(b) Second term

$$H_2O\text{-}\boxed{Pt}\text{-}Br^- + Br^- \rightleftharpoons H_2O\text{-}\boxed{Pt}\text{-}Br\cdots Br^{2-} \qquad (13)$$

$$H_2O\text{-}\boxed{Pt}\text{-}Br\cdots Br^{2-} \rightleftharpoons \boxed{Pt}\text{-}Br\cdots Br^{2-} + H_2O \qquad (14)$$

$$Br^- + \boxed{Pt}\text{-}Br\cdots Br^{2-} \longrightarrow Br\text{-}\boxed{Pt}\text{-}Br\cdots Br^{3-} \qquad (15)$$

$$Br\text{-}\boxed{Pt}\text{-}Br\cdots Br^{3-} \rightleftharpoons Br\text{-}\boxed{Pt}\text{-}Br^{2-} + Br^- \qquad (16)$$

Assuming (13), (14), and (16) are rapid equilibria and (15) is the rate-determining step, we get the rate equation below

$$d[Pt(CN)_4Br_2{}^{2-}]/dt = k_{15}K_{13}K_{14}[Pt(CN)_4Br(OH_2)^-][Br^-]^2 \qquad (17)$$

By combining the rate equations from the two mechanisms, we arrive at the rate law for the formation of *trans*-$Pt(CN)_4Br_2{}^{2-}$ on the basis of the above detailed mechanisms (eq 2′).

$$d[Pt(CN)_4Br_2{}^{2-}]/dt = (k_{11}K_{10} + k_{15}K_{13}K_{14}[Br^-])[Pt(CN)_4Br(OH_2)^-][Br^-] \qquad (2')$$

It appears that the anation of *trans*-$Pt(CN)_4Br(OH_2)^-$ by bromide ion is subject to an acceleration by bromide ion of the same sort that was observed in the base hydrolysis of *trans*-$Pt(CN)_4Br_2{}^{2-}$.[1] A dissociative mechanism is postulated in both cases; and the association of a bromide ion with the reactant apparently shifts the equilibrium of the dissociation probably by increasing the electron density on the central metal ion. As in the case of the hydrolysis, we must consider the possibility that a redox mechanism, described previously,[2] is operative here. In the present system this possibility seems highly unlikely because such a process would only result in the formation of bromine and $Pt(CN)_4{}^{2-}$, the starting material. This should reduce the rate of reaction. The anation reaction appears to fortify our contention that a reduction of this sort does not occur in this system.

It is interesting to compare the results of this study with those of the anation of $Co(CN)_5OH_2{}^{2-}$ by halide ions.[7] In both cases a limiting SN1 mechanism is consistent with the rate law found. The term which is second order in bromide ion complicates this interpretation in the present system. The rate of formation of *trans*-$Pt(CN)_4Br_2{}^{2-}$ is much greater than the rate of formation of $Co(CN)_5Br^{3-}$. The low enthalpy of activation indicates that the difference in rates results from the instability of aquo complexes of platinum(IV).

Acknowledgment. We wish to acknowledge with thanks the financial assistance provided for this work by the U. S. Atomic Energy Commission.

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New Multidentate Ligands. VII. Ethylenediamine-N,N′-diacetic-N,N′-di(methylenephosphonic) Acid[1]

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Received October 31, 1968

Abstract: Synthesis, acid-base equilibria, and metal ion chelating tendencies of the new ligand, ethylenediamine-N,N′-diacetic-N,N′-di(methylenephosphonic) acid are reported. On the basis of potentiometric equilibrium measurements of hydrogen ion concentrations at 25° and ionic strength 1.00 (KNO_3), acid dissociation constants of the ligand and the equilibrium constants for the interactions of the ligand with some representative metal ions have been evaluated. Probable structures of the metal chelates formed in solution are suggested on the basis of a comparison of their stabilities with those of analogous ligands.

The synthesis and metal binding tendencies of a new class of chelating ligands containing aminophosphonate groups have been reported by Martell and coworkers.[3,4] By means of potentiometric studies, they determined the acid dissociation constants and metal chelate formation constants for the ligands nitriloaceticdi(methylenephosphonic) acid (NADMP), nitriloacetic-β-propionicmethylenephosphonic acid (NAPMP), and N,N,N′,N′-ethylenediaminetetra(methylenephosphonic)acid (ENTMP). Schwarzenbach and coworkers[5] earlier reported the relatively strong chelating tendency of the phosphonate-containing ligand nitrilodiaceticmethylenephosphonic acid for Ca(II) ion.

In this paper, the synthesis and metal chelating tendencies of the new ligand, ethylenediamine-N,N′-diacetic-N,N′-di(methylenephosphonic) acid (EDAMP), are reported.

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[2] Department of Chemistry, Texas A&M University, College Station, Texas 77843.

[3] S. Westerback and A. E. Martell, *Nature*, 178, 321 (1956).

[4] S. Westerback, K. S. Rajan, and A. E. Martell, *J. Am. Chem. Soc.*, 87, 2567 (1965).

[5] G. Schwarzenbach, H. Ackermann, and P. Ruchstuhl, *Helv. Chim. Acta*, 32, 1175 (1949).

Experimental Section

Synthesis of Ethylenediamine-N,N'-diacetic-N,N'-di(methylenephosphonic) Acid. To chloromethylphosphonic acid (11 g) dissolved in 30 ml of water, sodium hydroxide pellets (*ca.* 6 g) were added slowly with stirring until a pH of 11 had been reached, and the solution was then saturated with sodium carbonate. Ethylenediamine-N,N'-diacetic acid (5 g) was dissolved in water (20 ml) and the pH of the solution brought to 11 by the addition of 40% sodium hydroxide solution. The sodium chloromethylphosphate was then added to the alkaline solution of ethylenediamine-N,N'-diacetic acid, and the mixture was gently refluxed for 90 hr and then neutralized with nitric acid and filtered. The filtrate was treated with an excess of lead nitrate to isolate the insoluble lead salt of EDAMP. The lead salt was filtered and washed with boiling water several times. The yield was 33 g. The free acid (EDADMP) was prepared from the lead salt by treatment of an aqueous suspension of the salt with hydrogen sulfide, separation of the lead sulfide by filtration, and evaporation of the filtrate under vacuum. The resulting pale yellow syrup was kept over calcium chloride in a vacuum desiccator and a viscous sticky mass was obtained. This was treated with absolute ethanol several times and dried over P_2O_5 in a vacuum desiccator for 1 week. The pale yellow crystalline solid thus obtained was very soluble in water and almost insoluble in absolute ethanol and insoluble in ether.

Anal. Calcd for $C_8H_{18}N_2O_{10}P_2 \cdot 2H_2O$: C, 24.0; H, 5.5; N, 7.0. Found: C, 23.8; H, 55; N, 7.3.

The starting material, ethylenediamine-N,N'-diacetic acid, is a well-known compound; however, there is only one report[6] of its preparation in the literature. The authors have reinvestigated the synthesis of this substance and have found a satisfactory method based on dicyanomethylation of ethylenediamine followed by acid hydrolysis of the dinitrile of the amino acid. The over-all yield of the product was 40–50%.

Potentiometric Measurements. The potentiometric studies of the equilibria involving proton and metal ion affinities of the ligand were carried out at 25° and an ionic strength of 1.00, which was maintained constant by the addition of KNO_3 to the experimental solution. Equilibrium measurements of the hydrogen ion concentrations were made with a Radiometer pH meter (Type PHM4) fitted with glass and calomel extension electrodes. The calibration of the electrode systems to give hydrogen ion concentration and the details of the experimental procedure are as described previously.[7]

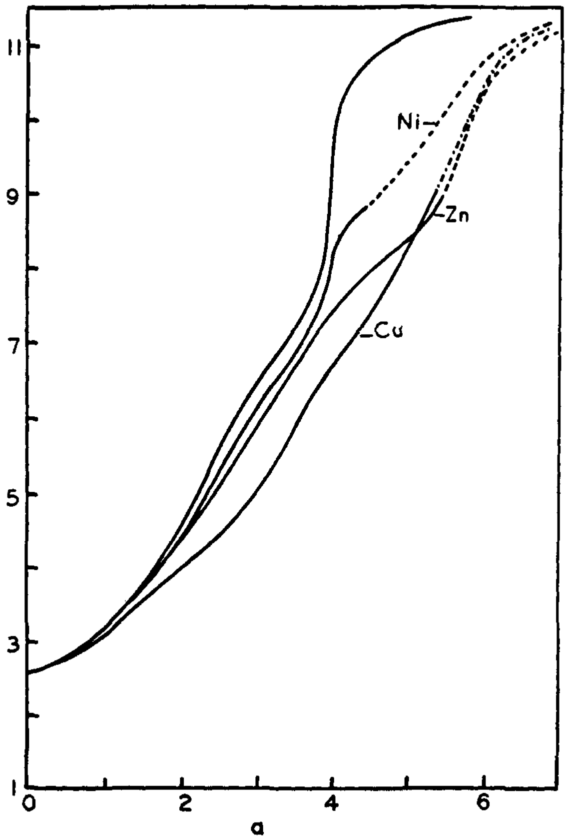

Figure 1. Potentiometric equilibrium curves of EDAMP and its metal chelates: —, 2.7 × 10^{-3} *M* EDADMP; Ni, Zn, and Cu each represent a system containing 2.7 × 10^{-3} *M* metal ion in the presence of an equivalent concentration of EDADMP; a = moles of base added per mole of ligand or metal ion; μ = 1.0 (KNO_3); t = 25°; broken lines indicate the formation of a precipitate in the system.

Results

Acid Dissociation Constants of the Ligand. The potentiometric titration curve of the ligand (EDADMP) (Figure 1), with inflections at 2 and 4 equiv of base per mole of the ligand indicates that the ligand has two strongly acid groups, two overlapping dissociations at intermediate pH, corresponding to the dissociation of a proton from each negative phosphonate group, and two high p*K*'s corresponding to the dissociation of protons from the amino groups. The acid–base neutralization steps of the ligand may be represented by the reaction steps in Scheme I.

The slope–intercept method was employed for graphical evaluation of each of the overlapping p*K*'s in the neutralization steps indicated in Scheme I, with the potentiometric data of Figure 1, and the dissociation constants thus obtained are presented in Table I.

Table I. Acid Dissociation Constants and Chelate Formation Constants of EDADMP and ENTMP[a]

Cation	Complex formed[b]	Log of equilibrium constant EDADMP (H_6L)	ENTMP (H_8L)[c]
H^+	HL	11.2 ± 0.1	10.60
H^+	H_2L	10.6 ± 0.1	9.22
H^+	H_3L	7.72 ± 0.04	7.43
H^+	H_4L	5.46 ± 0.03	6.63
H^+	H_5L	3.52 ± 0.03	6.18
H^+	H_6L	2.83 ± 0.03	5.05
H^+	H_7L		2.72
H^+	H_8L		1.46
Mg^{2+}	MgH_2L	3.4 ± 0.1	
Ca^{2+}	CaL		5.74
Mn^{2+}	MnL		9.40
	MnH_2L	3.9 ± 0.1	
Co^{2+}	CoH_2L	3.7 ± 0.1	
Ni^{2+}	NiH_2L	3.7 ± 0.1	
Cu^{2+}	CuL	12.7 ± 0.5	16.1 ± 0.4
	CuHL		13.3 ± 0.3
	CuH_2L	6.3 ± 0.5	11.6 ± 0.3
	CuH_3L		
	CuH_4L	3.2 ± 0.1	
Zn^{2+}	ZnH_2L	4.2 ± 0.1	

[a] μ = 1.0 *M*(KNO_3); 25°. [b] Reaction involved corresponds to combination of metal ion or proton shown with appropriate ligand moiety to give complex formed. [c] Data taken from Westerback, Rajan, and Martell.[4]

Interaction with Metal Ions. The reactions of this ligand with a number of alkaline earth and transition metal ions as well as a few tervalent ions were examined by means of potentiometric equilibrium measurement of hydrogen ion concentration. Typical potentiometric curves of the metal chelate systems involving Ni^{2+}, Zn^{2+}, and Cu^{2+} ions are illustrated in Figure 1. The titration curves of the Co(II), Mn(II), and Mg(II) chelates coincide with that of the Ni(II) curve shown. The Ca(II), Sr(II), and Ba(II) chelate systems each gave

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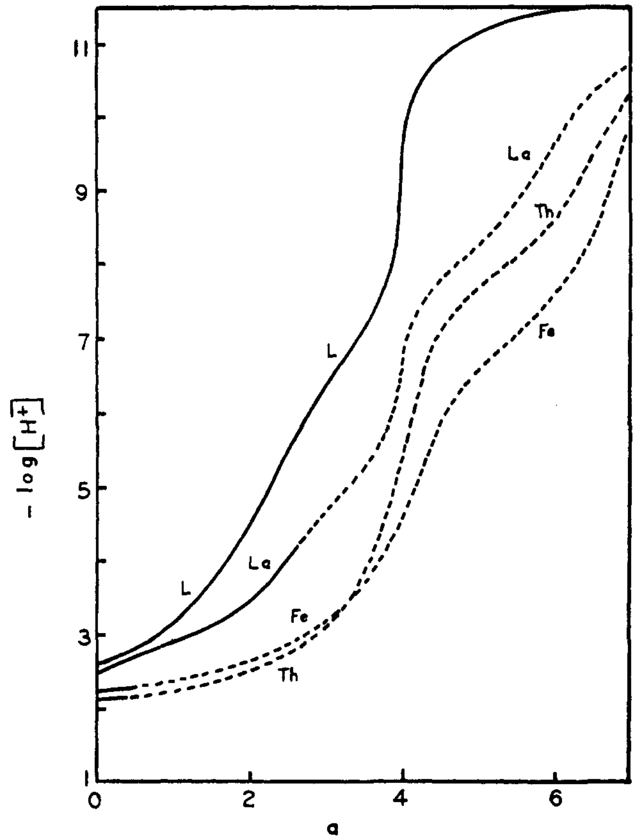
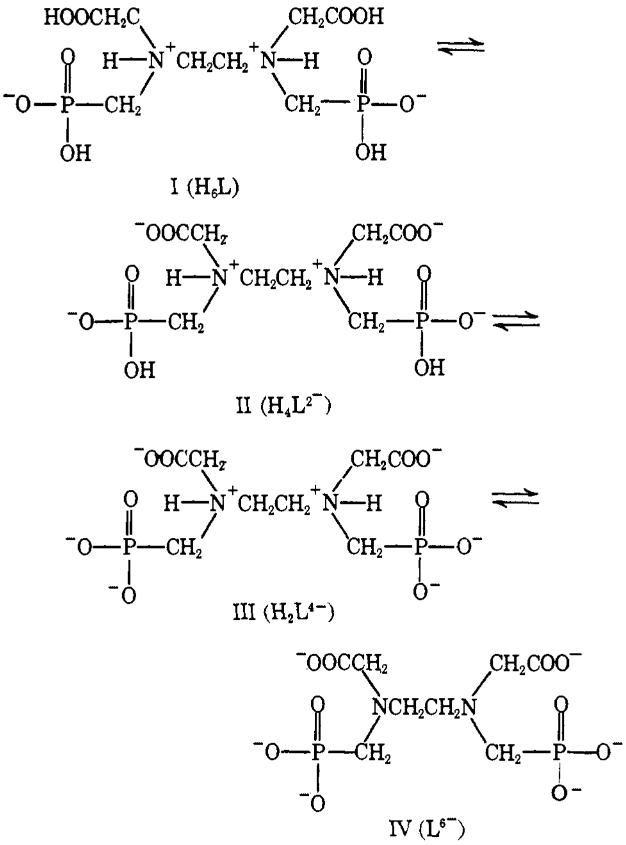


Figure 2. Potentiometric equilibrium curves of EDAMP and its metal chelates: L = 2.7 × 10^{-3} M EDADMP; Fe, La, and Th each represent a system containing 2.7 × 10^{-3} M metal ion in the presence of an equivalent concentration of EDADMP; a = moles of base added per mole of ligand or metal ion; μ = 1.0 (KNO_3); t = 25°; dotted lines indicate the separation of solid from the solution.

Scheme I



I (H_6L)

II (H_4L^{2-})

III (H_2L^{4-})

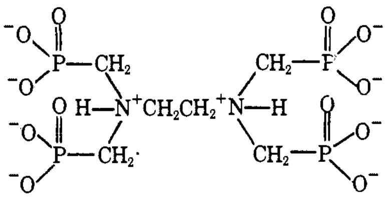
IV (L^{6-})

potentiometric titration curves superposable on that of the free ligand over most of the pH range. The interactions of Fe(III), La(III), and Th(IV) ions resulted in the separation of solid precipitate over most of the pH range of the titration (Figure 2). These titration curves were therefore employed only for the determination of stoichiometry of chelate formation, and as rough measures of the stabilities of the metal chelates formed.

Formation constants of Mg(II), Ni(II), Mn(II), Zn(II), and Cu(II) chelates were determined from the data of Figure 1, and the results are presented in Table I.

Discussion

It is of interest to compare the acid-base characteristics of the ligand EDADMP with those of ethylenediaminetetra(methylenephosphonic) acid (ENTMP)[4] and EDTA. The dissociation steps of EDADMP and ENTMP are quite similar except that the intermediate buffer region of the former involves the dissociation of two protons rather than four, in accordance with the fact that only two phosphonic acid groups are present. Although the functional groups of EDADMP would indicate that its acid-base behavior might be intermediate between that of EDTA and ENTMP, the proton association constants of EDADMP given in Table I show that the expected trend is not borne out experimentally. The first two association constants of the fully dissociated form of EDADMP are larger than those of ENTMP, in spite of the higher charge of the latter. Apparently a negatively charged acetate group is more base strengthening than a phosphonate group in compounds III and V.



V, ENTMP (diprotonated form)

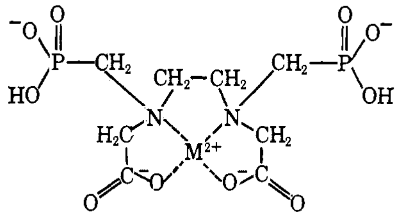
The titration curves (Figure 1) and the equilibrium data shown in Table I indicate that Ni(II), Co(II), Mn(II), and Mg(II) ions interact very weakly with the more acid forms of the ligand, *i.e.*, H_6L to H_2L^{4-}. Above pH 8.5, these metal ions react more strongly with the HL^{5-} and L^{6-} species, but precipitation takes place. The affinity of the Zn(II) ion for the ligand is a little stronger than those of Ni(II), Co(II), Mg(II), and Mn(II) ions. The tendency of Cu(II) to form a chelate with this ligand is relatively quite strong. The deviations shown for copper(II) are somewhat misleading in that they do not reflect uncertainties in the data (the titration curves are accurately reproducible from the constants given), but the latitude in the choice of the successive complementary constants that may be employed for accurate representation of the equilibrium data. Although strong interactions were indicated for Fe(III), La(III), and Th(IV) ions (Figure 2), the titration data could not be used for the calculation of the appropriate equilibrium constants because of the separation of solid phase throughout the pH range of the titration.

Table II. Comparison of Chelating Tendencies of NTA and EDTA with Analogous Aminophosphonate Ligands

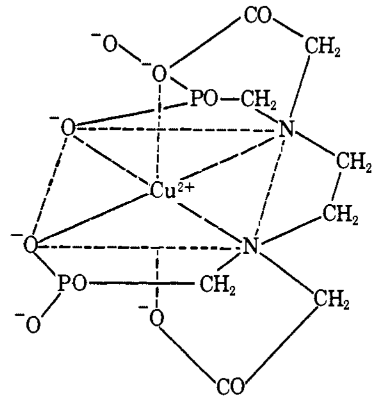
Cation	Complex formed	Log of equilibrium constant NTA[a]	NDAP[b]	NADMP[e]	EDADMP[d]	ENTMP[c]	EDTA[e]
H^+	HL	9.73	10.76	10.80	11.2 ± 0.1	10.60	10.26
H^+	H_2L	2.49	5.57	6.37	10.6 ± 0.1	9.22	6.16
H^+	H_3L	1.89	2.25	5.01	7.72 ± 0.04	7.43	2.67
H^+	H_4L		2.00	2.00	5.46 ± 0.03	6.63	2.00
H^+	H_5L			1.73	3.52 ± 0.03	6.18	
H^+	H_6L				2.83 ± 0.03	5.05	
H^+	H_7L					2.72	
H^+	H_8L					1.46	
Mg^{2+}	MgL	5.41	6.28		3.4 ± 0.1[f]		8.69
Ca^{2+}	CaL	6.41	7.18	6.17		5.74	10.59
Sr^{2+}	SrL	4.98	5.59				
Mn^{2+}	MnL	7.44		7.00	3.9 ± 0.1[f]	9.4	14.04
Cu^{2+}	CuL	12.68		12.53	12.7 ± 0.5	16.1 ± 0.4	18.8

[a] G. Schwarzenbach and H. Ackermann, *Helv. Chim. Acta*, **31**, 1029 (1948). [b] Reference 5. [c] Reference 4. [d] This work. [e] G. Schwarzenbach and E. Freitag, *Helv. Chim. Acta*, **34**, 1492 (1951).

On the basis of the potentiometric equilibrium data, the combination of Mg(II), Co(II), Mn(II), and Zn(II) ions with the ligand anion H_2L^{4-} through the displacement of four protons suggests the arrangement of ligands given in VI.



VI, diprotonated chelate of EDADMP
(M^{2+} represents Mg(II), Co(II), Mn(II), and Zn(II) ions)



VII, Cu(II) chelate of EDADMP

The coordination of Cu(II) ion with L^{6-} anion at high pH may be represented by formula VII, which indicates a distorted octahedral structure in which the carboxylate groups are assigned the more remote, less strongly bound, coordination sites above and below the plane of the strong coordinate bonds of the copper(II) ion. It is not known with data presently available whether these sites are occupied by carboxylate or phosphonate oxygens. On the basis of relatively large variations in basicity, the relative coordinating tendencies of ligand donor groups are considered to be $-PO(OH)O^- < -COO^- < PO_3^{2-}$. The arrangement of the coordinate bonds suggested for the copper(II) complex in formula VII is based on the well-known approximate square-planar geometry of the four strong coordinate bonds around the Cu(II) atom. Accordingly, the diprotonated Cu(II) complex would have the two carboxylate oxygens in the plane of the basic nitrogen atoms. Structural conclusions arrived at in this way are further strengthened by the p*K* of the diprotonated species, CuH_2L^{2-}, which is much higher than that expected for a free carboxyl group, but not much different from an uncoordinated monoprotonated phosphonate group.

Similarly the much lower p*K* for CuH_4L indicates that the Cu(II) ion must be coordinated to two monoprotonated phosphonate groups, and to the two basic nitrogen atoms of the tetraprotonated ligand.

Because of the generally nonparallel nature of the equilibrium and stability constants listed in Table I (which is mainly due to precipitation of EDADMP chelates at high pH), it is not possible to make direct comparisons between the unprotonated chelates of EDTA, EDADMP, and ENTMP. From the relative stabilities of the copper(II) chelates of these ligands, however, it seems that the formation constants of EDADMP chelates are unexpectedly low, and not intermediate between those of EDTA and ENTMP.

The acid dissociation constants and some representative metal chelate formation constants of the ligands nitrilotriacetic acid (NTA), nitrilodiaceticmethylenephosphonic acid (NDAP), nitriloaceticdimethylenephosphonic acid (NADMP), ethylenediaminediaceticdimethylenephosphonic acid (EDADMP), ethylenediaminetetramethylenephosphonic acid (ENTMP), and ethylenediaminetetraacetic acid (EDTA) are presented in Table II. The increased metal-binding affinity obtained through the substitution of one acetate group in nitrilotriacetic acid (NTA) by a methylenephosphonate group in NDAP, reported by Schwarzenbach, *et al.*,[5] is not continued in going to the ligand NADMP. Further, the stability constants of both EDADMP and ENTMP chelates are smaller than those of EDTA, indicating that the substitution of two and four methylenephosphonate groups results in an over-all decrease in metal chelate stabilities. The observed increase in metal ion affinity for one phosphonate group, and the decrease that occurs with two or more phosphonate groups on the ligand, may be understood if the high negative charge of this donor group is considered. The larger negative charge of the phosphonate groups greatly increases the coulombic repulsions between the ligand donor groups that must be brought together to form metal chelate rings with the metal ion. When two or more phosphonate groups are present in the ligand, apparently these repulsions become great enough to decrease the formation constants for the combination of the ligand with divalent metal ions.

It is possible that this effect is overcome sufficiently with metal ions of higher charge, however, so that increased stabilities would be obtained with two or more phosphonate groups on the chelating ligand. The data needed to test this interpretation are being gathered and will be the subject of a subsequent publication.

New Multidentate Ligands. VIII. Metal Complexes of N,N′-Diglycylethylenediamine in Aqueous Solutions[1]

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Contribution from the Department of Chemistry, Texas A&M University, College Station, Texas. *Received July 15, 1968*

Abstract: The specific coordinating tendencies of the synthetic ligand, N,N′-diglycylethylenediamine, toward Cu(II) and Ni(II) ions have been studied as a model for peptide–metal binding. The coordination compounds formed are unique in that hydrogen ions are displaced by these metal ions from the amide linkages, and in the formation of a low pH polynuclear copper(II) chelate that depolymerizes to a mononuclear chelate in alkaline solution. The copper(II) chelate, CuL^{2+}, releases amide protons in two distinct steps, to give the species $Cu_2(H_{-1}L)_2^{2+}$ and CuH$_{-2}$L. On the other hand, the nickel(II) chelate of the neutral ligand, NiL^{2+}, loses both amide protons simultaneously to give the chelate NiH$_{-2}$L. Cobalt(II) and zinc(II) ions do not displace the peptide protons, forming only the "ordinary" complexes, ML^{2+}, in which the metal ion is coordinated to the neutral ligand. In the types of reactions with metal ions, the ligand resembles triglycine and tetraglycine, but contrasts with these and other peptides in the manner in which it forms polynuclear copper(II) chelates. Electronic spectra of the Cu(II) and Ni(II) chelates formed are measured and discussed.

Metal complexes of N,N′-diglycylethylenediamine (DGEN) were first studied by Pfeiffer and Saure[2] in their investigation of the biuret reaction with a series of ligands containing amide groups. They found that the copper(II)-DGEN complex, as well as biuret complexes, has a deep violet color in alkaline solution. For such complexes, they suggested a structure in which a proton is displaced from the amide group coordinated to the copper(II) ion. They also suggested that nickel(II) chelates of these compounds have similar structures. The stability constants of DGEN complexes of various metal ions were first reported by Chakraburtty and coworkers from their potentiometric studies.[3] These authors[3] first observed that the "ordinary" complexes of DGEN with copper(II) and nickel(II) react further with alkali hydroxide, and interpreted the reaction as hydrolysis of the metal complexes.

Subsequently, similar reactions were observed in systems of copper(II)[4–14] and nickel(II)[6,15,16] complexes of many amino acid peptides, and it is now established that, in acidic or near neutral pH, the peptide protons, not those of coordinated water molecules, are being dissociated in such systems.[4–16] The displacement of the peptide or amide protons is also known in the solid state of both copper(II)[6,17,18] and nickel(II)[6,17] chelates. Direct evidence for the peptide proton dissociation was obtained from aqueous (D$_2$O) infrared studies[13,14,16] for complexes in solution. The result of X-ray crystallographic studies[18] has shown unequivocally the peptide proton displacement in the solid and the coordination of the resulting negative-peptide groups to metal ion.

All of the copper(II) and nickel(II) complexes of peptides and amides known so far, in which the peptide or amide protons are displaced, have at least one amino group in the ligand. Thus, it appears that the presence of the strongly coordinating amino group(s) may be necessary for strong chelation which stabilizes the complex resulting from displacement of the amide protons. In this respect, DGEN appeared to be an ideal ligand for the study of metal–peptide interactions because it has two amino groups, one on each end of the chain, and the chelate rings resulting from the displacement of the peptide protons would all be five membered. Thus DGEN is expected to form the negative-peptide

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(1) This work was supported by the U. S. Atomic Energy Commission under Contract No. AT (40-1) 3621 with Texas A&M Research Foundation.

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