New Insights into M(II)−Hydroxamate Interactions: The Electro-Analytical Behavior of Metal(II) Complexes Involving Monohydroxamic Acids and Diamines in an Aqueous Medium

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The binary and ternary systems of Cu(II), Co(II), Ni(II), Zn(II), Cd(II), Mn(II), Mg(II), and Ca(II) metal ions with the hydroxamic acids, acetohydroxamic acid (Aha), benzohydroxamic acid (Bha), and salicylhydroxamic acid (Sham), and diamines, ethylenediamine (en), 1,3-diaminopropane (dapr), and *o*-phenylenediamine (*o*-pda), were investigated potentiometrically at 25 °C and $I = 0.10\ \text{mol}\cdot\text{dm}^{-3}$ ($NaNO_3$) in aqueous solution. The acid−base properties of the ligands were investigated. The potentiometric titration curves show that the ternary complexes are formed in a stepwise manner. The stability constants of the binary and ternary complexes were calculated on the basis of computer analysis of titration data. The order of stability of the binary and ternary complexes in terms of the nature of hydroxamic acids, diamines, and metal ions was investigated and discussed. The relative stability of ternary complex species is expressed in terms of $\Delta\log K$ and % R.S. parameters. The distribution of binary and ternary complexes in solution was evaluated. Evaluation of the effect of temperature of the medium on both the ionization process of the ligands and complex formation for the M(II)−en−Sham (M(II) = Cu(II), Co(II), and Ni(II)) ternary systems has been studied along with the corresponding thermodynamic parameters. The complexation behavior of ternary complexes is ascertained using conductivity measurements. In addition, confirmation of the formation of ternary complexes in solution has been performed using cyclic voltammetry measurements.

Introduction

Hydroxamic acids $R_C(CO)N(R_N)OH$ (R_C = alkyl/aryl; R_N = alkyl/aryl or H) are among the most well studied compounds due to their significance in so many fields.[1] Naturally occurring hydroxamic acids are involved as low-molecular weight iron chelators in the microbial transport of iron (siderophores) and play a key role in facilitating the proper function of enzymes in electron and oxygen transport and other life-sustaining processes.[2–4] Hydroxamic acids have a high binding affinity to a range of transition metal ions. These acids inhibit a wide variety of enzymes including matrix metalloproteinase[1,5–7] or urease.[8] There is no doubt that the inhibitory effect is in correlation with the chelation of the catalytic metal center by the hydroxamate function. Therefore, clarification of their metal-complexing properties in binary and ternary systems involving hydroxamic acids could be of considerable interest.

Diamines play an important role in processes of living organisms. These compounds are present in practically all kinds of cells,[9–11] and their concentration is particularly high in young cells, e.g., cancer cells.[12,13] The diamine−bioligand interactions are observed in the range of pH in which the diamine is protonated while the bioligand is deprotonated. The coordination properties of the diamines present in biological systems are important for the role they play in various cell processes.[14]

Complexation equilibria for binary and ternary systems involving ribonucleotides and salicylhydroxamic acid have been investigated, in our laboratory, potentiometrically.[15] Formation of binary and ternary complexes of di- and trivalent metal ions with some selected aliphatic and aromatic hydroxamic acids and some amino acids or nucleic acid components has been studied by us using the same technique.[16] Equilibrium studies on Th(IV), UO_2(II), Ce(III), and La(III) with the considered hydroxamic acids were also studied by us[17] potentiometrically.

In view of the above studies, it seems to be of considerable interest, therefore, to conduct several investigations covering binary and ternary complexes of Cu(II), Co(II), Ni(II), Cd(II), Mn(II), Mg(II), and Ca(II) metal ions involving hydroxamic acid and diamine ligands.

Experimental Section

Materials and Solutions. Acetohydroxamic acid (Aha) and benzohydroxamic acid (Bha) were Sigma products. Salicylhydroxamic acid (Sham) was purchased in a pure form from Nasr Pharmaceutical Chemicals Co., Egypt. The purity of hydroxamic acids and the concentrations of the stock solutions were determined using Gran's method. Ethylenediamine (en), 1,3-diaminopropane (dapr), and *o*-phenylenediamine (*o*-pda) were purchased from Aldrich Chemical Co. and used without further purification. The metal salts were provided by BDH as nitrates. Stock solutions of the metal salts were prepared in double-distilled water, and the metal concentration was standardized with the disodium salt of EDTA. Carbonate-free sodium hydroxide (titrant, prepared in $0.10\ \text{mol}\cdot\text{dm}^{-3}$ ($NaNO_3$) solution) was standardized potentiometrically with KH phthalate (Merck AG). A nitric acid solution ($\approx 0.04\ \text{mol}\cdot\text{dm}^{-3}$) was prepared and used after standardization. Sodium hydroxide, nitric acid, and sodium nitrate were from Merck p.a.

Apparatus and Procedure. pH measurements were performed using a Metrohm 702 titroprocessor equipped with a 665 dosimat (Switzerland). The precision of the instrument was (± 0.001) pH unit. The pH titrations were carried out in an 80 cm^3 commercial double-walled glass vessel. The ionic strength of

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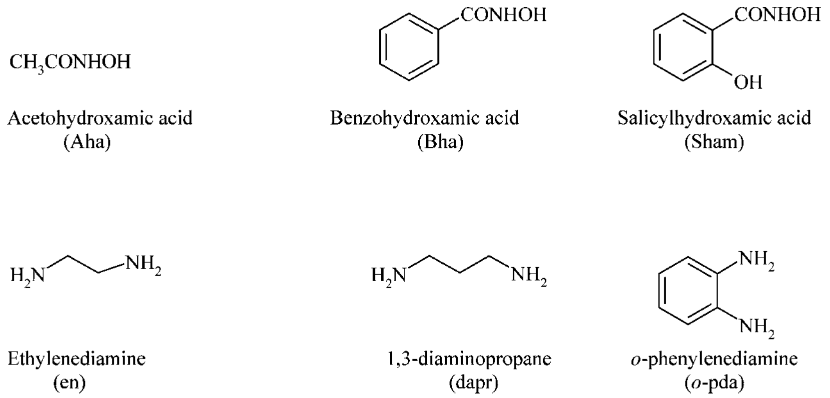
Table 1. Summary of Experimental Parameters for the Potentiometric Measurements

Systems	Protonation processes of ligands: hydroxamic acids (Aha, Bha, and Sham) and diamines (en, dapr, and *o*-pda) Binary: Aha/Bha/Sham, en/dapr/*o*-pda with Cu(II), Co(II), Ni(II), Zn(II), Cd(II), Mn(II), Mg(II), and Ca(II) in water solution Ternary: Aha/Bha/Sham and en/dapr/*o*-pda with the same metal ion mentioned above in water solution
Solution composition	[ligand] range ($1 \cdot 10^{-3}$ to $6 \cdot 10^{-3}$) $\text{mol} \cdot \text{dm}^{-3}$; metal/ligand ratio ranging from 1:1 to 1:6 for binary systems and the ratios 1:1:1 and 1:2:2 for ternary systems; ionic strength 0.10 $\text{mol} \cdot \text{dm}^{-3}$ electrolyte ($NaNO_3$)
Experimental method	pH-metric titration of 50 cm^3 samples in the range of pH 2 to 11.5
Instrument	SM 702 Metrohm automatic titrator with a combined pH glass electrode equipped with a 665 dosimat and a magnetic stirrer (Switzerland)
Calibration	By titrating HNO_3 solution (0.10 $\text{mol} \cdot \text{dm}^{-3}$) against a standard NaOH solution at (the same temperature as the solution under study) and 0.10 $\text{mol} \cdot \text{dm}^{-3}$ ($NaNO_3$)
T (°C)	(25 to 55) °C
n_{tot}[a]	100 to 120
n_{tit}[b]	4 to 6
Method of calculation	Computer program based on unweighted linear least-squares fit

[a] Number of titration points per titration. [b] Number of titrations per titration curve.

Scheme 1



the solutions was maintained at 0.10 $\text{mol} \cdot \text{dm}^{-3}$ by using the desired concentration of ($NaNO_3$) solution as supporting electrolyte, and temperature was adjusted inside the cell at the desired temperature, by circulating thermostatted water using an oil-thermostatted setup. A computer program (GLEE, glass electrode evaluation)[18] has been used for the calibration of a glass electrode, in terms of pH, by titrating HNO_3 at the same temperature and at $I = 0.10\ \text{mol} \cdot \text{dm}^{-3}$ ($NaNO_3$) against NaOH standard solution. The resulting titration data were used to calculate the standard electrode potential $E°$ and K_w for water before each experiment. The investigated solutions were prepared (total volume 50 cm^3) and titrated potentiometrically against standard CO_2-free NaOH (0.10 $\text{mol} \cdot \text{dm}^{-3}$) solution. A stream of nitrogen was passed throughout the titration cell to exclude the adverse effect of atmospheric carbon dioxide.

The ligand concentrations were varied in the range ($1 \cdot 10^{-3}$ to $6 \cdot 10^{-3}$) $\text{mol} \cdot \text{dm}^{-3}$. Three to six different metal-to-ligand ratios, ranging from 1:1 to 1:6, and the ratios 1:1:1 and 1:2:2 (metal:primary ligand:secondary ligand) for the ternary systems were used. The initial estimates of the ionization constants of the ligands and the stability constants of binary and ternary complexes were calculated adopting the Irving and Rossotti technique.[19,20] These equilibrium constants were refined with a computer program based on an unweighted linear least-squares fit.

Each of the investigated solutions was thermostatted at the required temperature with a precision of ± 0.10 °C, and the solutions were left to stand at this temperature for about 15 min before titration. Magnetic stirring was used during all titrations. About 100 to 120 experimental data points were available for evaluation in each system. The titration was repeated at least four times for each titration curve. The complexes are quite stable up to high pH values. In all cases, no calculations have been performed beyond the precipitation point; hence, the hydroxyl species likely to be formed after this point could not be studied. A summary of the experimental details, for the potentiometric measurements, is given in Table 1.

Conductometric Measurements. Conductometric titrations were followed with a HANNA conductivity meter HI-98304.

Table 2. Dissociation Constants (± SD) of Hydroxamic Acids and Stability Constants of their 1:1 and 1:2 Binary Complexes at 25 °C and $I = 0.10\ \text{mol} \cdot \text{dm}^{-3}$ ($NaNO_3$)

	Aha		Bha		Sham	
	$pK_{a1} = 9.35 \pm 0.01$		$pK_{a1} = 8.60 \pm 0.03$		$pK_{a1} = 7.40 \pm 0.02$, $pK_{a2} = 9.78 \pm 0.01$	
cation	$\log K^{M}_{ML}$	$\log K^{ML}_{ML_2}$	$\log K^{M}_{ML}$	$\log K^{ML}_{ML_2}$	$\log K^{M}_{ML}$	$\log K^{ML}_{ML_2}$
Cu(II)	8.20 ± 0.03	5.89 ± 0.03	7.60 ± 0.02	3.34 ± 0.01	13.10 ± 0.01	3.42 ± 0.01
Zn(II)	5.71 ± 0.02	4.72 ± 0.05	5.07 ± 0.01	4.32 ± 0.02	5.94 ± 0.03	3.99 ± 0.03
Ni(II)	5.62 ± 0.05	4.57 ± 0.02	5.10 ± 0.04	3.67 ± 0.01	6.08 ± 0.02	3.92 ± 0.02
Co(II)	4.86 ± 0.03	3.47 ± 0.01	4.81 ± 0.05	3.38 ± 0.03	6.37 ± 0.05	4.55 ± 0.04
Cd(II)	4.50 ± 0.01	–	4.37 ± 0.03	3.25 ± 0.04	5.81 ± 0.03	–
Mn(II)	4.48 ± 0.02	3.90 ± 0.02	4.35 ± 0.01	3.05 ± 0.02	5.50 ± 0.01	–
Mg(II)	–	–	–	–	3.11 ± 0.02	–
Ca(II)	–	–	–	–	3.06 ± 0.02	–

Table 3. Dissociation Constants of Diamines and Stability Constants of their 1:1, 1:2, and 1:3 Binary Complexes at 25 °C and $I = 0.10$ mol·dm^{-3} ($NaNO_3$)

	En			Dapr						*o*-pda
	$pK_{a1} = 7.00 \pm 0.01$, $pK_{a2} = 10.40 \pm 0.02$			$pK_{a1} = 8.55 \pm 0.01$, $pK_{a2} = 10.65 \pm 0.03$						$pK_{a2} = 4.60 \pm 0.02$
cation	$\log K_{MA}^{M}$	$\log K_{MA_2}^{MA}$	$\log K_{MA_3}^{MA_2}$	$\log K_{MA}^{M}$	$\log K_{MA_2}^{MA}$	$\log K_{MA_3}^{MA_2}$	$\log K_{MHA}^{M}$	$\log K_{MHA_2}^{MA}$	$\log K_{MHA_3}^{MA_2}$	$\log K_{MA}^{M}$
Cu(II)	10.48 ± 0.01	9.20 ± 0.03	7.25 ± 0.02	9.74 ± 0.02	7.30 ± 0.03	4.44 ± 0.02	15.61 ± 0.01	9.50 ± 0.02	6.52 ± 0.03	5.14 ± 0.01
Zn(II)	5.68 ± 0.03	5.04 ± 0.01	4.04 ± 0.01	5.85 ± 0.03	3.65 ± 0.02	–	10.54 ± 0.01	7.85 ± 0.03	–	3.90 ± 0.03
Ni(II)	7.42 ± 0.02	6.15 ± 0.05	4.21 ± 0.04	6.34 ± 0.01	4.28 ± 0.02	2.92 ± 0.01	12.89 ± 0.02	8.29 ± 0.02	–	4.35 ± 0.02
Co(II)	5.40 ± 0.01	4.56 ± 0.03	–	4.99 ± 0.03	3.97 ± 0.03	–	10.12 ± 0.02	7.87 ± 0.01	–	2.98 ± 0.05
Cd(II)	5.25 ± 0.04	4.55 ± 0.01	–	4.74 ± 0.01	–	–	9.32 ± 0.01	8.43 ± 0.02	–	–
Mn(II)	5.10 ± 0.02	4.25 ± 0.03	–	4.49 ± 0.04	–	–	8.92 ± 0.02	8.04 ± 0.02	–	–
Mg(II)	–	–	–	–	–	–	5.84 ± 0.01	–	–	–
Ca(II)		–	–	–	–	–	5.23 ± 0.02	4.98 ± 0.01	–	–

The following mixture was titrated conductometrically against 0.10 mol·dm^{-3} NaOH solution: $1 \cdot 10^{-2}$ mol·dm^{-3} metal(II) ion (10 cm^3) + $1 \cdot 10^{-2}$ mol·dm^{-3} hydroxamic acid (10 cm^3) + $1 \cdot 10^{-2}$ mol·dm^{-3} diamine (10 cm^3). Diamines were prepared in the diprotonated form.

Cyclic Voltammetry Measurements. Cyclic voltammetric measurements were collected using potentiostat/galvanostate wenking PGS 95 with a single compartment voltammetric cell equipped with a platinum working electrode[21,22] (area = 0.50 cm^2), a Pt-wire counter electrode, and a SCE as a reference electrode. In a typical experiment, a sample volume of 25 cm^3 containing the free metal ion $1 \cdot 10^{-3}$ mol·dm^{-3} M(II) (a), $1 \cdot 10^{-3}$ mol·dm^{-3} M(II) + $1 \cdot 10^{-3}$ mol·dm^{-3} hydroxamic acid (b), $1 \cdot 10^{-3}$ mol·dm^{-3} M(II) + $1 \cdot 10^{-3}$ mol·dm^{-3} diamine (c), and $1 \cdot 10^{-3}$ mol·dm^{-3} M(II) + $1 \cdot 10^{-3}$ mol·dm^{-3} hydroxamic acid + $1 \cdot 10^{-3}$ mol·dm^{-3} diamine (d) was used. The ionic strength of the studied solutions was adjusted at 0.10 mol·dm^{-3} using a ($NaNO_3$) solution. All solutions were investigated in water at 25 °C. The solutions were purged with nitrogen for 120 s, and then the potential was scanned at the scan rate 25 mV·s^{-1} from (+ 0.20 to −0.60) V.

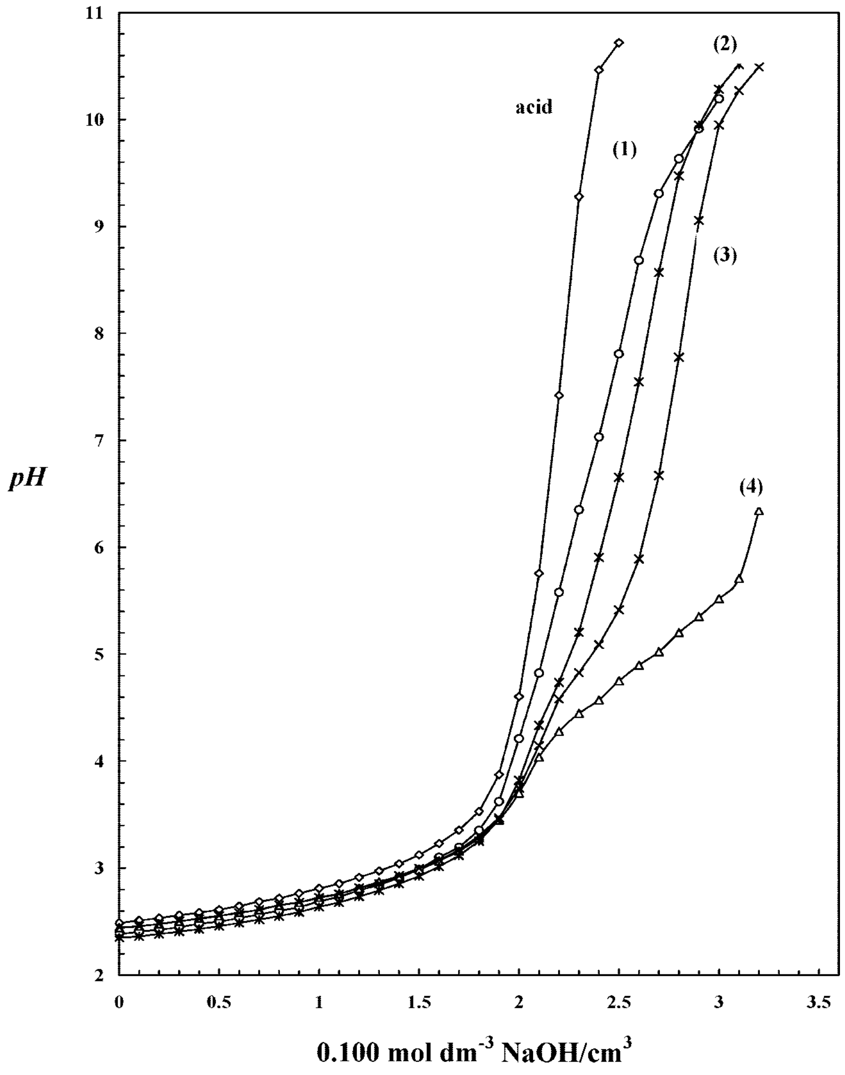


Figure 1. Potentiometric pH−titration curves for the en (1) and for the Cu(II)−en system at 25 °C and $I = 0.10$ mol·dm^{-3} ($NaNO_3$); 2, 1:6; 3, 1:4; and 4, 1:1 metal-to-ligand ratios; $C_{en} = 1 \cdot 10^{-3}$ mol·dm^{-3}.

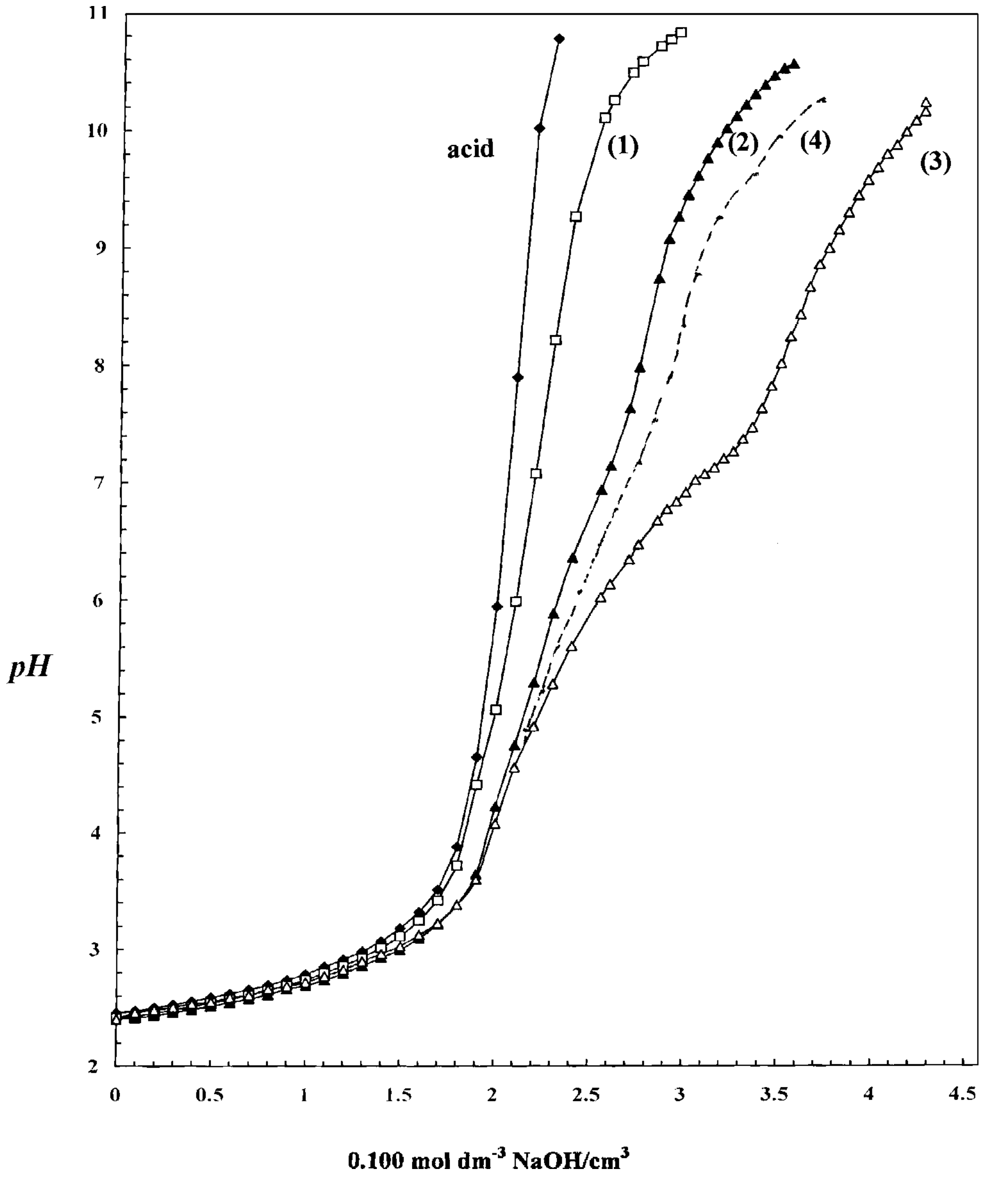


Figure 2. Potentiometric pH−titration curves for the Zn(II)−en−Aha system at 25 °C and $I = 0.01$ mol·dm^{-1} (NaNo$_3$): 1, Aha; 2, Zn(II)−en (1:1); 3, Zn(II)−en−Aha (1:1:1); 4, composite curve.

Table 4. Stability Constants for the Mixed-Ligand Complexes Formed in Metal Ion−en−Hydroxamic Acid Systems at (25 ± 0.1) °C and $I =$ 0.1 mol·dm^{-3} (NaNO$_3$)

	$\log K^{\mathrm{MA}}_{\mathrm{MAL}}$			$\log \beta^{\mathrm{M}}_{\mathrm{MAL}}$			$\Delta \log K$			% R.S.		
cation	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham
Cu(II)	7.25 ± 0.02	7.40 ± 0.04	7.65 ± 0.01	17.73	17.88	18.13	−0.95	−0.20	−5.45	−11.58	−2.63	−41.60
Zn(II)	5.15 ± 0.04	5.26 ± 0.03	5.50 ± 0.02	10.83	10.94	11.18	−0.56	0.19	−0.44	−9.80	3.74	−7.41
Ni(II)	5.20 ± 0.06	5.23 ± 0.02	5.35 ± 0.03	12.62	12.65	12.77	−0.42	0.13	−1.45	−7.47	2.54	−23.80
Co(II)	3.35 ± 0.03	4.05 ± 0.06	4.58 ± 0.04	8.75	9.45	9.98	−1.51	−0.76	−1.79	−31.06	−15.80	−28.10
Cd(II)	3.34 ± 0.05	3.79 ± 0.08	4.35 ± 0.01	8.59	9.04	9.60	−1.16	−0.58	−1.46	−25.80	13.27	−25.10
Mn(II)	3.28 ± 0.01	3.48 ± 0.08	3.64 ± 0.02	8.38	8.58	8.74	−1.20	−0.87	−1.86	−26.78	−20.00	−33.80
Mg(II)	3.23 ± 0.02	3.43 ± 0.02	3.52 ± 0.05	–	–	–	–	–	0.41	–	–	13.18
Ca(II)	3.22 ± 0.06	3.28 ± 0.04	3.44 ± 0.01	–	–	–	–	–	0.38	–	–	12.40

Results and Discussion

Dissociation Constants of the Free Ligands. The formulas of the investigated ligands are shown in Scheme 1. The proton dissociation constants of the hydroxamic acids have been determined at 25 °C and $I = 0.10$ mol·dm^{-3} (NaNO$_3$). The results obtained are in good agreement with data found in the literature[23,24] (Table 2). The difference in the pK_a values for Aha, Bha, and Sham has been discussed in our previous work.[16] Also, the values of pK_{a1} and pK_{a2} for en and dapr are in good agreement with the reported values (Table 3).[25,26] It is observed that the pK_a's increase slightly in the case of dapr compared with en. This is probably due to the increased electron-donating effect of the alkyl chain. The lower basicity of *o*-pda compared with aliphatic diamines may be attributed to the delocalization of the electron pair on the nitrogen atoms toward the π orbitals of the aromatic ring.[27]

Stability Constants of Binary Complexes. Titration curves for en and Cu(II)−en systems are shown as a representative

Table 5. Stability Constants for the Mixed-Ligand Complexes Formed in Metal Ion−dapr−Hydroxamic Acid Systems at (25 ± 0.1) °C and I = 0.10 mol·dm^{-3} (NaNO$_3$)

	log K^{MA}_{MAL}			log K^{MHA}_{MHAL}			log β^{M}_{MAL}			log β^{M}_{MHAL}		
cation	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham
Cu(II)	5.85 ± 0.01	6.02 ± 0.02	7.00 ± 0.02	6.15 ± 0.02	8.14 ± 0.03	10.26 ± 0.01	15.59	15.76	16.74	21.66	23.75	25.87
Zn(II)	3.84 ± 0.03	4.25 ± 0.01	4.97 ± 0.03	5.16 ± 0.03	5.36 ± 0.04	8.67 ± 0.03	9.69	10.10	10.82	15.70	15.90	19.21
Ni(II)	3.86 ± 0.05	4.00 ± 0.02	5.19 ± 0.02	5.15 ± 0.04	6.34 ± 0.01	8.03 ± 0.04	10.20	10.34	11.53	18.40	19.23	20.92
Co(II)	3.34 ± 0.03	3.46 ± 0.04	4.16 ± 0.03	4.58 ± 0.01	4.77 ± 0.03	7.78 ± 0.02	8.33	8.45	9.15	14.70	14.89	17.90
Cd(II)	3.22 ± 0.02	3.25 ± 0.05	4.12 ± 0.01	4.55 ± 0.02	4.57 ± 0.02	7.39 ± 0.01	7.96	7.99	8.86	13.87	13.89	16.71
Mn(II)	3.20 ± 0.02	3.22 ± 0.03	3.54 ± 0.03	4.57 ± 0.03	4.76 ± 0.01	7.79 ± 0.05	7.68	7.69	8.03	13.49	13.68	16.71
Mg(II)	3.19 ± 0.01	3.20 ± 0.01	3.43 ± 0.01	4.17 ± 0.04	4.32 ± 0.01	4.95 ± 0.01	–	–	–	10.01	10.16	10.79
Ca(II)	–	3.19 ± 0.02	3.37 ± 0.01	3.94 ± 0.02	4.19 ± 0.03	4.33 ± 0.02	–	–	–	9.17	9.42	9.56

	Δ log K			% R.S.		
cation	Aha	Bha	Sham	Aha	Bha	Sham
Cu(II)	−2.35	−1.58	−6.10	−28.65	−20.78	−46.56
Zn(II)	−1.87	−0.82	−0.97	−32.74	−16.17	−16.33
Ni(II)	−1.76	−1.01	−0.89	−31.32	−19.80	−14.63
Co(II)	−1.52	−0.65	−2.21	−31.27	−28.07	−34.70
Cd(II)	−1.28	−1.12	−1.65	−28.44	−25.63	−28.39
Mn(II)	−1.28	−1.13	−1.96	−28.57	−25.97	−35.64
Mg(II)	–	–	0.32	–	–	10.28
Ca(II)	–	–	0.31	–	–	10.13

Table 6. Stability Constants for the Mixed-Ligand Complexes Formed in Metal Ion−*o*-pda−Hydroxamic Acid Systems at (25 ± 0.1) °C and I = 0.10 mol·dm^{-3} (NaNO$_3$)

	log K^{MA}_{MAL}			log β^{M}_{MAL}			Δ log K			% R.S.		
cation	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham	Aha	Bha	Sham
Cu(II)	3.68 ± 0.01	4.35 ± 0.03	4.58 ± 0.02	8.82	9.49	9.72	−4.52	−3.25	−8.52	−55.12	−42.76	−65.03
Zn(II)	3.46 ± 0.03	3.48 ± 0.02	3.98 ± 0.01	7.36	7.38	7.88	−2.25	−1.59	−1.96	−39.40	−31.36	−32.99
Ni(II)	3.35 ± 0.05	3.86 ± 0.01	4.24 ± 0.03	7.70	8.21	8.59	−2.27	−1.24	−1.84	−40.39	−24.31	−30.26
Co(II)	3.19 ± 0.02	3.43 ± 0.05	3.65 ± 0.04	6.17	6.41	6.63	−1.67	−1.38	−2.72	−34.36	−28.69	−42.70
Cd(II)	3.10 ± 0.04	3.11 ± 0.05	3.36 ± 0.02	–	–	–	−1.40	−1.26	−2.45	−31.11	−28.83	−42.17
Mn(II)	3.08 ± 0.02	3.09 ± 0.03	3.30 ± 0.03	–	–	–	−1.40	−1.26	−2.20	−31.25	−28.96	−40.00
Mg(II)	3.08 ± 0.03	3.07 ± 0.02	3.26 ± 0.04	–	–	–	–	–	0.15	–	–	4.82
Ca(II)	2.85 ± 0.05	3.01 ± 0.02	3.25 ± 0.02	–	–	–	–	–	0.19	–	–	6.20

example in Figure 1. Analysis of the complexed ligand pH-metric titration curves indicates that the addition of metal ion to the free ligand solution shifts the buffer region of the ligand to lower pH values. This shows that a complex formation reaction proceeds by the releasing of protons from such ligands. Although the 1:1 and 1:2 constants for M(II) with diamines or hydroxamic acid binary complexes were reported earlier by others,[12,23,25] we have again redetermined them at 25 °C and I = 0.10 mol·dm^{-3} (NaNO$_3$), since it is essential that for a proper comparison of the binary and

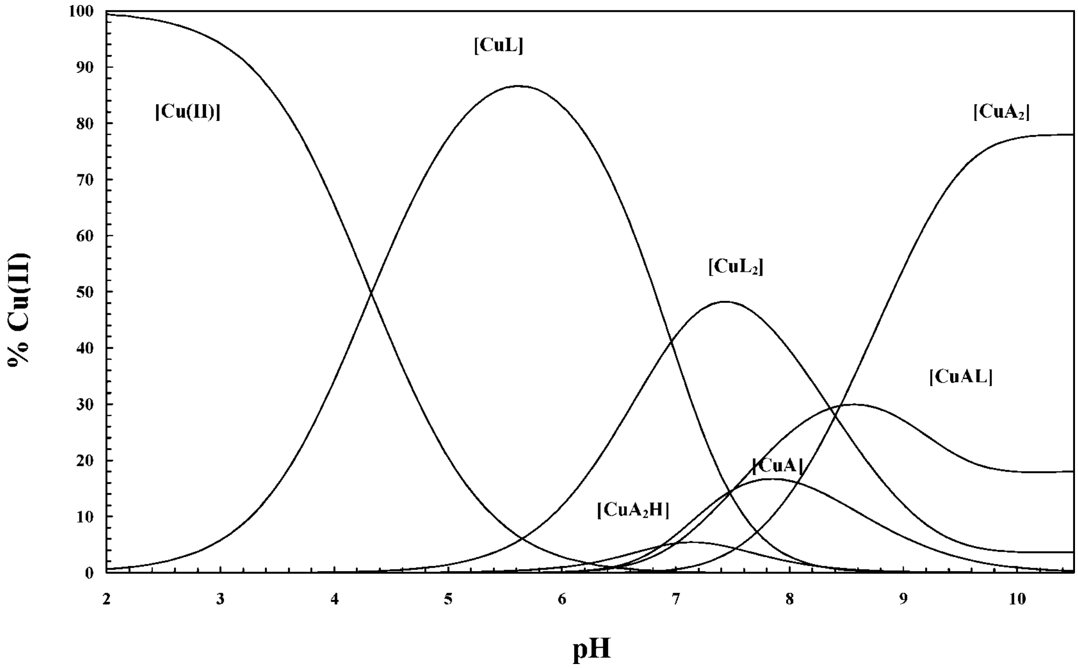


Figure 3. Representative concentration distribution curves as a function of pH calculated for the Cu(II)−dapr−Aha system in the ratio 1:2:2 at 25 °C, I = 0.10 mol·dm^{-3} (NaNO$_3$), and $C_{\text{ligand}} = 1 \cdot 10^{-3}$ mol·dm^{-3}.

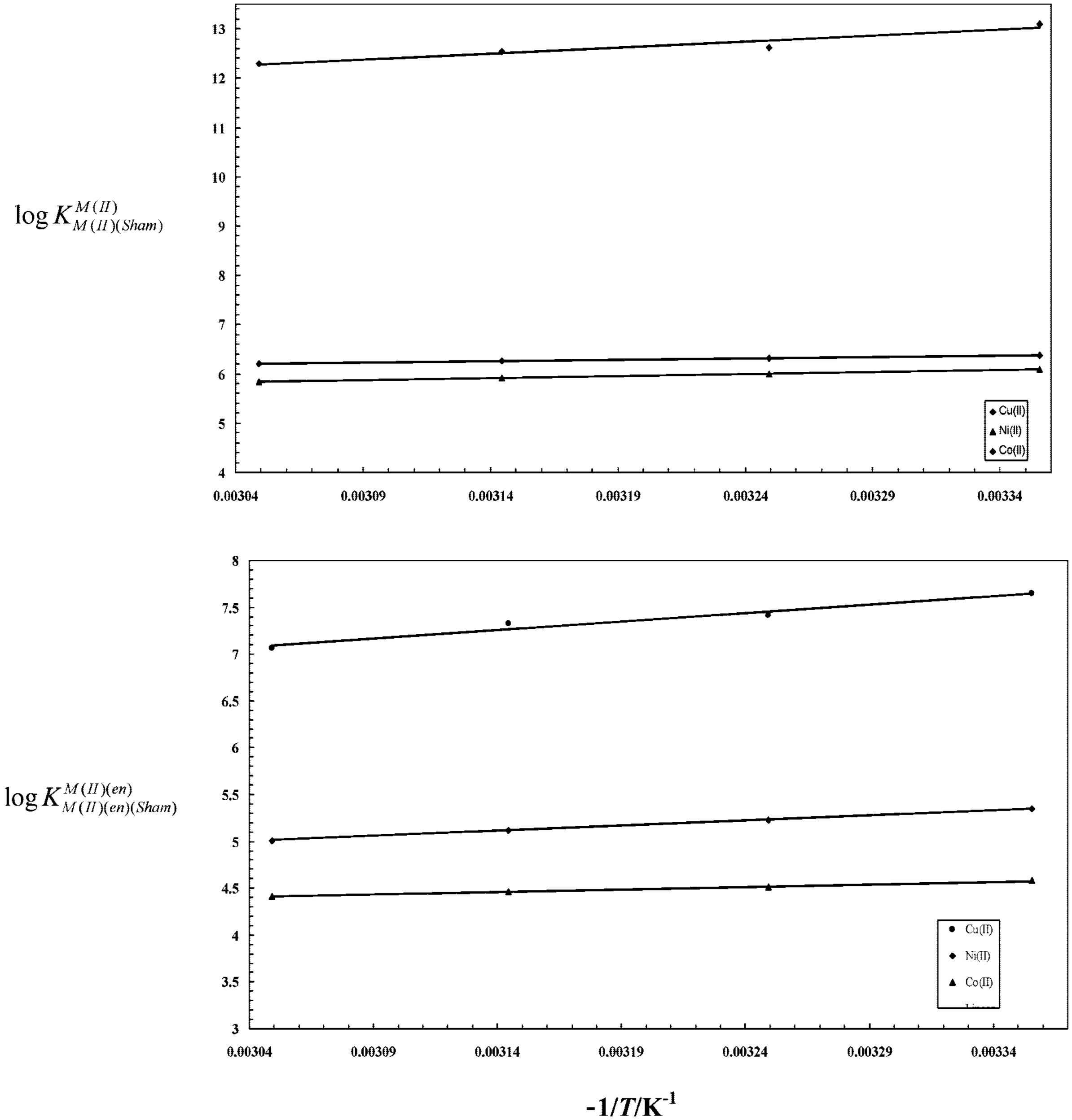


Figure 4. Plot of log $K^{\mathrm{M(II)}}_{\mathrm{M(II)(Sham)}}$ and log $K^{\mathrm{M(II)(en)}}_{\mathrm{M(II)(en)(Sham)}}$ vs $-1/T$ at $I = 0.10$ mol·dm^{-3} (NaNO$_3$).

ternary constants they should be evaluated under identical experimental conditions.

Examination of the stability constants of the binary complexes (Tables 2 and 3) leads to the following remarks:

(a) The observed order of stability of binary systems with respect to the ligand hydroxamic acid is Sham > Aha > Bha. The increased stability of the Sham binary complexes relative to those of the other hydroxamic acids may be attributed to an additional interaction of the phenolic group with the metal ion. The relative stabilities of the binary complexes of Aha and Bha follow their relative basicities, since it is well-known that the increase in basicity of a ligand increases the stability of its metal complexes.

(b) In the systems formed by the diamines en and dapr, it can be observed that the species M(II)−en are slightly more stable than the species M(II)−dapr which can be attributed to the fact that the five-membered ring of M(en) is more stable.[14]

(c) The dapr forms both protonated and deprotonated binary complexes, whereas en forms only deprotonated ones. This behavior is similar to that reported recently by Da Silva et al.[14] The difference (log $K^{\mathrm{M}}_{\mathrm{MHA}}$ − log $K^{\mathrm{M}}_{\mathrm{MA}}$) amounts to 5.87 for Cu(II), 6.55 for Ni(II), 4.49 for Zn(II), 5.13 for Co(II), 4.58 for Cd(II), and 4.43 for Mn(II)−dapr binary systems. The lowering of this difference can be ascribed to coordination of dapr with the metal ion.

(d) The results indicate that *o*-pda does not form very stable complexes with the metallic divalent ions because of its relatively weak basicity compared with the aliphatic diamines and because of the large steric requirements of the ligand.

(e) Also, it can be observed that the stability constants of the different 1:3 metal−ligand (en or dapr) complexes are lower than those of the corresponding 1:2 complex species and stability constants of the latter complexes are lower than those of the corresponding 1:1 systems, as expected from statistical consideration. The reduction in the values of stepwise constants is principally due to the fact that the entropy contribution to the free energy change becomes less favorable from one step to the next.

Table 7. Thermodynamic Quantities Associated with the Dissociation of the Sham or en Ligands and the Interaction of Metal Ions with the Ligands at 1:1 and 1:1:1 Molar Ratio, $I = 0.10\ \mathrm{mol \cdot dm^{-3}}$ ($NaNO_3$)

		pK_a's or log K			
ligand or complex	cation	t/°C = 25	t/°C = 35	t/°C = 45	t/°C = 55
Sham	H	7.40 ± 0.02	6.85 ± 0.01	6.53 ± 0.02	6.32 ± 0.03
	H	9.78 ± 0.01	9.69 ± 0.02	9.63 ± 0.03	9.57 ± 0.01
(1:1) binary complex of Sham	Cu(II)	13.10 ± 0.01	12.62 ± 0.01	12.55 ± 0.02	12.29 ± 0.01
	Ni(II)	6.08 ± 0.02	6.00 ± 0.03	5.91 ± 0.01	5.84 ± 0.02
	Co(II)	6.37 ± 0.05	6.31 ± 0.01	6.27 ± 0.03	6.21 ± 0.01
En	H	7.00 ± 0.01	6.88 ± 0.01	6.80 ± 0.02	6.75 ± 0.03
	H	10.40 ± 0.02	10.20 ± 0.02	10.12 ± 0.03	9.97 ± 0.01
(1:1) binary complex of en	Cu(II)	10.48 ± 0.01	10.33 ± 0.02	10.11 ± 0.01	9.92 ± 0.03
	Ni(II)	7.42 ± 0.02	7.36 ± 0.04	7.30 ± 0.01	7.25 ± 0.02
	Co(II)	5.40 ± 0.01	5.35 ± 0.02	5.31 ± 0.04	5.28 ± 0.01
(1:1:1) ternary complex involving en and Sham	Cu(II)	7.65 ± 0.01	7.42 ± 0.02	7.32 ± 0.01	7.06 ± 0.04
	Ni(II)	5.35 ± 0.03	5.23 ± 0.01	5.12 ± 0.01	5.01 ± 0.02
	Co(II)	4.58 ± 0.04	4.51 ± 0.03	4.46 ± 0.02	4.41 ± 0.02

ligand or complex	cation	$\Delta H°$ / $\mathrm{kJ \cdot mol^{-1}}$	$\Delta G°$ / $\mathrm{kJ \cdot mol^{-1}}$	$\Delta S°$ / $\mathrm{J \cdot mol^{-1} \cdot K^{-1}}$
Sham	H	96.16	42.24	−179.69
	H	17.42	55.82	−128.29
(1:1) binary complex of Sham	Cu(II)	−47.04	−74.77	91.56
	Ni(II)	−15.14	−34.70	65.63
	Co(II)	−9.00	−36.36	91.70
En	H	22.71	59.34	−122.47
	H	8.77	39.94	−102.88
(1:1) binary complex of en	Cu(II)	−35.81	−59.82	80.92
	Ni(II)	−20.42	−42.35	73.80
	Co(II)	−7.28	−30.82	78.89
(1:1:1) ternary complex involving en and Sham	Cu(II)	−36.41	−43.66	24.06
	Ni(II)	−21.18	−30.54	31.40
	Co(II)	−10.31	−26.14	53.03

Stability Constants of Ternary Complexes. A representative set of experimental titration curves for the Zn(II)−en−Aha system are displayed in Figure 2. The existence of a ternary complex is proved by comparison of the mixed ligand titration curve with the composite curve obtained by graphical addition of the secondary ligand (Aha) titration data to that of the 1:1 metal−primary ligand (en) titration curve. Therefore, it is assumed that, in the presence of both ligands, diamine (A) interacts first with the metal ion forming a 1:1 MA binary complex which is then followed by interaction of the hydroxamic acid, i.e., the ternary complex formation could be considered as stepwise equilibria (eqs 1 and 2).

$$\mathrm{M} + \mathrm{A} \rightleftharpoons \mathrm{MA} \qquad K_{\mathrm{MA}}^{\mathrm{M}} = \frac{[\mathrm{MA}]}{[\mathrm{M}][\mathrm{A}]} \tag{1}$$

$$\mathrm{MA} + \mathrm{L} \rightleftharpoons \mathrm{MAL} \qquad K_{\mathrm{MAL}}^{\mathrm{MA}} = \frac{[\mathrm{MAL}]}{[\mathrm{MA}][\mathrm{L}]} \tag{2}$$

The overall stability constant $\beta_{\mathrm{MAL}}^{\mathrm{M}}$ may be represented by eq 3

$$\mathrm{M} + \mathrm{A} + \mathrm{L} \rightleftharpoons \mathrm{MAL} \qquad \beta = \frac{[\mathrm{MAL}]}{[\mathrm{M}][\mathrm{A}][\mathrm{L}]} = K_{\mathrm{MAL}}^{\mathrm{MA}} \cdot K_{\mathrm{MA}}^{\mathrm{M}} \tag{3}$$

The $\beta_{\mathrm{MAL}}^{\mathrm{M}}$ constant expresses the stability of the mixed-ligand species, and it does not represent the binding strength between L and M(II) ions directly in the presence of A. This effect is much better reflected by the equilibrium constant, $K_{\mathrm{MAL}}^{\mathrm{MA}}$, calculated according to eq 4

$$\log K_{\mathrm{MAL}}^{\mathrm{MA}} = \log \beta_{\mathrm{MAL}}^{\mathrm{M}} - \log K_{\mathrm{MA}}^{\mathrm{M}} \tag{4}$$

This latter reaction constant (the reaction is shown as eq 2) indicates how tightly L is bound to the simple M(II)−A complex.

Based on the ternary complex stability constant values (Tables 4 to 6), the following conclusions could be drawn:

(a) The observed order of stability of ternary systems with respect to the ligand hydroxamic acid is Sham > Bha > Aha. The increased stability of Sham ternary complexes relative to those of the other hydroxamic acid ligands can be attributed to an additional interaction of the OH group with the metal ion.

(b) Protonated 1:1:1 ternary complexes involving dapr are found to be more stable than the corresponding deprotonated ones which can be ascribed to extra hydrogen bonding of dapr's proton with the oxygen atom of the hydroxamic acid molecule. This behavior is similar to that published recently for Cu(II)−polyamine−ATP ternary systems.[14]

(c) The complex stability of the ternary systems with respect to the metal ion present follows the order: Zn(II) < Cu(II) > Ni(II) > Co(II) > Mg(II) > Ca(II). The order of stability in the case of transition metal ions is that which is expected on the basis of their position in the Irving−Williams series. In the case of the alkaline earth metal ions, the order may be attributed to the difference in the ionic radii of the cations.

Estimation of the concentration distribution of various complex species in solution provides a useful picture of metal ion binding in biological systems. A species distribution diagram for the Cu(II)−dapr−Aha system is reported in Figure 3. The formation of [CuAL] starts at pH 7.50, reaches a maximum concentration (29.99 % total copper) at pH 8.57, and decreases to 18.33 % when [$\mathrm{CuA_2}$] becomes predominant. The predominance of [$\mathrm{CuA_2}$] (77.66 %, pH 10.10) is partly caused by the high ligand:metal ratio (2:1) which had to be used to avoid precipitation. The concentration distribution of various complex species existing in solution as a function of pH was obtained using the SPECIES program.

In most cases, the relative stability of the mixed-ligand species [MAL] is expressed in terms of the Δ log K parameter (the constant due to the equilibrium [MA] + [ML] = [MAL] + M), which is a way to characterize the tendency toward

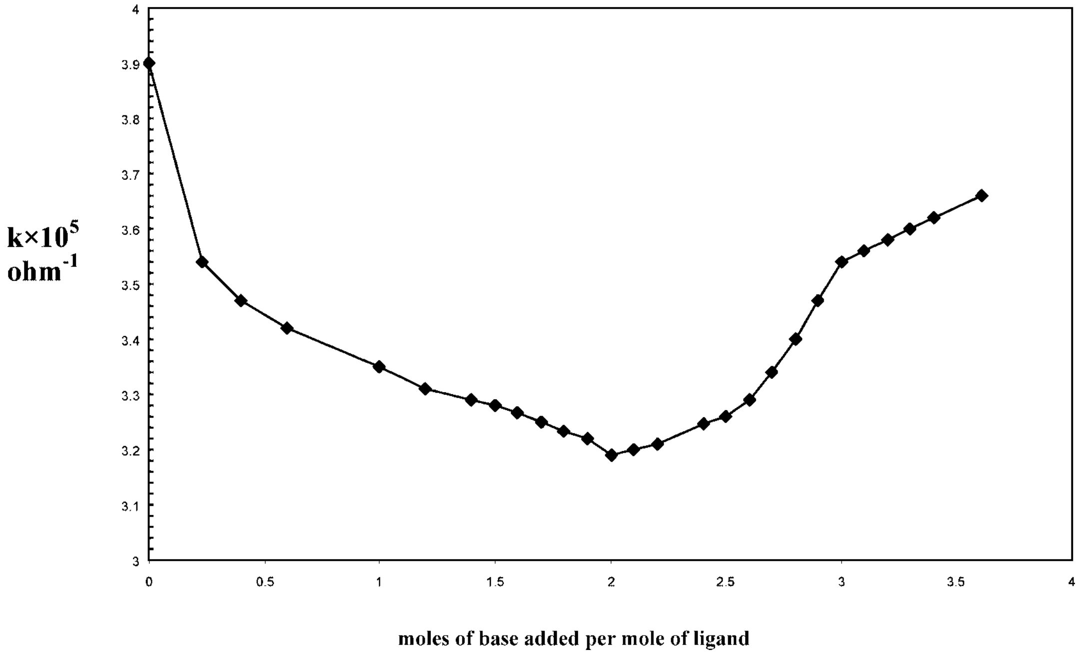


Figure 5. Conductometric titration curve for the Cu(II)−en−Aha system.

formation of mixed-ligand complexes. Generally, negative values of Δ log *K* were obtained (Tables 4 to 6) as expected from statistical considerations. It is worthy to mention that the highly negative Δ log *K* values in the case of ternary systems involving the aromatic diamine, *o*-pda, may be due to M→Nπ bond formation. This behavior is similar to those observed previously.[28,29] Another parameter, percent relative stabilization (% R.S.) to quantify the stability of a ternary complex may be defined as

$$\%\,\mathrm{R.S.} = [(\log K_{\mathrm{MAL}}^{\mathrm{MA}} - \log K_{\mathrm{ML}}^{\mathrm{M}})/\log K_{\mathrm{ML}}^{\mathrm{M}}]\cdot 100 \quad (5)$$

and the values obtained agree with the Δ log *K* values.

The effect of temperature of the medium on the dissociation of Sham and en ligands and the stability of their 1:1 binary and 1:1:1 ternary complexes with Cu(II), Co(II), and Ni(II) metal ions was also investigated at $I = 0.10\ \mathrm{mol\cdot dm^{-3}}$ ($NaNO_3$). The values of the protonation and binary (1:1) equilibrium constants for Sham and en were found to be linearly dependent on the inverse of temperature, indicating negligible change in heat capacity for each of these protonation and complexation reactions.[30] Figure 4 shows a plot of log $K_{\mathrm{M(II)(Sham)}}^{\mathrm{M(II)}}$ and log $K_{\mathrm{M(II)(en)(Sham)}}^{\mathrm{M(II)(en)}}$ vs $-1/T$ at $I = 0.10\ \mathrm{mol\cdot dm^{-3}}$ ($NaNO_3$). The equilibrium constants have been evaluated at four different temperatures [(25, 35, 45, and 55) °C] and along with the thermodynamic quantities and the values obtained are cited in Table 7. The values of $\Delta H°$ for the ionization of the ligands are found to be positive indicating the endothermic nature of the deprotonation process. The positive values of the standard free energy change ($\Delta G°$) for the dissociation processes of the ligands denote these processes are not spontaneous. Also, the

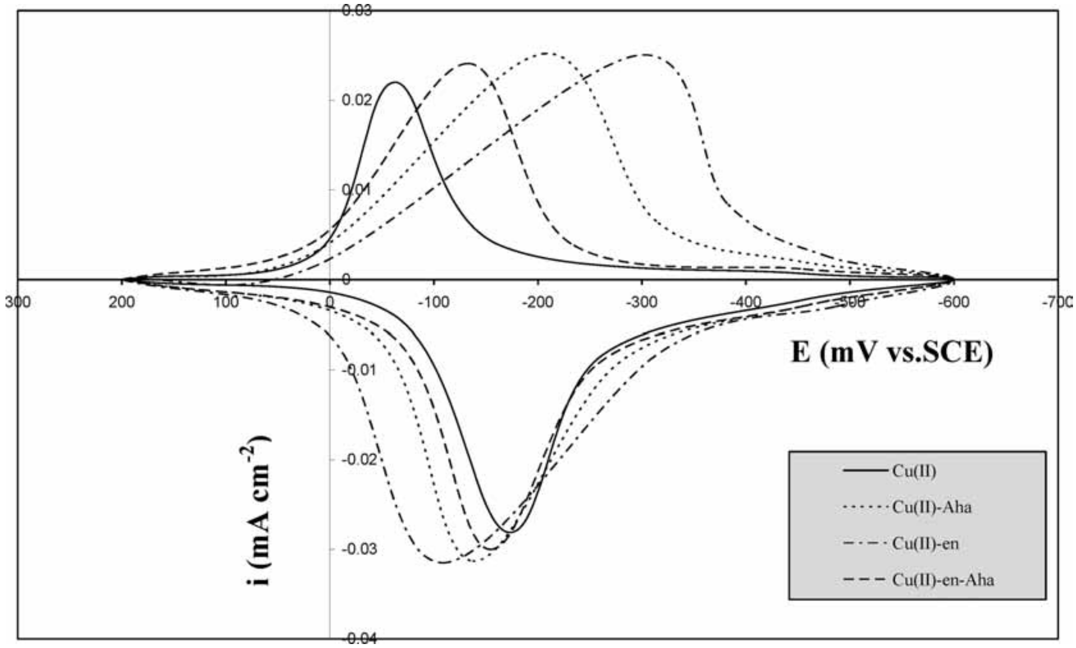


Figure 6. Cyclic voltammogram for the Cu(II)−en−Aha system at 25 °C, $I = 0.10\ \mathrm{mol\cdot dm^{-3}}$ ($NaNO_3$), and pH 5.80 with a scan rate of 25 mV·s⁻¹.

negative values of $\Delta S°$ are pointing to increased ordering due to association. The values of the formation constants decrease with temperature because the formation reactions are exothermic (Le Chatelier's principle). The values of enthalpy changes ($\Delta H°$) for the binary and ternary systems investigated are negative. It is of interest to note that the $\Delta H°$ values for the ternary systems studied are more negative as compared to those of the corresponding binary ones and ensure that despite the steric hindrance due to the primary ligand, en, the bond is stronger in the ternary complex formation.[31] However, the data show that the $\Delta H°$ values are highly negative in the case of the Cu(II)−Sham 1:1 binary system compared to the other Cu(II) binary and ternary systems investigated (Table 7). This behavior can be attributed to the high stability of 1:1 Cu(II)−Sham binary complex species ($\log K^{\mathrm{Cu(II)}}_{\mathrm{Cu(II)(Sham)}} = 13.10 \pm 0.01$) as shown in Table 2. The complex formation process is spontaneous in nature, as characterized by the negative $\Delta G°$ values. The values of $\Delta S°$ substantiate the suggestion that the different binary and ternary complexes are formed due to coordination of the ligand anion to the metal cation. Furthermore, the positive values of $\Delta S°$ suggest also a desolvation of the ligands, resulting in weak solvent−ligand interactions, to the advantage of the metal ion−ligand interaction.[32]

To ascertain the mode of chelation of the investigated ternary systems, a conductometric titration curve of the ternary complex containing Cu(II) with en and Aha, taken as representative, is shown in Figure 5. The titration curve shows an inflection at $a = 2$ (a = moles of base added per mole of ligand), probably corresponding to the neutralization of two protons resulting from the formation of the Cu(II)−en binary complex. Between $2 < a < 3$, the slight increase of conductance is due to the formation of the ternary complex and is associated with the release of one proton from the secondary ligand (Aha). Beyond $a = 3$, the conductance increases more uniformly due to the presence of excess alkali.

Confirmation of the formation of the ternary complexes in solution has been studied using the cyclic voltammetry technique. The binary and ternary systems involving Cu(II), en, and Aha have been selected for conducting this study. Figure 6 represents the cyclic voltammograms for the reduction of $1 \cdot 10^{-3}$ $\mathrm{mol \cdot dm^{-3}}$ Cu(II) in the absence and presence of the investigated ligands ($1 \cdot 10^{-3}$ $\mathrm{mol \cdot dm^{-3}}$) at $I = 0.10$ $\mathrm{mol \cdot dm^{-3}}$ $\mathrm{NaNO_3}$, 25 °C, and pH = 5.80 at a scan rate = 25 $\mathrm{mV \cdot s^{-1}}$. It is quite clear that the cyclic voltammograms of the binary and ternary complexes are quite different and the cathodic peaks are slightly shifted to more negative potentials as well, indicating the formation of binary and ternary complexes in solution. The main features of the voltammograms are a two-electron oxidation step and two-electron reduction steps at negative potentials for the complex species investigated. Comparing the values of the reduction potentials of the three systems investigated, it is clear that the stability of complexes follows the order:

$$\mathrm{Cu(II)-en}(E_{\mathrm{red}} = -295) > \mathrm{Cu(II)-Aha}(E_{\mathrm{red}} = -206) > \mathrm{Cu(II)-en-Aha}(E_{\mathrm{red}} = -133)$$

This order is in accordance with the results obtained by potentiometric−pH titrations under the same conditions as shown in Tables 2 to 4. The voltammetric behavior is shown to be quasireversible for all investigated systems, and the irreversibility phenomena increases according to the sequence

$$\mathrm{Cu(II)-en} \rightarrow \mathrm{Cu(II)-Aha} \rightarrow \mathrm{Cu(II)-en-Aha}$$

Conclusion

The present work describes metal(II) complexes involving monohydroxamic acids and diamines in an aqueous medium. The complex formation equilibria were investigated to ascertain the composition and stability constants of the complexes. The concentration distribution diagrams of the complexes were evaluated. The effect of the temperature of the medium on the dissociation process of the ligands and complex formations for the M(II)−en−Sham (M(II) = Cu(II), Co(II), and Ni(II)) ternary systems has been studied along with the corresponding thermodynamic parameters. The mode of chelation of ternary complexes is ascertained using conductivity measurements. Confirmation of the formation of ternary complexes in solution has been performed using cyclic voltammetry measurements. Investigated ternary complexes involving hydroxamic acids and diamines may have interesting biological activity. This would require specially designed research conducted by specialists in biology.

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