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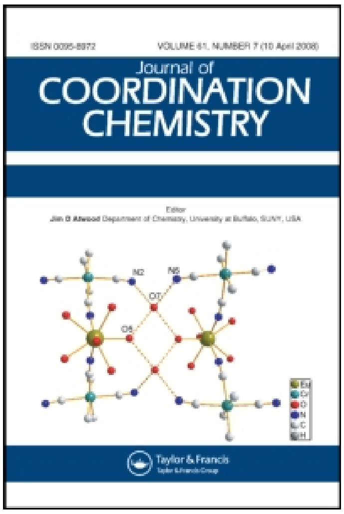

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NEW MULTEDENTATE LIGANDS XII: Chelating Tendencies of N,N'-Ethylenediaminediacetic-N,N'-Diacethydroxamic Acid

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NEW MULTIDENTATE LIGANDS XII

Chelating Tendencies of N,N′-Ethylenediaminediacetic-N,N′-Diacethydroxamic Acid[1]

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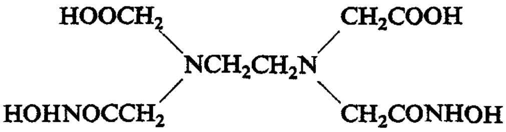
(*Received January* 21, 1971)

Quantitative equilibrium studies of a new multidentate ligand, N,N′-ethylenediaminediacetic-N,N′-diacethydroxamic acid (EDTA—DX, H_4L) are described. Its acid-base and metal-ligand reaction stoichiometries have been determined and the corresponding proton and metal ion association constants have been calculated from potentiometric data. Stabilities of normal chelates ML^{n-4}, and their protonation constants are reported for Mg(II), Co(II), Ni(II), Cu(II), Zn(II), and Fe(III), and an additional dissociation constant is determined for the iron chelate FeL^-. The probable chelate structures in solution have been deduced by analysis of infrared and proton magnetic resonance spectra in D_2O solution, and of electronic spectra in aqueous solution.

It has been shown that suitably designed multidentate ligands containing individual specific donor groups can be useful in demonstrating previously unknown coordinating properties of these functional groups.[3] For example, the ligands DGENTA (diglycylethylenediaminetetraacetic acid) and EDDAG—DA (N,N′-ethylenediaminediacetylglycine-N,N′-diacetic acid) provided the first examples of metal ion promoted dissociation of amide protons by Co(II) and Fe(III)[3]. In that publication,[3] other examples of strongly coordinating groups were suggested for incorporation into a ligand containing auxiliary amino and carboxylate donor groups. These were peptide, hydrazide, imide, hydroxyalkyl and hydroxamide groups.

The hydroxamide group was chosen for this study because of its widespread importance[4] in certain biological iron transport substances, in analytical chemistry as a selective donor group for Fe(III) and because of its interesting structure. In all previous studies, the hydroxamide group was "forced" to act as a bidentate donor since auxiliary donor groups were lacking. Thus Schwarzenbach *et al.*[5,6] have concluded from a potentiometric study of the simple acethydroxamic acid and from an optical comparison with sideramines that the hydroxamic acid group is a typical bidentate donor behaving very much like acetylacetone towards various metal ions. More recently, Lindner and Gottlicher[7] determined the crystal structure and Epstein and Straub[8] measured the Mossbauer spectra of ferric benzhydroxamides. Here again binding to the metal was found to occur through both oxygen atoms of the donor. It does seem fairly well established that in the absence of metal ions the hydroxamide group exists in the keto form.[9,10]

The purpose of this work is to establish the metal-binding characteristics of the hydroxamido group when it is present in a multidentate ligand. Towards this end, N,N′-ethylenediaminediacetic-N,N′-diacethydroxamic acid (EDTA—DX **1**) was synthesized and its interaction with various metal ions were studied, and the results are now reported. This compound may be considered the dihydroxamic acid derivative of EDTA, and on that basis is of theoretical interest to coordination chemists for comparison of its coordination tendencies with the very extensive studies completed on EDTA.



1, EDTA-DX

EXPERIMENTAL

Reagents

EDTA-DX† Hydroxylamine solution was prepared by neutralizing 5.6 g (0.08 mol) of finely divided hydroxylamine hydrochloride suspended in 30 ml methanol with 4.5 g potassium hydroxide in 30 ml

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† *Note added in proof:* Following the completion of this work, a method of preparation of EDTA-DX from EDTA dianhydride has been described by J. L. Herz and S. C. Chaberek, *Dutch Patent* No. 7008537 (Dec. 15, 1970).

methanol and filtering off the inorganic salt formed. To the filtrate were added 6.7 g (0.02 mol) of EDTA-diethyl ester and 4.5 g of potassium hydroxide in 30 ml methanol and the solution was allowed to react at room temperature for three days. The product was precipitated with 20% hydrochloric acid and the gummy precipitate was crystallized from a minimum amount of water by adjusting the pH with solid potassium carbonate and diluting with double the amount of methanol. The product was recrystallized from water/methanol. Yield 4.0 g.

*Anal.*Calcd. for $C_{10}H_{16}N_4O_8K_2 \cdot H_2O$: C,28.83; H, 4.36; N, 13.45; K, 18.77
Found: C, 28.56; H, 4.43; N, 13.27; K, 18.52.

Reagent grade metal nitrates were used and were standardized by titration with EDTA.[11] Ethylenediaminediacetic acid was obtained from Pfaltz and Bauer and was recrystallized several times from water/ethanol.

Measurements

Potentiometric measurements—Titration Appropriate aliquots of standard solutions of metal ion, nitric acid, solid ligand, and potassium nitrate were diluted to 50.00 ml with distilled water and titrated with 0.1 M standard CO_2-free NaOH while $-\log [H^+]$ was measured by means of a Beckman Research pH meter fitted with E-2 glass and calomel extension electrodes calibrated in the usual way.[3] The experimental solutions were all originally 0.100 M in KNO_3 and 0.004–0.002 M in metal and/or ligand. The titrations were performed under anaerobic conditions in a thermostatically jacketed glass cell at 25.00 ± 0.05°.

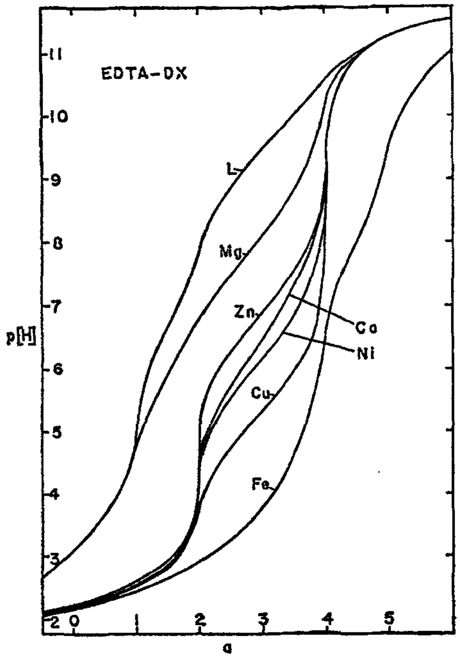


FIGURE 1 Potentiometric equilibrium curves for the addition of base to N,N′-ethylenediaminediacetic-N,N′-diacethydroxamic acid (EDTA—DX, H_4L) in the absence of and in the presence of equimolar amounts of Mg(II), Co(II), Ni(II), Cu(II), Zn(II), and Fe(III) ions; pH = $-\log [H^+]$; a = moles of base added per mole of ligand present.

Spectra The infrared spectra were measured on a Beckman IR-12 with 0.050 mm matched AgCl cells containing 0.10 M solutions in the sample cell and D_2O in the reference cell.

The electronic spectra were measured with a Cary 14 spectrophotometer using 1.00 cm matched quartz cells at 25° and 0.10–0.0010 M concentration.

The nuclear magnetic resonance spectra were obtained with a Varian A-60 nmr spectrometer using 0.15 M solutions (D_2O) at about 37°.

RESULTS

Stability constants

EDTA-DX The potentiometric titration curve of the free ligand is shown in Figure 1. One proton per mole of ligand dissociates between $a = 0$ and $a = 1$ (where a = moles of base added per mole of ligand present), a second dissociates between $a = 1$ and $a = 2$, and at higher pH, two more dissociate between $a = 2$ and $a = 4$. The first four protonation constants obtained for the fully-dissociated ligand, L^{4-}, by a computer-simulated titration curve with an overall fit of $\sigma = \pm 0.017$ pH units are $\log K_1^H = 9.93$, $\log K_2^H = 9.00$, $\log K_3^H = 6.67$, and $\log K_4^H = 3.48$. A fifth protonation constant was found to have a value of about 1.55 log units. The protonation constants determined in this research are defined by the general formula,

$$K_n^H = [H_nL^{(n-4)+}]/([H_{n-1}L^{(n-5)+}][H^+]).$$

EDTA—DX Metal ion interaction The EDTA—DX curves obtained with 1:1 molar ratios of ligand to Mg(II), Fe(III), Co(II), Ni(II), Cu(II), and Zn(II) ions are shown in Figure 1. The complex equilibria may be represented by

$$M^{n+} + H_2L^{2-} \rightleftharpoons MH_2L^{(n-2)+} \quad K_{MH_2L} \qquad (1)$$

$$ML^{(n-4)+} + H^+ \rightleftharpoons MHL^{(n+3)-} \quad K^H_{MHL} \qquad (2)$$

$$MHL^{(n-3)+} + H^+ \rightleftharpoons MH_2L^{(n-2)+} \quad K^H_{MH_2L} \qquad (3)$$

The equilibrium curves with Zn(II), Co(II), Ni(II), and Cu(II) have their first buffer region up to $a = 2$ and their second buffer region involving two protons between $a = 2$ and $a = 4$. With Mg(II), complex formation equilibria set in only at $a = 1$ and the second proton dissociation overlaps the metal complex formation curve. With Fe(III) the second two-proton dissociation reaction overlaps formation of the complex at much lower pH, and an additional single proton dissociation is evident at about pH = 8 between $a = 4$ and $a = 5$. At still higher pH, the titration curve provides indication of further proton displacement from the metal complex.

For the divalent ions whose formation regions are well separated from the buffer region between $a = 2$ and $a = 4$, the formation constant corresponding to equation (1) was calculated from the following equations which were derived from the appropriate mass and charge balance relationships:

$$K_{MLH_2} = \frac{(T_M - [M])\cdot A_1}{[M]\cdot(T_L - T_M + [M])} \tag{4}$$

$$M^{2+}] = \frac{[A_1\cdot B - 2\cdot A_1\cdot T_M - A_2\cdot T_L + A_2\cdot T_M}{A_2 - 2\cdot A_1}$$

T_M = total analytical metal ion concentration

T_L = total analytical ligand concentration

$A_1 = 1 + K_3{}^H\cdot[H^+] + K_3{}^H\cdot K_4{}^H\cdot[H^+]^2 + K_3{}^H\cdot K_4{}^H\cdot K_5{}^H\cdot[H^+]^3$

$A_2 = 2 + K_3{}^H\cdot[H^+] - K_3{}^H\cdot K_4{}^H\cdot K_5{}^H\cdot[H^+]^3$

$B = [H^+] + [Na^+] - K_w/[H^+] - [\text{acid}]$

acid = concentration of excess mineral acid (i.e. below $a = 0$).

The Mg(II) formation constant K_{MH_2L} was calculated by first estimating K^H_{MHL} and $K^H_{MH_2L}$ (equations 2 and 3) from the data between $a = 3$ and $a = 4$, and then substituting these values into the following expression for the equilibrium constant:

$$K_{MH_2L} = \frac{A_2\cdot(T_L - A_1\cdot B/A_2)}{(X_1 - A_1\cdot X_2/A_2)\cdot[M^{2+}]\cdot\left(B - \dfrac{X_2\cdot(T_L - A_1\cdot B/A_2)}{(X_1 - A_1\cdot X_2/A_2)}\right)} \tag{5}$$

$$[M^{2+}] = T_M - \frac{X_1\cdot(T_L - A_1\cdot B/A_2)}{(X_1 - A_1\cdot X_2/A_2)}$$

$A_1 = 1 + K_3{}^H\cdot[H^+] + K_3{}^H\cdot K_4{}^H\cdot[H^+]^2$

$A_2 = 2 + K_3{}^H\cdot[H^+]$

$X_1 = 1 + 1/(K^H_{MH_2L}\cdot[H^+]) + 1/(K^H_{MHL}\cdot[H^+]^2)$

$X_2 = 2 + 3/(K^H_{MH_2L}\cdot[H^+]) + 4/(K^H_{MHL}\cdot[H^+]^2)$

In all cases the two overlapping ML-proton association equilibrium constants K^H_{MHL} and $K^H_{MH_2L}$, defined by equations 2 and 3, were calculated in two ways, both of which agreed to better than ± 0.01 log units. For the first, a computer linear least squares fit to the form $y = m\cdot x + b$ was made, where

$$y = \frac{(4\cdot T_M - B)}{[H^+]\cdot(3\cdot T_M - B)} \qquad x = \frac{(2\cdot T_M - B)\cdot[H^+]}{(3\cdot T_M - B)}$$

and therefore $K^H_{MHL} = -b$ and $K^H_{MH_2L} = m/K^H_{MHL}\cdot$ In the second, an iterative computer program was used to simulate the portion of the pH curve from $a = 2$ to $a = 4$. The solution was obtained in terms of $[H^+]$, rather than as a function of a values, as is customary in conventional programs.

Table I contains a summary of the equilibrium

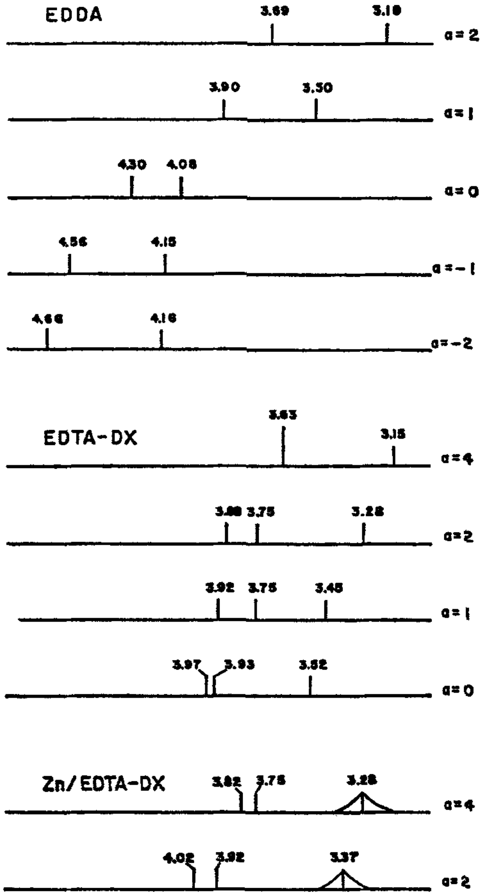


FIGURE 2 Nmr spectra of N,N′-ethylenediaminediacetic acid (EDDA) and of N,N′-ethylenediaminediacetic-N,N′-diacethydroxamic acid (EDTA—DX, H_4L) in the absence of and in the presence of an equimolar ratio of Zn(II) ion; solvent = D_2O; a = moles of base added per mole of ligand present; chemical shifts are given in terms of δ values.

constants describing the complex metal-ligand-proton interactions in aqueous solution.

Spectra

The ligand IR spectra presented in Table II were measured at *a* = 0, 1, 2, and 4. The carbonyl band assignments were made by comparison with known systems;[3,12,13] however, the hydroxamide assignments in D_2O solution are new.

The metal-complex IR spectra are presented in Table III. The interpretation of these spectra is not as straightforward as those of the ligand alone because with metal present, at *a* = 4, the carbonyl spectrum collapses into one band or at best a shoulder is visible. However, this IR information is useful not only from the viewpoint of the observed peaks, but also because conclusions may be drawn from the absence of certain absorptions.

Since it is not generally possible to obtain nmr spectra of paramagnetic species, nmr spectra of the transition metal ion complexes studied are not reported. Excellent nmr spectra of the EDTA—DX and EDTA—DX—Zn(II) systems were obtained and are reported as a function of *a* values in Figure 2. For comparison EDDA nmr spectra of the 1:1 EDDA—Zn(II) complex were measured and are also included in Figure 2. As the hydroxamide groups dissociate with Zn^{2+} present, the peaks at *a* = 2 shift toward higher field, yet the resonance

TABLE I

Equilibrium constants for the interaction of EDTA-DX with metal ions[a, b]

		Log K					
Symbol	Equilibrium quotient	Mg^{2+}	Fe^{3+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
K_{MH_2L}	$\frac{[MH_2L^{(n-2)+}]}{[M^{n+}][H_2L^{2-}]}$	3.29	10.80	9.69	11.0	10.7	9.60
K^H_{MHL}	$\frac{[MHL^{(n-3)+}]}{[ML^{(n-4)+}][H^+]}$	8.73	4.60	7.31	6.81	5.79	7.47
$K^H_{MH_2L}$	$\frac{[MH_2L^{(n-2)+}]}{[MHL^{(n-3)+}][H^+]}$	7.54	2.98	5.77	5.62	4.88	6.35
K^H_X	$\frac{[ML^{(n-4)+}]}{[MLOH^{(n-5)+}][H^+]}$		8.07				

[a] Medium consists of 0.10 M KNO_3; t = 25°.

[b] Log values of successive proton association constants of ligand are 9.93, 9.00, 6.67 and 3.48.

TABLE II

Carbonyl infrared stretching frequencies of EDTA-DX in D_2O, cm^{-1}

a[a]	$\overset{\oplus}{-}\mathrm{COOH}$	$-\mathrm{COOH}$	$\oplus\!-\!\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHOH}$	$-\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHOH}$	$\overset{\oplus}{-}\mathrm{COO}^-$	$-\mathrm{COO}^-$	$-\mathrm{CONHO}^-$
0	1720	1682	1650sh	1631	1590		
1		1680	1650	1631	1588		
2				1647 1632		1583	
4						1582	1624

[a] a = moles of base added per mole of ligand present.

TABLE III

Carbonyl stretching frequencies of metal EDTA–DX complexes in D_2O, cm^{-1}

Metal Ion	a[a]	$\mathrm{M^{n+}\ldots\overset{\vee}{N}CH_2\overset{\overset{O}{\|}}{C}NHOH}$	$\mathrm{-COO^{-}\ldots M^{n+}}$	$\mathrm{(-CONHO^{-})\ldots M^{n+}}$
Cu^{2+}	2	1663	1607	
	4			1601
	5[b]		~1575	1600
Ni^{2+}	2	1653	1604	
	4			1598
Co^{2+}	2	1653	1604	
	4	1630[c]		1614
Zn^{2+}	2	1656	1603	
	4			1596
Mg^{2+}	2	1659	1606	
	4	1647[c]	1603	
		~1620sh		
Fe^{3+}	2		1643	~1625sh
	4		1570	1621, 1655sh
	5		1594	~1620sh

[a] a = moles of base added per mole of ligand present.
[b] two moles of metal per mole of ligand employed.
[c] see discussion.

at 3.3 δ maintains its very complicated multiplet indicating that a symmetrical chelate has formed.

Perhaps the most useful proof of chelate structure involving metal assisted hydroxamide proton dissociation is contained in the electronic spectra presented in Table IV. An example of the pH dependence of UV and visible spectra (copper 1:1 system) is presented in Figure 3. For comparison electronic spectral data for analogous EDDA chelates have also been measured and are included in Table IV.

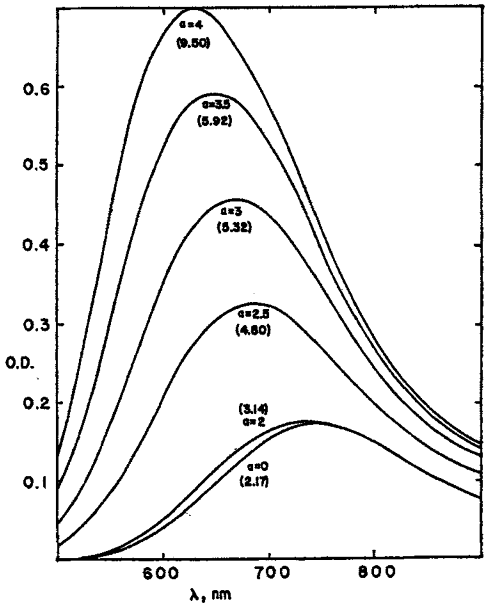


FIGURE 3 Electronic spectra of the 1:1 Cu(II)-N, N′-ethylenediaminediacetic-N,N′-diacethydroxamic acid chelate at 4.00×10^{-3} M concentration in H_2O; O.D. = optical density medium contains 0.100 M KNO_3; temperature = 25 ± 1°

DISCUSSION AND CONCLUSIONS

EDTA—DX

EDTA—DX, **1**, is a tetrabasic ligand whose structure can be considered as consisting of an EDDA (N,N′-ethylenediaminediacetic acid) backbone with two acethydroxamic acid groups substituted on the nitrogen atoms. Acethydroxamic acid[14] itself possesses a pK_a of 9.35. It is fairly well established that the proton dissociates from the oxygen atom,[15] for even N-benzoyl-N-phenylhydroxylamine[16] shows acidic properties with a pk_a of 8.2. Therefore, the values for log K_1^H and log K_2^H of 9.93 and 9.00 are normal for EDTA—DX and may be considered as arising from the successive protonations of the oxygens of the hydroxamide groups in the tetranegative ligand, L^{4-}. At $a = 4$, the IR spectrum (Table II) of the ligand L^{4-} in the carbonyl region is appropriately found to consist of two bands with

TABLE IV

Electronic spectra of EDTA—DX and EDDA chelates[a]

Metal[d] Ion	a[e]	EDTA—DX[b] λ_{max}	EDTA—DX[b] ϵ_{max}	EDDAB[c] λ_{max}	EDDAB[c] ϵ_{max}
Cu^{2+}	2	735	46	672	98
	4	615	200		
Ni^{2+}	2	302	14	303	15
		377	16	370	7
		593	8	610	4
		770	~1	760	1
		1025	21	1015	12
	4	303 band covered			
		377	17		
		570	14		
		795	shoulder		
		925	24		
Co^{2+}	2	298 band covered		298	23
		490	10	500	9
		510	10	525	8
		~1100	3	~1110	5
	4	450sh	~7		
		~500sh	weak		
		~1025	4		
[f]Fe^{3+}	2	425sh	~1000		
	4	375sh	~2000		

[a] Taken at 25° at concentrations of ~0.1 – 0.001 M

[b] EDTA—DX = N,N′-ethylenediaminediacetic acid-N,N-diacethhydroxamic acid.

[c] EDDA = N,N′-ethylenediaminediacetic acid.

[d] 1:1 molar ratios of metal ion to ligand employed in all cases.

[e] a = moles of base added per mole of acid form of the ligand initially present.

[f] extremely intense charge transfer band in *uv* ($\epsilon \gg$ 10,000) trailing into visible region.

TABLE V

Chelate stability constants, and protonation constants

Metal Ion	Log K EDTA—DX[a]	Log K EDDA[b,c]	Log K EDDAG—DA[d]
Mg^{2+}	3.29	3.9	
Co^{2+}	9.69	11.2	10.47
Ni^{2+}	11.0	13.5	10.68
Cu^{2+}	10.7	16.2	11.23
Zn^{2+}	9.6	11.1	
H^+	6.67	9.57	7.37
H^+	3.48	6.48	4.38

[a] This research; EDTA—DX – dihydroxamic acid of EDTA.

[b] EDDA formation constants from S. Chaberek and A. E. Martell, *J. Am. Chem. Soc.* **74**, 6228 (1952); EDDA = N,N′-ethylenediaminediacetic acid.

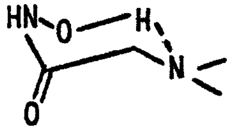
[c] EDDA protonation constants from L. C. Thompson, *J. Inorg. Nucl. Chem.* **24**, 1083 (1962).

[d] EDDAG—DA constants from reference 3; EDDAG—DA = N,N′-ethylenediaminediacetylglycine-N,N′-diacetic acid.

the 1624 cm^{-1} absorption corresponding to the $-CONHO^-$ carbonyl stretch.

It is even more striking to compare K_3^H and K_4^H of EDTA—DX with the corresponding K_1^H and K_2^H of EDDA and K_3^H and K_4^H of EDDAG—DA, all of which are listed in Table V. The fact that the K^H values of EDTA—DX are lower by a factor of some 10^3 than the corresponding constants of EDDA reveals that the hydroxamide substituent is about 10^1 times better than the amide group at attenuating the basicity of the inner nitrogen atoms of the EDDA substructure. Since the lowest K^H of EDTA—DX is 3.48, there is a strong possibility that this macroscopic constant is a weighted average of at least several microscopic constants involving protonation of N (of EDDA substructure) and/or the O of the carboxyl group. This latter possibility is strongly supported by the multibanded C=O IR spectrum (Table II) at $a = 0$. The nmr spectra also offer supporting evidence in this connection. From Figure 2 it appears that the ethylenic group resonances of EDDA shift from 0.30 to 0.60 ppm downfield upon successively protonating the amino groups. Furthermore, the acetate methylene resonance in going from $a = 0$ to $a = 1$ shifts 0.40 ppm upfield and in going from $a = 1$ to $a = 2$ this resonance shifts 0.21 ppm upfield. Keeping these values in mind, the protonation scheme for EDTA—DX becomes clear when in going from $a = 0$ to $a = 1$ only a very small shift of 0.07 ppm upfield is observed for the ethylenic protons. The larger shift of 0.17 ppm upfield in going from $a = 1$ to $a = 2$ is closer to that associated with the deprotonation of one of the inner nitrogens.

Further comparing EDTA—DX and EDDA spectra at $a = 1$, the 3.92 δ resonance is readily assigned to the acetate methylene, and the 3.75 δ resonance is assigned to the hydroxyamidoacetic methylene protons. From a similar comparison at $a = 2$, a reversal is noted where the higher field resonance at 3.75 δ is now the one associated with the carboxylate groups, and the methylene protons of the hydroxyamidoacetic group are characterized by a resonance at 3.88 δ. The reversal of chemical shift is reasonable for the following reasons: 1, it is very unlikely (as would be the case with the alternative assignment) that with the removal of a proton from a nitrogen atom, there would be no shielding change for the hydroxamic acid methylene, an unusually small change for the acetate methylene, and a normal change for the ethylenic methylene; 2, if the value of 3.75 δ at $a = 2.0$ were assigned to the acetate methylene, and the value 3.88 δ were assigned to the hydroxamic acid methylene, the observed shifts from $a = 1$ to $a = 2$ would be normal for all methylene groups except the latter; and 3, the unusually small upfield shift of the hydroxamic acid methylene resonance can be rationalized on the basis of probable hydrogen bond formation between the hydroxamic acid hydroxyl proton and the basic (deprotonated) nitrogen atom, to give the hydrogen bonded chelate ring illustrated by formula **2**.



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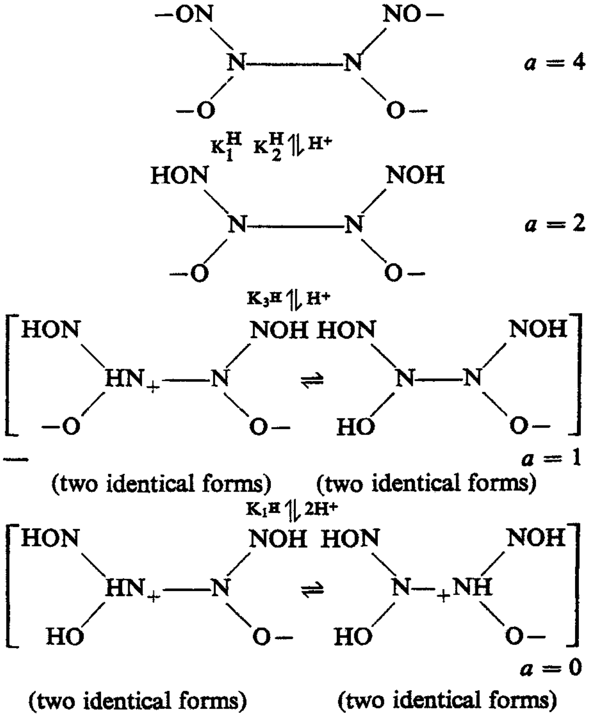
As observed, the ethylenic and acetate methylenes would not be greatly affected by such hydrogen-bonded chelate ring formation, and would be expected to have normal upfield shifts when the basic nitrogen atom is deprotonated.

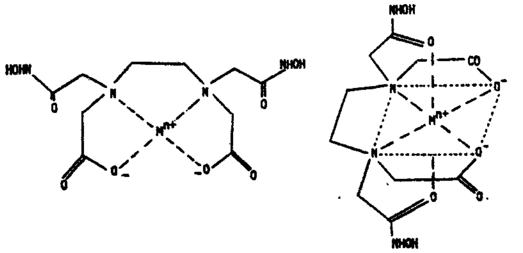
From the above discussion, the protonation scheme of EDTA—DX starting with the most deprotonated form, can now be set forth schematically as illustrated in Scheme 1.



SCHEME I

EDTA—DX Complexes at Low pH

The similarity of the 1:1 titration curves shown in Figure 1 for divalent ions indicates that Zn(II), Co(II), Ni(II), Cu(II) and as is indicated below, even Mg(II) and Fe(III), behave similarly in 1:1 metal—EDTA—DX systems. In general, the initial complex formed up to $a = 2$ is most reasonably concluded to be of the substituted EDDA type, **3**. In the Mg(II) case complex formation sets in only from $a = 1$ and further reaction overlaps the formation part of the curve. The Fe(III) formation curve is also overlapped by subsequent proton dissociation reactions.



a. Planar complex b. Octahedral complex

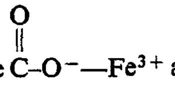
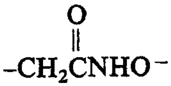
3 Low pH M—EDTA—DX chelate, $MH_2L^{(n-2)+}$

The intrinsic basicity toward protons of the tertiary amino nitrogens of EDTA—DX is a factor of about 10^3 less than in the EDDA case as shown in Table V and is due to electron withdrawing influence of the hydroxamide carbonyl group one carbon atom away. Accordingly, the coordinating tendency is similarly reduced in going from EDDA complexes to EDTA—DX complexes of the type illustrated by formula **3**. Because of its preference for 4-coordination, the comparison of these two ligands for Cu(II) can be restricted to the two amino nitrogens and the two carboxylate groups. Thus the lowering of the stability constant by $10^{5.5}$ is fully ascribed to the electronic —I effect of the hydroxamidic carbonyls. The remaining metal ion formation constants with EDTA—DX listed in Table V are all lower than those of EDDA. The greatest drop occurs with Cu(II), and the smallest with Mg(II), with the octahedral ions of Co(II), Ni(II) and Zn(II) showing intermediate effects. When the stabilities of the normal metal complexes for EDDA and EDTA—DX are compared, the large drop in stability for Cu(II) and the minimal effect observed for the Mg(II) complex are reflections of the relative coordinating tendencies of these two metal ions for basic nitrogen atoms. It is assumed as a first approximation that the coordinating tendencies of the acetate donor groups are not much different for these two ligands.

For the octahedral metal ion it is expected that there would be additional coordination with the relatively very weak carbonyl oxygen donors of the hydroxamic acid groups as illustrated by 3b. This seems to be evidenced by the fact that the decreases in stability observed for Co(II), Ni(II), and Zn(II) complexes are very much less than that of Cu(II). Another, though minor, factor working towards increased stability of the EDDA—DX chelates of octahedral metal ions is the favorable entropy factor due to the fact that the ligand is sexadentate for metal ions of coordination number six.

In addition to thermodynamic arguments based on equilibrium data, electronic spectra provide additional support for structures 3a and 3b, for complexes initially formed when the metal ion interacts with the ligand at low pH. There is very strong similarity between the visible spectra of EDTA—DX and EDDA chelates. The absorption bands of the Cu(II)—EDTA—DX complex at $a = 2$, for example, are shifted to lower energies with a concomitant loss in intensity when compared to the Cu(II)—EDDA spectra. This is in agreement with EDTA—DX being a weaker base than EDDA, thus exerting a weaker field, so that the spectrum of EDTA—DX chelate with Cu(II) lies both in intensity and position somewhere between those of $Cu(H_2O)_6{}^{2+}$ and Cu(II)—EDDA. Comparing the behaviour of the other metal ions listed in Table IV, it is seen that their spectra are remarkably similar, with slight shifts and only moderate changes in intensity, when going from the EDDA to the EDTA—DX chelate. Thus the weakening of the ligand field, which is so evident in the Cu(II) case, is compensated for somewhat by the effect of having the hydroxamido carbonyl groups bound in say the axial positions 3b to complete the octahedral field, displacing two molecules of water. Other arrangements of the oxygen donors in 3b are of course also possible, but such variants would not alter this interpretation of the spectra.

The infrared spectra shown in Table III provide further support for these suggestions. At $a = 2$, there are two types of carbonyl groups present in each coordinated ligand. The carboxyl bound to the metal ion absorbs at around 1603–1607 cm^{-1} and probably merits no further attention apart from noting that it is in the expected place. The other IR carbonyl band is assigned to the acethydroxamide group. Its position should be shifted to longer wave lengths by metal ion coordination, but because of the weak interactions involved, the shifts should be small and should depend mostly on the charge of the metal ion. In the case of the Cu(II) complex, 3a, the hydroxamic acid carbonyl absorption occurs at 1663 cm^{-1}, an increase of 32 wave numbers over the IR carbonyl frequency of the uncoordinated aminoacethydroxamic acid group, and 13 wave numbers over that of the N-protonated aminoacethydroxamic group. This large increase in carbonyl frequency indicates the strong electron withdrawal effect of coordination of the nitrogens (formula 3a) by the Cu(II) ion which tends to shift electrons from the carbonyl oxygen toward the coordinated metal, thus increasing the bond order in the carbonyl group. Coordination of Ni(II), Co(II), and Zn(II) gives a carbonyl frequency about 10 cm^{-1} lower than is observed for the Cu(II) complex. This decrease in frequency is ascribed to two effects, the lesser interaction of the amino nitrogen with these metal ions, and coordination of the carbonyl oxygen of the hydroxamic acid group in octahedral complexes illustrated by 3b. The latter interaction would decrease the bond order of the carbon-oxygen double bond, thus lowering its vibrational frequency.

At $a = 2$, the Fe(III) ion is completely bound to the ligand, and metal ion induced proton dissociation of the ligand has occurred to a considerable extent. The  $\overset{\overset{O}{\|}}{C}\text{–}O^{-}\text{—}Fe^{3+}$ absorption frequency in this case is rather high, 1643 cm^{-1}, indicating strong metal ion interaction with one of the acetate oxygens, thus increasing the vibrational frequency of the uncoordinated carbonyl group. The shoulder at ~ 1625 cm^{-1} should be the carbonyl frequency of the negative acethydroxamate group,  $\text{-}CH_2\overset{\overset{O}{\|}}{C}NHO^{-}$. The negative charge on the donor group lowers the carbonyl frequency to the point where it is very much lower than the carbonyl frequency in the Cu(II) complex without proton dissociation. Comparison with the octahedral Co(II), Ni(II) and Zn(II) complexes would be more appropriate, however, since the Fe(III) complex is probably octahedral or distorted octahedral, with six donor groups of the ligand and perhaps one or more water molecules coordinated to the Fe(III) ion. On this basis, it is considered more appropriate to discuss probably coordinate bond types for FeHL and FeL^- below, along with consideration of other metal complexes at high pH.

For the low pH complexes, little additional structural information is provided by the electronic spectra presented in Table IV and in Figures 3 and 4. In the case of Fe(III) complexes, the characteristic bands involving *d* orbitals, are only shoulders on a very large transfer charge band.

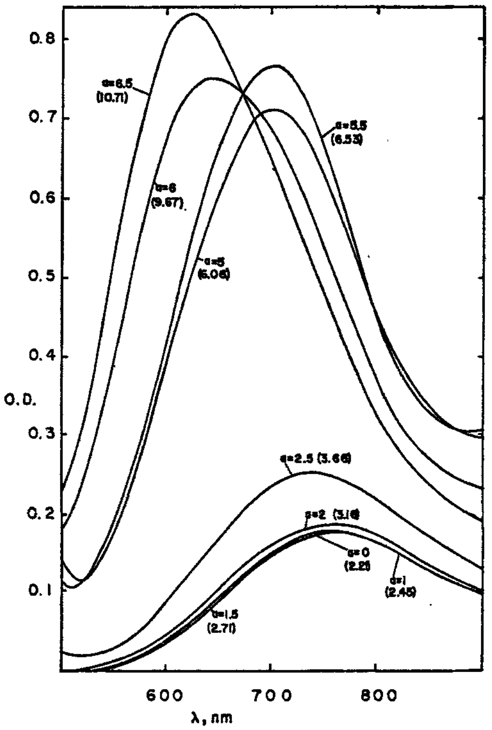
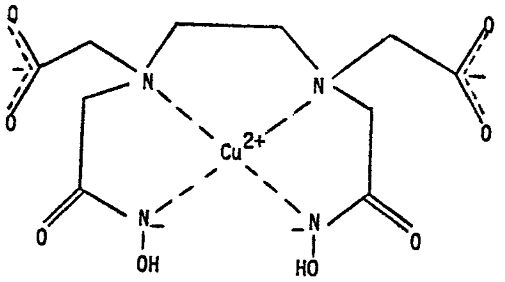


FIGURE 4 Electronic spectra of the binuclear complex containing two gram ions of Cu(II) per mole of N,N'-ethylenediaminediacetic-N,N'-diacethydroxamic acid (EDTA—DX) at 3.30×10^{-3} M concentration in 0.100 M aqueous KNO_3; O.D. = optical density; temperature —25 ± 1°.

Similarly, little additional structural information can be gained from the nmr spectra presented in Figure 2 for the Zn(II) chelate, other than that the spectra are consistent with the interpretations described above for low pH complexes and described below for high pH complexes.

EDTA—DX Complexes at High pH

As base is added past $a = 2$ (Figure 1), the hydroxamide groups of the 1:1 Cu(II), Ni(II), Co(II) and Zn(II) complexes begin to dissociate. Although the pK's for these metal ion-assisted dissociation reactions vary between two extremes, the difference between the two successive dissociation constants (i.e. K^H_{MHL} and $K^H_{MH_2L}$) for deprotonation of the acethydroxamic acid groups vary over a relatively narrow range, from slightly less than to a little more than one log K unit. This in itself is evidence for a strong tendency of the ligand to form symmetrical, highly stable complexes of the type ML^{2-}. The simplicity of the nmr spectra (Figure 2) at $a = 4$ for the Zn(II) ions is in agreement with the conclusion that a symmetrical complex is formed. The structure suggested for the high pH Cu(II) chelate, CuL^{2-}, is represented by **IV**. The negative hydroxamate donors coordinate the Cu(II) ion much more strongly than do the carboxylate groups, which are displaced in the transition from CuH_2L to CuL^{2-}. There is of course the possibility that the carboxylate groups are weakly coordinated to Cu(II) above and below the plane of the four coordinated nitrogen atoms, with metal-oxygen bonds that would be considerably longer than the planar metal-nitrogen bonds.

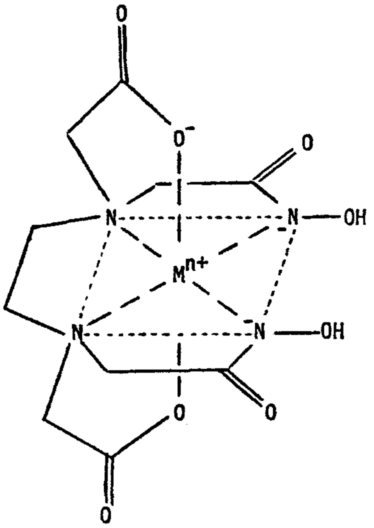


4 High pH chelate of Cu—EDTA—DX, CuL^{-4}

However, the coordinate bonds indicated in **4** are believed to represent the only strong interactions between the copper(II) ion and the ligand at high pH. This is in accord with the probable carboxylate carbonyl vibrational frequency which is buried under the 1601 cm^{-1} peak assigned to the coordinated hydroxamate carbonyl (Table III). The position of the carboxylate band in **4** may be close to but a little higher than that of the free aminocarboxylate group (1582 cm^{-1}, Table II). Further support for the fundamental change in coordinate bonding from **3*a*** to **4** is provided by the electronic spectra of the Cu(II) complexes presented in Table IV. In going from $a = 2$ to $a = 4$, there is a fundamental change in the nature of the spectra, involving a shift to lower wave length and a fourfold decrease in intensity.

The potentiometric and spectral data for the

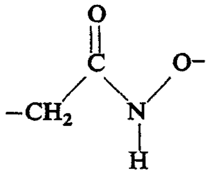
Ni(II), Co(II), Zn(II), and Fe(III) for complexes of the type ML^{n-4} are compatible with an octahedral arrangement of donor groups indicated in **5**. The negative hydroxamate donors in **5** may be interchanged with the carboxylate groups, so that **5** is actually one of three possible conformations of the ligand.



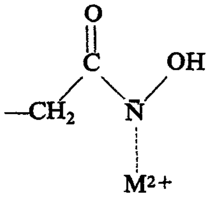
5 High pH octahedral chelates of EDTA—DX, ML^{n-4}

The infrared data in Table III are in conformity with structure **5**, the high pH absorption bands occurring at 1598 and 1596 cm^{-1} for Ni(II) and Zn(II), respectively. These bands represent a combination of coordinated carboxylate and hydroxamate groups. The band at 1614 cm^{-1} for Co(II) is considered somewhat anomalous. The interaction of the hydroxamate group with the Fe(III) ion is expected to be much stronger than with the divalent metal ions, and is characterized by an absorption band which is about 20 cm^{-1} higher in frequency. If the metal ions were coordinated to the carbonyl oxygens, increasing the coordination tendency would lower the frequency. Thus the observations are in accord with hydroxamate nitrogen coordination, as indicated in Formulas **4** and **5**, rather than with hydroxamate carbonyl oxygen coordination, the type that prevails at low pH.

It is interesting to note that the carbonyl frequency of the uncoordinated ionized hydroxamate group has a frequency considerably higher, by about 25 cm^{-1}, than do the ionized hydroxamate groups coordinated to divalent metal ions. A possible rationalization of this observation would be offered by assuming that deprotonation induced by coordination occurs at the nitrogen atom, as indicated by the following.



6a $\nu_{C=O} \cong 1624$ cm^{-1}



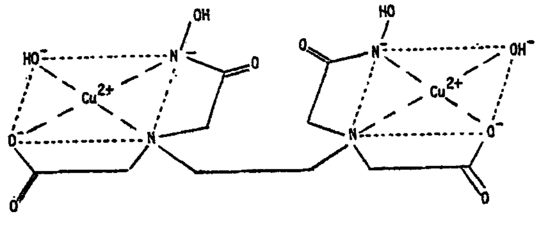
6b $\nu_{C=O} \cong 1600$ cm^{-1}

Amide type resonance in **6b** would place more negative charge on the carbonyl oxygen, in spite of coordination with a divalent metal ion, than would amide resonance in **6a**, thus accounting for the direction of the shift of carbonyl frequencies.

The increase in carboxylate carbonyl frequency of the Fe(III) complexes that occurs when FeL^- goes to $FeOHL^{2-}$ does not seem to have a clear explanation with the data presently available. It is possible that the dissociation of a coordinated water molecule, or dissociation of a second proton from the hydroxamic acid group would eliminate or decrease hydrogen bonding to the uncoordinated carbonyl oxygens of the carboxylate groups, thus increasing their vibrational frequencies. In any case it is the carboxylate carbonyl frequencies of **5** that are abnormally low, while that observed for the $FeOHL^{2-}$ complex seems quite normal.

Cu(II)—EDTA—DX 1:2 *System*

Since the Cu(II) ion is four coordinate and the ligand EDTA—DX is potentially sexadentate, systems containing a 2:1 molar ratio of copper(II) ion to ligand were investigated. At $a = 2$ and less, the 2:1 visible spectrum (Figure 4) was found to be identical with that of a 1:1 spectrum (Figure 3). The solution was deep blue. Above $a = 2$, the solution began to turn green and at about $a = 2.5$ a green precipitate was formed. This precipitate redissolved on the addition of five equivalents of base. As more base was added, a further buffered region was obtained which indicated reaction of a



7 2:1, Cu(II)—EDTA—DX chelate

total of at least six moles of base per mole of ligand. The visible changes in the spectra are summarized in Figure 4. The clear isosbestic point indicates a 1:1 stoichiometry involving only two species. To accommodate these data, the high pH binuclear structure (at maximum deprotonation) for this 2:1 system is suggested as shown in **7**. Dissociation of the extra protons (above $a = 4$) result in the direct coordination of two hydroxide ions with the complex, one for each free (acquo) coordination site on each metal ion. The arrangement of donor groups about the Cu(II) ions at six equivalents of base $Cu_2(OH)_2L^{2-}$ is believed to be represented by **7**, while the neutral insoluble green complex that was observed is also believed to be binuclear and represented by an arrangement of donor groups similar to **7**, with the hydroxide ions replaced by water molecules.

REFERENCES

1. This work was supported by a research grant, No. A-259, from the Robert A. Welch Foundation.
2. To whom inquiries may be addressed, Texas A & M University.
3. R. J. Motekaitis and A. E. Martell, *J. Am. Chem. Soc.* **92,** 4223 (1970).
4. J. B. Neilands, *Structure and Bonding* **1,** 59 (1966).
5. G. Anderegg, F. L'Eplattenier, G. Schwarzenbach, *Helv. Chim. Acta.* **46,** 1409 (1963).
6. G. Schwarzenbach and K. Schwarzenbach, *Helv. Chim. Acta.* **46,** 1930 (1963).
7. H. J. Lindner and S. Gottlicher, *Acta. Cryst.* **25,** 832 (1969).
8. L. M. Epstein and D. K. Straub, *Inorg. Chem.* **8,** 453 (1969).
9. R. E. Plapinger, *J. Org. Chem.* **24,** 802 (1959).
10. H. P. Fritz and O. E. Van Stetten, *Z. Naturforsch.* **24,** 947 (1969).
11. G. Schwarzenbach and H. Flaschka, *Complexometric Titrations* (Methuen & Co. Ltd., Second English Edition, 1969).
12. A. E. Martell in *Recent Topics in Coordination Chemistry* (S. Misumi and K. Ueno, Ed., Special Publication No. 84, Nankado, Tokyo, Japan, 1968) pp. 47–67.
13. K. Nakamoto in *Spectroscopy and Structure of Metal Chelate Compounds*, K. Nakamoto and P. J. McCarthy, S. J. (John Wiley & Sons, Inc., N.Y., 1968), pp. 276–281.
14. G. Anderegg, G. F. L'Eplattenier and G. Schwarzenbach, *Helv. Chim. Acta*, **46,** 1400 (1963).
15. F. Mathis, *Bull. Soc. Chim. France*, D9–22 (1953).
16. G. K. Schweitzer and M. M. Anderson, *J. Inorg. Nucl. Chem.*, **30,** 1051 (1968).