SUPERQUAD was employed to refine the formation constants and, on the basis of the

Table 4. Cumulative and stepwise protonation complex-formation constants of 2-amino-*N*-hydroxypropanamide (ahpr) at 25 °C and $I = 0.5$ mol dm^{-3} (KCl)

	SUPERQUAD				GAUSS Z
	H^+	Co^{2+}	Ni^{2+}	Cu^{2+}	H^+
$\log \beta_{011}$	9.18(1)				9.18(1)
$\log \beta_{021}$	16.62(1)				16.61(1)
$\log K^{H}{}_2{}^a$	7.44(1)^b				7.43(1)
$\log \beta_{101}$		6.08(1)	6.92(1)	10.32(6)	
$\log \beta_{102}$		10.69(1)	14.06(1)	20.04(1)	
$\log \beta_{2-12}$				20.90(1)	
$\log \beta_{1-12}$		1.59(4)	5.82(2)	11.11(6)	
$\log \beta_{201}$		8.91(3)			
$\log K_2$		4.61(1)	7.14(1)	9.72(4)	
Z^c	352	373	364	367	352
U	1.107×10^1	2.233×10^3	9.457×10^2	1.836×10^3	$3.827 \times 10^{-3\,d}$
$\chi^{2\,e}$	13.91	28.27	8.62	33.59	
σ^f	0.18	2.46	1.62	2.25	$1.093 \times 10^{-5\,g}$
R^h					0.3%

[a] $\log K_n = \log \beta_{0n1} - \log \beta_{0n-11}$. [b] $\sigma(\log K_n) = [\sigma^2(\log \beta_{0n1}) + \sigma^2(\log \beta_{0n-11})/2]^{\frac{1}{2}}$. [c] Total number of experimental data points used in the refinement. [d] $U = \sum_{i=1}^{Z}(n_i^{\text{calc.}} - n_i^{\text{obs.}})^2$, where n_i is the observed (obs.) or calculated (calc.) average number of hydrogen ions bound to each central ligand molecule. [e] Observed χ^2; calculated value (6, 0.95) should be 12.6, where 6 is the number in degrees of freedom and 0.95 the confidence coefficient in the χ^2 distribution. [f] $\sigma = \left[\sum_{i=1}^{Z} w_i(E_i^{\text{obs.}} - E_i^{\text{calc.}})^2/(Z - m)\right]^{\frac{1}{2}}$, where m is the number of parameters to be refined. [g] $\sigma^2 = \sum_{i=1}^{Z}(n_i^{\text{calc.}} - n_i^{\text{obs.}})^2/(Z - m)$. [h] $R = \left[\sum_{i=1}^{Z}(n_i^{\text{obs.}} - n_i^{\text{calc.}})^2 / \sum_{i=1}^{Z}(n_i^{\text{obs.}})^2\right]^{\frac{1}{2}} \times 100$.

Table 5. Parameters (ε/dm^3 mol^{-1} cm^{-1}, ν/cm^{-1}, $\Delta\nu$/cm^{-1}) of the component bands obtained from Gaussian analysis of the absorption spectra of $[CuL_2(H_2O)_2]$, $[Cu(OH)L_2(H_2O)]^-$, and $[NiL_2(H_2O)_2]$, respectively (L = DL-alaninehydroxamate), *f* values refer to the oscillator strengths for the transitions[a]

Assignment	ε	ν	$\Delta\nu$	*f*
$[CuL_2(H_2O)_2]$				
$^2B_{1g} \longrightarrow {}^2A_{1g}$	29.29	16 797.8	4 000.1	5.3900×10^{-4}
	34.26^b	16 800.5	4 001.2	6.3052×10^{-4}
	53.71^c	16 800.2	4 001.1	9.886×10^{-4}
	33.58^d	16 799.2	4 147.8	6.404×10^{-4}
$^2B_{1g} \longrightarrow {}^2B_{2g}$	54.50	18 492.7	4 378.5	1.0977×10^{-3}
	48.00^b	18 501.4	4 374.6	9.6595×10^{-4}
	80.93^c	18 500.2	4 374.9	1.629×10^{-3}
	48.11^d	18 824.0	4 191.8	9.272×10^{-4}
$^2B_{1g} \longrightarrow {}^2E_g$	35.26	20 496.3	4 707.9	7.6367×10^{-4}
	36.10^b	20 500.1	4 705.8	7.8149×10^{-4}
	48.46^c	20 499.2	4 706.1	1.049×10^{-3}
	29.56^d	20 517.7	5 066.8	6.855×10^{-4}
$[Cu(OH)L_2(H_2O)]^-$				
$^2B_{1g} \longrightarrow {}^2A_{1g}$	39.59	17 304.2	4 402.4	8.0178×10^{-4}
$^2B_{1g} \longrightarrow {}^2B_{2g}$	52.50	19 305.9	4 533.3	1.0948×10^{-3}
$^2B_{1g} \longrightarrow {}^2E_g$	30.48	21 107.2	6 050.8	8.4834×10^{-4}
$[NiL_2(H_2O)_2]$				
$^1A_{1g} \longrightarrow {}^1B_{1g}$	50.51	19 799.9	3 480.4	8.0872×10^{-4}
	55.45^e	19 819.7	3 773.8	9.6267×10^{-4}
	53.98^f	19 779.8	3 818.7	9.4825×10^{-4}
$^1A_{1g} \longrightarrow {}^1A_{2g}$	60.00	23 898.2	5 281.5	1.4577×10^{-3}
	58.20^e	23 900.1	5 187.6	1.3888×10^{-3}
	56.20^f	23 892.8	5 187.1	1.3410×10^{-3}

[a] Relative standard deviation for the Cu^{2+}–ahpr system = 0.52; region of spectrum 14 286—27 778 and 12 579—25 000 cm^{-1} for Ni^{2+} and Cu^{2+}, respectively. [b] Cu^{2+}–adhb system. [c] Cu^{2+}–adhp system. [d] Cu^{2+}–ahpr system, ref. 35. [e] Ni^{2+}–adhb system. [f] Ni^{2+}–adhp.

usual numerical criteria, to select the initial sets of complexes. The final choice of the equilibrium models is demonstrated by the excellent matching of the experimental and calculated potentiometric data. In particular, when applying SUPERQUAD to obtain consistent chemical models to explain the entire set of potentiometric data, the standard deviations (σ) of the parameters refined ($\log \beta_{pqr}$), the agreement factor σ^2 (variance), the goodness-of-fit statistic χ^2, and the chemical meaning of the species complexed found in solution were taken into consideration for each hypothesis. The most consistent set

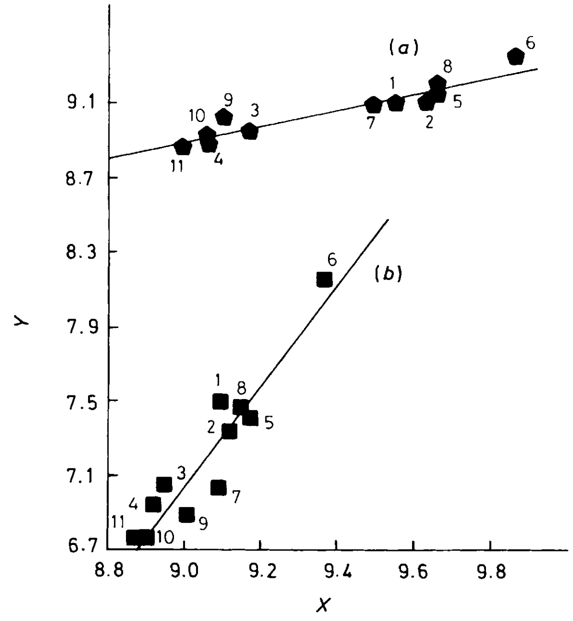

Figure 1. Relationship between (*a*) log K^{H}_{1} (protonation constant of α-amino group in aminohydroxamic acids) and log K^{H}_{1} (protonation constant of α-amino group of the corresponding amino acids) ($y = 4.8338 + 0.4502\ x$, correlation coefficient $r = 0.95$) and (*b*) log K^{H}_{2} (protonation constant of NHO^- group) and log K^{H}_{1} (protonation constant of α-amino group in aminohydroxamic acids) ($y = -15.7044 + 2.5286\ x$, $r = 0.93$). The lines drawn were obtained from a linear least-squares analysis of all the data: (1) aha = 2-amino-*N*-hydroxyacetamide;[27] (2) ahp = 2-amino-*N*-hydroxypentanamide;[27] (3) ahip = α-amino-*N*-hydroxy-1*H*-imidazole-4-propanamide;[28] (4) ahhpp = 2-amino-*N*-hydroxy-3-(*p*-hydroxyphenyl)propanamide;[25] (5) ahhe = 2-amino-*N*-hydroxyhexanamide (E. Leporati, *J. Chem. Soc., Dalton Trans.*, 1987, 421); (6) hasn = *N*-hydroxy-D-asparagine;[24] (7) ahinp = α-amino-*N*-hydroxy-1*H*-indole-3-propanamide [ref. as for (5)]; (8) ahpr (present work); (9) ahpp = 2-amino-*N*-hydroxy-3-phenylpropanamide;[38] (10) adhp = 2-amino-*N*,3-dihydroxypropanamide;[39] (11) adhb = 2-amino-*N*,3-dihydroxybutanamide[38]

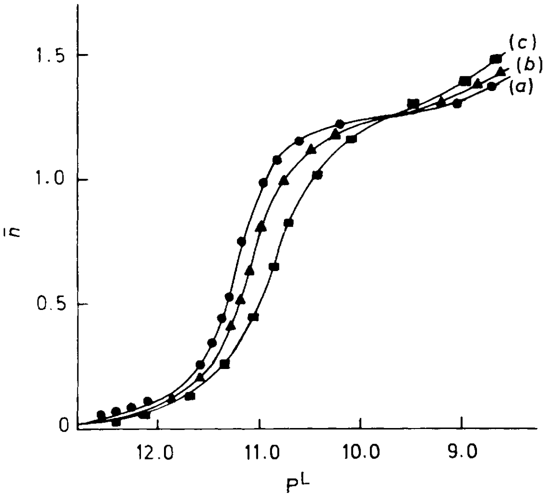

Figure 2. Formation curves for potentiometric titrations [runs 7(*a*), 8(*b*), and 9(*c*), Table 2] of the Cu^{2+} ahpr system

of complexes found, together with their respective formation constants, is shown in Table 4. As a result of comparisons between experimental and calculated titration curves, it is possible to verify the model selected. In the presence of metal ions the curves reveal an appreciable complexing capacity in the acidic media, especially for Cu^{2+}, which takes place by pH 3.0. The relative importance of the various species in each pH range is shown by the distribution diagrams for ahpr with Co^{2+}, Ni^{2+}, and Cu^{2+} (Figure 3).

A comparison of the stability constants of copper(II) complexes of DL-alaninehydroxamic acid with those reported[35] indicates that in general small differences are observed probably due to the different experimental conditions. Thus, complexation also in the light of previous studies can be explained by assuming that ahpr acts as a bidentate ligand co-ordinating to the metal ion (M) *via* the deprotonated NHO^- moiety and the nitrogen atom of the α-amino group, in contrast to the normal co-ordination of unsubstituted monohydroxamic acid.[42] The spectrophotometric study was carried out on a series of solutions, containing ahpr and copper(II) or nickel(II), with concentrations and pH values (Table 3) selected from those employed in the potentiometric titrations. Some typical absorption spectra obtained for the Cu^{II}–ahpr and Ni^{II}–ahpr systems at different pH values are reported in Figures 4 and 5. The only colour variation observed for the Cu^{II}–ahpr system is from intense green to purple, while for pH > 8.0 the colour changes from purple to reddish purple. Small bathochromic and hyperchromic shifts are observed at 537.0—544.0 nm, when the pH increases. The increase in absorption and shift to shorter wavelengths with increase in pH indicates greater complexation, until the formation of the last species complexed, $[Cu(OH)L_2]^-$, which predominates at basic pH. According to Narain and Shulka[43] the position of the absorption maxima for copper(II) complexes in water solution depends fundamentally on the number of Cu–N interactions. The absorption spectra (Figure 4) of the Cu^{II}–ahpr system exhibit, in general, approximately the same changes with increasing pH to those observed for the corresponding aminohydroxamic acid system. Small differences are observed in the energy of the characteristic absorption maxima. The maximum in the range 620—650 nm generally is typical for Cu^{II} co-ordinated by two nitrogen atoms of amino or amido groups. Since the hydrolysed binuclear complex $[Cu_2(OH)L_2]^+$, which reaches a concentration of *ca.* 60.0% total copper at pH 3.922 [curve (1) (*a*), Figure 4] and *ca.* 88.0% at pH 4.476 [curve (2) (*a*), Figure 4] exhibits $\lambda_{max.}$ at 657 and 648 nm respectively, it is possible to conclude that every copper ion is co-ordinated by two nitrogen atoms of ahpr. In the same way, CuL_2 complexes with dipeptides show an absorption peak at 540—560 nm. Therefore, the appearance of the absorption maxima at 563 nm [Figure 4(*a*), curve (4); Figure 4(*b*), curve (5)] for the Cu^{II}–ahpr system suggests the co-ordination of one copper ion by two ligands forming two five-membered chelate rings and four Cu–N bonds. The co-ordination in the complex $[CuL_2]$ involves two nitrogens of the α-amino and deprotonated NHO^- groups. The species $[CuL_2]$ reaches a maximum concentration of 99.05% total copper at pH 6.5 [Figure 3(*a*)]. Associated with the shift of the bands in the range 547—647 nm [Figure 4(*a*) and (*b*)] is the change of colour from intense green to purple in acidic media, while for pH > 8.0 the colour changes from purple to reddish purple. From spectra in Figure 4(*a*) and (*b*) a distinctive isosbestic point can be seen at *ca.* 593 nm. This corresponds to an equilibrium between the only species $[Cu_2(OH)L_2]^+$ and $[CuL_2]$ [Figure 3(*a*); each reaches a concentration of 50% total copper at pH 5.36], which are predominant from pH 3.8 to 8.5. Studies of the equilibria existing between Cu^{II} and other analogous aminoalkanehydroxamic acids[23,35] have indicated the presence of an OH^- ion, acting as a bridge in the binuclear species,[23] which originates from the displacement of a proton from a co-ordinated water molecule in the $[CuL]^+$ units to give the complex $[Cu_2(OH)L_2]^+$. According to Billo[44] the ligand-field contribution of

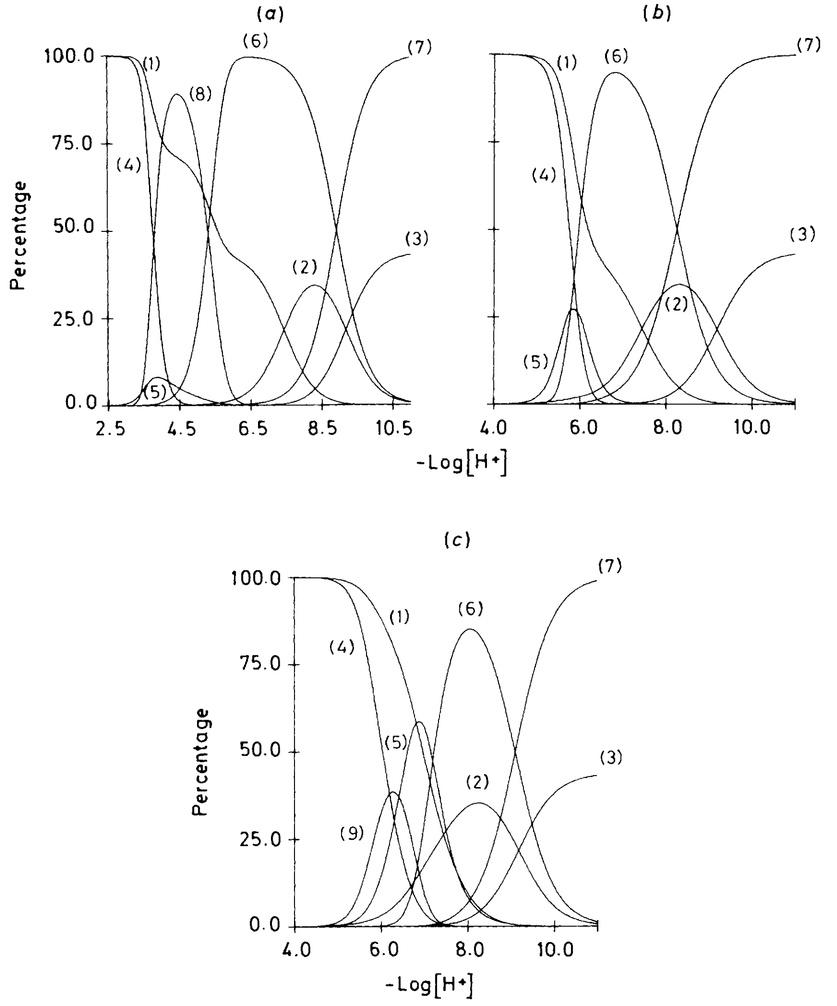

Figure 3. Typical distribution diagrams for M^{2+}–ahpr systems. The percentage of each species has been calculated from the data for a hypothetical solution of metal ions (0.0031 mol dm^{-3}) and ahpr (0.011 mol dm^{-3}) by the HALTAFALL program (N. Ingri, W. Kakalowicz, L. G. Sillén, and B. Warnqvist, *Talanta*, 1967, **14**, 1261) and using a PLOTTER Calcomp 936. The concentrations of the species not containing metal were calculated as percentages of the total ligand, those containing metal as percentages of the total metal: (*a*) Cu^{2+}–ahpr, (*b*) Ni^{2+}–ahpr, (*c*) Co^{2+}-ahpr; (1) H_2L^+, (2) HL, (3) L^-, (4) M^{2+}, (5) $[ML]^+$, (6) $[ML_2]$, (7) $[M(OH)L_2]^-$, (8) $[Cu_2(OH)L_2]^+$, and (9) $[Co_2L]^{3+}$

each N (amino group) is generally equal to *ca.* 4 530 cm^{-1}, which means that the contribution of each nitrogen of the hydroxamate moiety in the $[CuL_2]$ complex with $\lambda_{max.}$ = 18 523 cm^{-1} corresponds to (18 523 − 9 060)/2 = 4 732 cm^{-1}.

For the hydrolysed binuclear species $[Cu_2(OH)L_2]^+$, with $\lambda_{max.}$ = 648 nm, if we suppose co-ordination of one alanine-hydroxamate group to each copper ion *via* the nitrogens of the α-amino and hydroxamate moiety, this would result in a contribution of 9 262 cm^{-1} to the enetgy of the *d*—*d* transitions. The two remaining groups would have to contribute *ca.* 3 081 cm^{-1} each, in order to arrive at the observed $\lambda_{max.}$ = 648 nm (15 425 cm^{-1}) for the complex $[Cu_2(OH)L_2]^+$. This value (3 081 cm^{-1}) is in good agreement with the predicted contribution of an OH^- or H_2O group (*ca.* 3 010 cm^{-1}) which occupies equatorially the fourth position in the co-ordination sphere of each copper ion. When the pH is increased from 3.814 to 4.774 [Figure 4(*b*)] small hypsochromic and high hyperchromic effects (range 648—660 nm) are observed; as the pH increases above 4.774, a simultaneous decrease in the band intensity (hypochromic shift) occurs with changes to shorter wavelengths (hypsochromic effect) and an increase in the absorption (hyperchromic effect) with a maximum at 563 nm [Figure 4(*b*), curve (5)] thus shifting to smaller wavelengths is observed. The molar absorption coefficients ε_{pqr} in the region 400—795 nm for the Cu^{2+}-ahpr system together with the formation constants of the complexes were refined by handling the specific set of experimental absorbance data (Table 3, 22 solutions, 80 wavelengths, 1 760 points) by using the program SQUAD (Figure 6). It is well known that any curve reported in Figure 6 may be considered to be the sum of an infinite number of Gaussian components. However, it is possible to assume that a unique fitting between a wide number of different models could be obtained if the relative symmetry is taken into account. At this point a careful and detailed Gaussian analysis of the experimental spectrum of $[CuL_2(H_2O)_2]$ and $[Cu(OH)L_2(H_2O)]^-$ (Figure 6) was carried out, using the computer program NLIN (SAS Institute Inc. SAS User's Guide: Statistics, Version 5 Edition, Cary Nc. SAS Institut Inc., 1985, p. 576); in particular the parameters of the component bands and related maxima positions are carefully determined. The electronic spectra of most octahedral and pseudo-octahedral complexes of Cu^{II} are explainable by the doublet term system displaying one (in the case of octahedral) or more absorption bands. The theoretical energy levels for a d^9 free copper

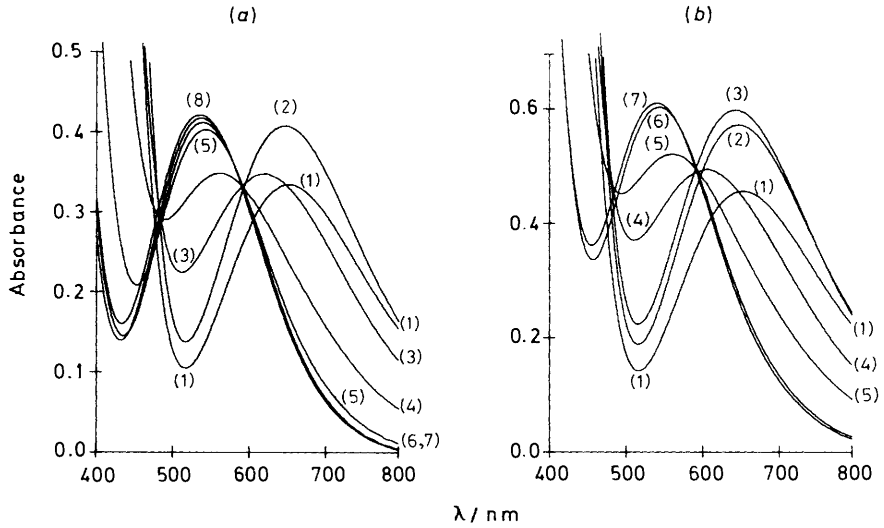

Figure 4. Plots of experimental absorbance data *versus* wavelength for solutions of the Cu^{2+}–ahpr system; (*a*) runs 10(1), 9(2), 8(3), 7(4), 6(5), 5(6), 4(8) (Table 3), and (7), pH 8.391, $[H_2L^+] = 1.3978 \times 10^{-2}$, $[Cu^{2+}] = 4.5497 \times 10^{-3}$ mol dm^{-3}; (*b*) runs 3(2), 2(3), 1(4) (Table 3), and (1), pH 3.814, $[H_2L^+] = 1.3369 \times 10^{-2}$, $[Cu^{2+}] = 6.5273 \times 10^{-3}$ mol dm^{-3}, (5), pH 5.779, $[H_2L^+] = 1.3712 \times 10^{-2}$, $[Cu^{2+}] = 6.6947 \times 10^{-3}$ mol dm^{-3}, (6), pH 7.049, $[H_2L^+] = 1.3821 \times 10^{-2}$, $[Cu^{2+}] = 6.7479 \times 10^{-3}$ mol dm^{-3} and (7), pH 9.218, $[H_2L^+] = 1.3904 \times 10^{-2}$, $[Cu^{2+}] = 6.7884 \times 10^{-3}$ mol dm^{-3}. The program VISION with the PLOTTER Calcomp 936 was used

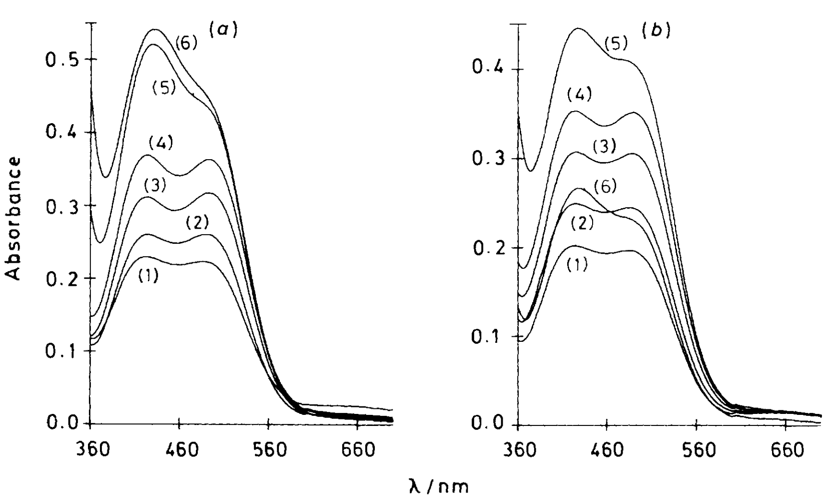

Figure 5. Plots as in Figure 4 but for the Ni^{2+}–ahpr system: (*a*) runs 27(1), 26(2), 25(3), 24(4), 23(5) (Table 3), and (6), pH 9.503, $[H_2L^+] = 1.0545 \times 10^{-2}$, $[Cu^{2+}] = 5.5060 \times 10^{-3}$ mol dm^{-3}; (*b*) runs 32(1), 31(2), 30(3), 29(4), 28(5), and 33(6) (Table 3)

configuration[45] in O_h and D_{4h} symmetry indicate that as many as three doublet–doublet transitions may be located in the electronic spectra of complexes with D_{4h} symmetry. However, experimental absorption spectra for such compounds rarely exhibit more than two absorption bands; only in some cases is it possible to observe all three absorption bands.[46] Seldom are they completely separated from other. However the major complication is that, between of splittings which are small compared to band widths, sometimes one band is totally hidden by the other two so that it does not even appear as a shoulder. To obtain a realistic model, it is necessary to apply a possible reduction in the symmetry of the system so that O_h and D_{4h} would be the possible effective symmetries of the system investigated. Most copper(II) complexes which are usually green or blue are tetragonally distorted with four short metal–nitrogen bonds in one equatorial plane (*xy*) and two longer metal–water bonds on the axis perpendicular to that plane; then the assumption of D_{4h} symmetry may be adequate to account for the spectral band locations. Moreover the Gaussian analyses, based on the non-linear Gauss-Newton least-squares method which allowed O_h (one band) and D_{4h} (three bands) symmetry, were different in terms of the relative standard deviation, as previously reported for the copper(II)—L-alanine-hydroxamic acid complex.[35] The assignments and calculated maxima positions of the component bands (Figure 7, and Table 5) are based on the following assumptions: the effective symmetry about the copper ion is D_{4h} and the ligand-field models proposed for $[CuL_2(H_2O)_2]$ and $[Cu(OH)L_2(H_2O)]^-$ complexes are adequate to derive the spectral parameters. In this case the term B_{1g} will be the ground state and three-spin allowed transitions from the $^2B_{1g}$ state to the other doublet states are expected. The relative energy order of these transitions ($^2A_{1g} < {}^2B_{2g} < E_g$) will depend on the axial metal–water interaction and their energies in terms of the parameters *Dq*, *Ds*, and *Dt* have been obtained from the following expressions (2)—(4).[47]

$$\nu_1 = E(B_{1g} \longrightarrow A_{1g}) = -4Ds - 5Dt \qquad (2)$$

$$\nu_2 = E(B_{1g} \longrightarrow B_{2g}) = 10Dq \qquad (3)$$

	$[CuL_2(H_2O)_2]$	$[Cu(OH)L_2(H_2O)]^-$
$Dq = \nu_2/10$	1 849.3	1 930.6
$Ds = 1/7(\nu_2 - \nu_1 - \nu_3)$	−2 685.9	−2 729.4
$Dt = 1/35\{[4(\nu_3 - \nu_2) - 3\nu_1]\}$	−1 210.8	−1 277.3

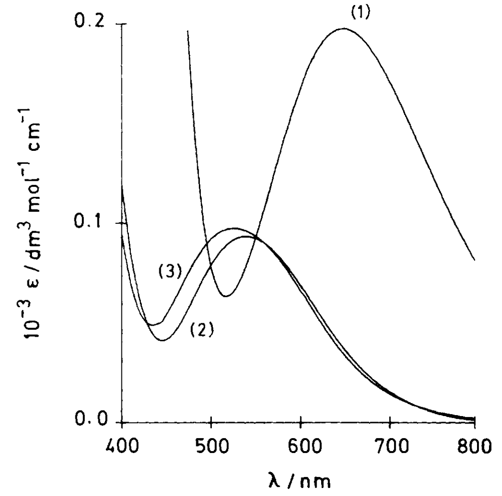

Figure 6. Plots of the molar absorption coefficients (ε) of the three complexed species in the Cu^{2+}–ahpr system at 25 °C obtained by the program SQUAD with the PLOTTER Calcomp 936; (1) $[Cu_2(OH)L_2]^+$, (2) $[CuL_2]$, and (3) $[Cu(OH)L_2]^-$

$$\nu_3 = E(B_{1g} \longrightarrow E_g) = 10Dq - 3Ds + 5Dt \qquad (4)$$

By using the maxima positions of the component bands (Table 5) the ligand-field parameters *Dq*, *Ds*, and *Dt* were obtained.

Table 5 and Figure 7 summarize the results of spectral resolution, the parameters of the components bands and their oscillator strengths for the Cu^{2+}–ahpr, Ni^{2+}–ahpr, and other analogous systems, respectively. There is excellent agreement between the parameters calculated (ν, ε, *f*, Δν) for the different systems meaning that a similar behaviour (thermodynamic stability, structure, configuration, all bond strengths, co-ordination environments) takes place through the $[CuL_2(H_2O)_2]$ complex formation. The small differences observed in the values (*Dq* and ε) could be due to various factors: *Dq* (inversely proportional to the fifth power of the metal–ligand distance) is very sensitive to changes in the metal–ligand distance; the metal–ligand bonds will be vibrating so that the internuclear distance is constantly fluctuating. Thus the larger crystal-field parameter *Dq* for $[Cu(OH)L_2(H_2O)]^-$ reflects, in addition to the electrostatic interaction between the metal ion and ligand, the covalent σ and π capability of the ligand; the increment in the molar intensity (ε) of the component bands for the Cu^{2+}–adhp system involves a change from centrosymmetric to weakly acentric molecules. The energies for a tetragonal distortion are commonly given in terms of the radial parameters *Ds* and *Dt* which are slightly different for $[Cu(OH)L_2(H_2O)]^-$. Since the equatorial and axial bond lengths may differ, distinction is made between the axial and equatorial radial parameters. The molar absorption coefficients ε_{pqr} (Figure 8) in the range 360—700 nm

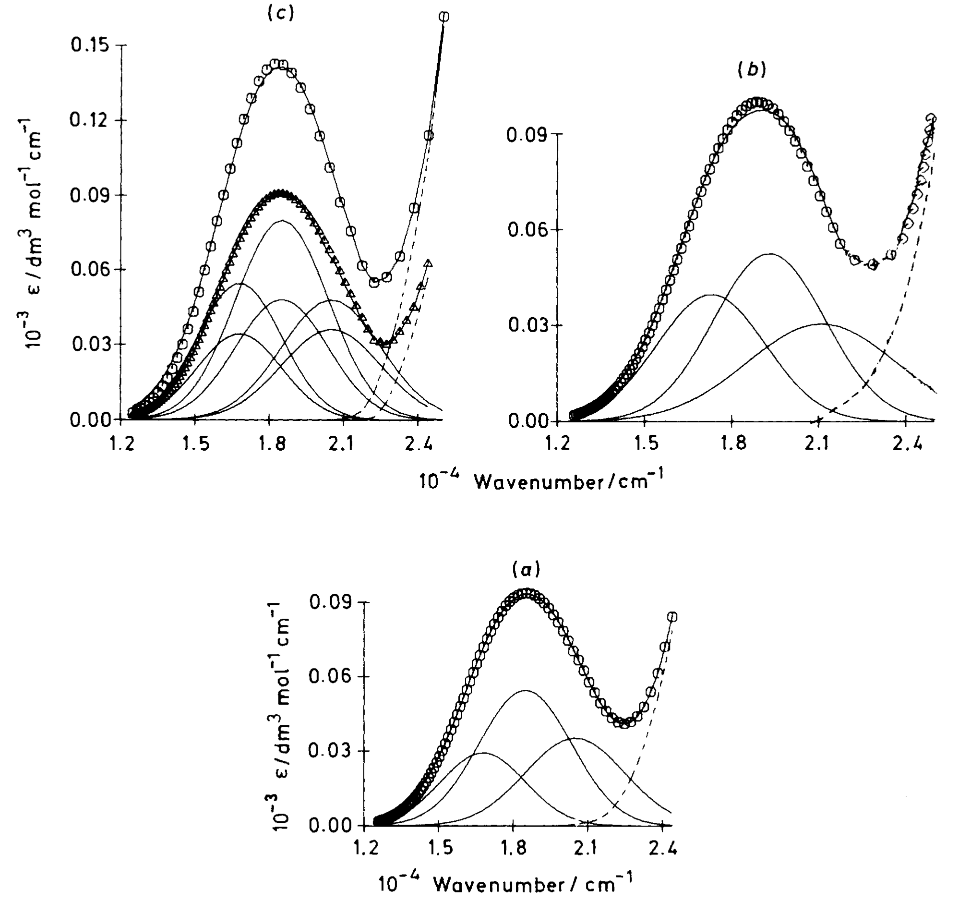

Figure 7. Absorption spectra [experimental (symbols) and calculated spectrum; (——, composite bands, ----, unassigned band)]: (*a*) $[CuL_2(H_2O)_2]$, (*b*) $[Cu(OH)L_2(H_2O)]^-$, where L^- = DL-alaninehydroxamate; (*c*) $[CuL_2(H_2O)_2]$, where L^- = serinehydroxamate (○) or = DL-threoninehydroxamate (△)

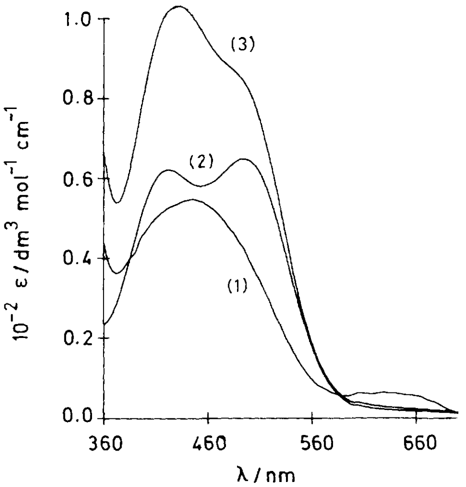

Figure 8. Plots of the molar absorption coefficients (ε) of the three complexes species in the Ni^{2+}-ahpr system at 25 °C obtained by the program SQUAD: (1) $[NiL]^+$, (2) $[NiL_2]$, and (3) $[Ni(OH)L_2]^-$

for the Ni^{2+}-ahpr system were refined as previously described[34,38] and the sum of the squared residuals between observed and calculated values obtained by SQUAD (1 035 experimental points) by using 15 solutions (Table 3) and 69 wavelengths for each solution was 1.602×10^{-1} (standard deviation in the absorbance data 1.391×10^{-2}). Gaussian analysis was carried out on the electronic spectrum of $[NiL_2(H_2O)_2]$ (Figure 8, Table 5) by using the computer program NLIN. In nickel(II) complexes of glycinehydroxamic acid[23,48] a N,N-co-ordination was found for $[NiL_2]$ and $[Ni(OH)L_2]^-$, respectively. In the solid state the co-ordination is *trans*[19] and *cis*[20] square planar. Square-planar derivatives of nickel(II) are commonly orange or red. The *d–d* spectra of nickel(II) complexes consist of a single broad asymmetric peak in the 20 000—24 000 cm^{-1} region which is well separated from the charge-transfer bands. Typical absorption spectra for the Ni^{2+}-ahpr system are reported in Figure 5 for the range pH 5.957—9.503. In a nickel complex of this kind three Gaussian components would be expected for complexes of D_{4h} symmetry with no ligands co-ordinated along the z axis: the ground state is $^1A_{1g}$ and two component bands may be tentatively assigned as ν_2 at 19 800 cm^{-1} ($^1A_{1g} \longrightarrow {}^1B_{1g}$) and ν_3 23 898 cm^{-1} ($^1A_{1g} \longrightarrow {}^1A_{2g}$) transitions in square-planar symmetry by comparison with observed spectra of analogous compounds[38,39] (Table 5) and of nickel(II) complexes of confirmed square-planar configuration.[47,48] The only other transition expected in this region for a low-spin nickel(II) complex of D_{4h} symmetry lying below 28 000 cm^{-1} ($^1A_{1g} \longrightarrow {}^1E_g$) is probably a charge-transfer band, not observed experimentally. Since the 1:2 nickel complex, according to X-ray investigations,[19,20] is N,N-co-ordinated forming five-membered rings, a similar co-ordination for the ML species *via* the nitrogens of the α-amino (NH_2) and deprotonated NHO^- groups is suggested, as previously reported for nickel complexes of glycinehydroxamic acid[27,48] and serinehydroxamic acid (adhp).[39]

The NiL_2 complex being square planar, the small difference in log K for NiL and NiL_2 [$\Delta\log K = \log K_2 - \log K_1 = 0.23$] can be explained if it corresponds to an octahedral (NiL) to square-planar (NiL_2) transformation. Moreover, the logarithm of the second stepwise formation constant ($\log K_2$) for the Ni^{2+}-ahpr system is appreciably greater than that of the first ($\log K_1$). The reason for this behaviour may lie in the ability of Ni^{2+} to form square-planar complexes; when a second ligand is bonding facially in a bidentate manner the two five-membered chelate rings in the complex $[NiL_2]$ are much more stable than one five-membered ring in $[NiL]^+$.

The bonding mode in $[ML]^+$ and $[ML_2]$, *etc.* complexes of aminohydroxamic acids so far examined is almost certainly not glycine-like, where the metal ion is bound through the carboxylate oxygen (CO_2^-) or the oxygen of the hydroxamate moiety ($CONHO^-$) and α-amino group only. The much higher stability of the 1:1 and 1:2 complexes of ahpr and other aminohydroxamic acids[24,25,27,28,38,39] with different metal ions compared with that of the corresponding complexes of the amino acids (*e.g.* D-aspartic acid, glycine, histidine, DL-norvaline, DL-tryptophan, L-tyrosine, DL-norleucine, serine, DL-alanine, *etc.*) can be attributed to co-ordination *via* the nitrogen atom of the α-amino group and the nitrogen of the NHO^- group. The Irving–Williams order is followed by the complexes $[ML]^+$, $[ML_2]$, and $[M(OH)L_2]^-$. The M^{II}-ahpr systems therefore probably satisfy different criteria for biological activities and analytical roles, strongly indicating M^{II}-ahpr complexes as suitable sources of metal ions as trace elements essential in animal nutrition. The results show that, at least at physiological pH, the assumption of an unco-ordinated α-amino group, which may be particularly active because of a possible surface-active role, is incorrect.

Acknowledgements

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