In a similar experiment methyl borate (8 mole per cent. based on lithium hydride) was added to the lithium hydride before addition of boron trichloride etherate. Reaction characteristics were almost identical with the above reaction in which no catalyst was used. The first diborane collected was of low purity. The final yield was 77%.

Boron trichloride gas was also passed directly into a lithium hydride–ether slurry. In a reaction between 3.1 moles of lithium hydride in 325 cc. of ether and 1.01 moles of boron chloride, exothermic reaction changed to endothermic when 0.65 mole of boron trichloride had been added. The 0.055 mole of diborane collected during the exothermic reaction was 93% pure. Remaining diborane analyzed to 100%; total yield of diborane, 0.384 mole; calculated, 0.517 mole.

Acknowledgment.—The authors wish to thank Dr. E. H. Winslow for his able assistance in devising analytical methods and directing their application, and Mr. L. B. Bronk for his analyses of active hydrogen-containing compounds.

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Stability of Metal Chelates. I. Iminodiacetic and Iminodipropionic Acids

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Acid dissociation constants of iminodiacetic acid and iminodipropionic acid, and the chelate stability constants of the corresponding anions with cupric, nickelous, cobaltous, zinc and cadmium ions are reported for a temperature of 30° and 0.1 ionic strength. The replacement of acetate groups by β-propionate groups in the ligand results in a considerable decrease in the stability of the chelate.

This is the first of a series of publications describing the effect of structure of the ligand on the stability of aqueous metal complexes. The chelating agents to be described are amino acids, soluble in water in the form of their salts, which have more or less ability to combine with the more basic metal ions, such as the alkaline earth metals, and having appreciable affinity for transition metals and other "heavy metal" ions. Thus all the compounds in this series may be classified as sequestering agents. A guiding principle in our investigation involves the selection of the two most useful sequestering agents known—ethylenediaminetetraacetic acid and nitrilotriacetic acid—as having more or less optimum structures. By changing these basic structures with respect to (1) variation of the number of acetic acid groups, and (2) replacement of these by other groups, it may be possible to draw logical conclusions concerning the basis of metal ion affinity in these compounds. Thus a quantitative study of the stabilities of the corresponding metal chelates may lead to a better understanding of the method of function of sequestering agents, and to the development of superior sequestering agents.

Iminodiacetic acid, $NH(CH_2COOH)_2$, and iminodipropionic acid, $NH(CH_2CH_2COOH)_2$, have not been investigated previously, with the exception of the former, for which dissociation constants and approximate stability constants with calcium and magnesium have been published. In the present paper, the dissociation constants and chelate stability constants with a number of metal ions of the first transition series are reported.

The structures of these complexing agents differ from that of the parent compound, nitrilotriacetic acid, $N(CH_2COOH)_3$, in that in the first an acetic acid group is replaced by a hydrogen, and in the second, both remaining acetic acid groups are replaced by β-propionic acid groups. In accordance with the now accepted theories[2] concerning the structure of aminopolycarboxylic acid–metal chelates, nitrilotriacetic acid is probably tetradentate. Hence the removal of an acetic acid group would be expected to render the resulting structure tridentate, and the stability of the chelate would thus be lowered. Indeed, the differences in calcium and magnesium formation constants for nitrilotriacetic acid and iminodiacetic acid reported by Schwarzenbach[3a,b] indicated a very dramatic drop in stability. The logarithms of the stability constants of the calcium and magnesium nitrilotriacetate ions, $Ca{\cdot}N(CH_2COO)_3^{-1}$ and $Mg{\cdot}N(CH_2COO^-)_3^{-1}$ were found by Schwarzenbach to be 6.41 and 5.41, respectively. On the other hand, the corresponding values for the iminodiacetic acid chelates, $Ca{\cdot}NH(CH_2COO)_2$, and $Mg{\cdot}NH(CH_2COO)_2$ were found to be only 3.41 and 3.66.

There is little quantitative information on the effect of replacement of an acetic acid group by propionic acid. Schwarzenbach[3a] found the logarithm of the stability constant of calcium with β-alanine-N,N-diacetic acid, $Ca{\cdot}OOCCH_2CH_2N(CH_2COO)_2^{-1}$, to be 5.04. This shows a drop of 1.37 log K units when compared to that of nitrilotriacetic acid.

Experimental

The experimental method consisted of potentiometric titration of the amino acid in the absence of and in the presence of the metal ion being investigated. The ionic strength was maintained constant by using 0.1 M KCl as a supporting electrolyte and by employing relatively very low concentrations of metal and amino acid. The titrations were carried out using both 1:1 and 2:1 ratios for amino acid to metal ion concentration. All measurements were carried out at 30 ± 0.02°.

Apparatus.—The titration assembly consisted of a Beckman model G pH meter with extension electrodes, and a glass reaction flask of about 250-ml. capacity. The titration vessel was fitted with a mercury seal stirrer and contained 9 necks sealed into the periphery to accommodate the microburet, glass and calomel electrodes, gas inlet and outlet, and a number of hydrogen and silver–silver chloride electrodes. The platinum (hydrogen) electrodes were of

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[1] F. C. Bersworth Postdoctoral Fellow, Clark University.

[2] Calvin and Martell, "The Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., New York, N. Y., 1952, chapter 4.

[3] (a) G. Schwarzenbach, H. Ackermann and P. Ruckstuhl, *Helv. Chim. Acta*, **32**, 1175 (1949); (b) G. Schwarzenbach, E. Kampitsch and R. Steiner, *ibid.*, **28**, 1133 (1945).

conventional design and were prepared according to the method of Weissberger.[4] The silver–silver chloride electrodes were prepared according to the directions of Shedlovsky and MacInnes.[5] In place of using standard buffers, the readings of the *p*H meter were checked by comparing with the hydrogen ion concentration calculated from the e.m.f. of the cell Ag, AgCl, KCl (0.1 *M*), H^+ (buffer), H_2–Pt determined with a Leeds and Northrup type K potentiometer. The comparisons were made over the whole *p*H range under the same experimental conditions as those employed in the regular runs, with complexing agent present. Thus a "calibration" curve was obtained which converted the *p*H readings to those obtainable by the hydrogen–silver–silver chloride cell, within the limits of accuracy of the *p*H meter. In making this calculation, it was assumed that the activity coefficient of the hydrogen ion is the mean ionic activity coefficient $\gamma_\pm$ of KCl at 30°. This value, 0.77, was obtained from the data of Shedlovsky and MacInnes.[6]

Reagents.—The potassium chloride and hydrogen chloride employed were prepared from J. T. Baker Analyzed materials and the hydrochloric acid was standardized by a conventional method. Carbonate-free potassium hydroxide was prepared by the method of Schwarzenbach and Biedermann.[7] The metal solutions, prepared from reagent grade chemicals, were made up in the form of 0.0333 *M* stock solution (μ = 0.100) and standardized by the method of Jones and Martell.[8] This procedure involves titration with ethylenediaminetetraacetic acid and will be described in a subsequent publication. The iminodiacetic acid was obtained through the courtesy of the Dow Chemical Company. After several recrystallizations from water, it was found to be analytically pure. Iminodipropionic acid was prepared by alkaline hydrolysis of a sample of iminodipropionitrile, kindly donated by the American Cyanamid Company. It was purified by a number of recrystallizations from aqueous ethanol followed by recrystallization from pure methanol.

Procedure.—The following procedure was employed in each run, the metal being left out for the determination of the acid dissociation constants. About 4×10^{-5} mole of amino acid was introduced into the titration cell and half the molar amount of metal ion was added. The solution was then made up to about 200 ml. with 0.1 *M* KCl. After thermal equilibrium was reached the *p*H was determined by taking a number of successive readings. The *p*H readings were then taken after the addition of small increments of 0.1 *M* KOH until the *p*H reached 10.5–11.0. The solution was maintained free of carbon dioxide by passing through it CO_2-free nitrogen, which had previously been passed through a presaturator containing 0.1 *M* KCl. Similar determinations were made with a 1:1 molar ratio of complexing agent to metal ion.

Experimental Results.—The results of the experimental measurements are presented in graphic form in Figs. 1 and 2, for the 1:1 ratio of amino acid to metal ion, in Figs. 3 and 4 for 2:1 ratio of amino acid to metal ion. The *p*H values plotted were previously corrected by the calibration method described above. These titration curves indicate qualitatively the formulas of the metal chelates formed and the relative magnitudes of the acid dissociation constants. These facts were necessary in justifying the equations employed in the calculation of the equilibrium constants, described in the next section. Consideration of the significance of the titration curves obtained is reserved for the discussion of results.

Calculation of Acid Dissociation Constants.—The acid dissociation constants were calculated from the titration curves (Figs. 1 and 2) by a direct algebraic method, and by an adaptation of Bjerrum's method. The equilibria involved and dissociation constants to be determined are

$$H_2A \rightleftharpoons HA^- + H^+ \quad k_1 = (H^+)(HA^-)/(H_2A) \qquad (1)$$

$$HA^- \rightleftharpoons A^{-2} + H^+ \quad k_2 = (H^+)(A^{-2})/(HA^-) \qquad (2)$$

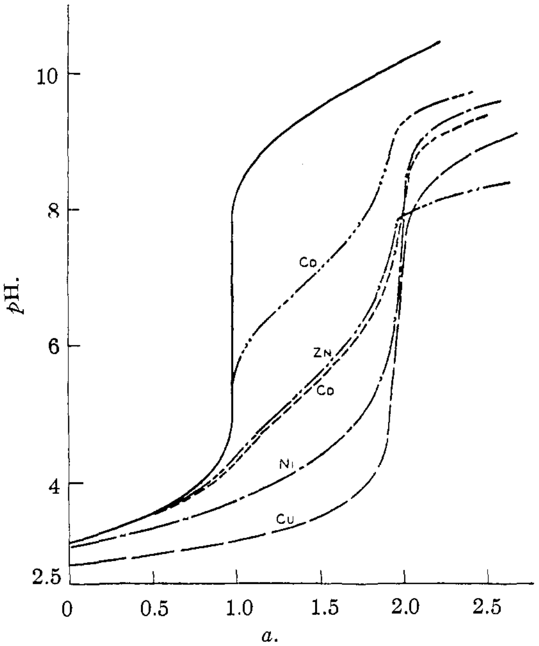

Fig. 1.—Titration curves of iminodiacetic acid (IMDA) $C_A/C_M = 1/1$: *a* = moles of base added per mole of acid.

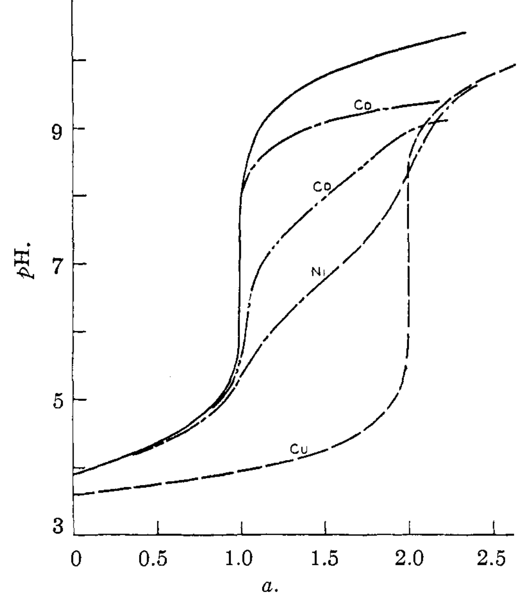

Fig. 2.—Titration curves of iminodipropionic acid (IMDP) $C_A/C_M = 1/1$: *a* = moles of base per mole of acid.

where H_2A represents iminodiacetic acid and iminodipropionic acid, and parentheses represent molar concentrations. Since $k_1 >>> k_2$, each dissociation stage was considered separately. If C_A represents the total concentrations of amino acid species and *a* represents the number of moles of base added per mole of amino acid present, it follows that in the low *p*H buffer region

$$C_A = (H_2A) + (HA^-) \qquad (3)$$

$$aC_A + (H^+) = (HA^-) \qquad (4)$$

Hence the first dissociation constant may be calculated from the relationship

$$k_1 = \frac{(H^+)[aC_A + (H^+)]}{C_A - [aC_A + (H^+)]} \qquad (5)$$

In the high-*p*H buffer region the concentration of the acid

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[4] Weissberger, "Physical Methods of Organic Chemistry," 2nd Ed., Vol. II, Interscience Publishers, Inc., New York, N. Y., 1945, p. 1722.

[5] T. Shedlovsky and D. A. MacInnes, THIS JOURNAL, 58, 1970 (1936).

[6] T. Shedlovsky and D. A. MacInnes, *ibid.*, 59, 503 (1937).

[7] G. Schwarzenbach and W. Biedermann, *Helv. Chim. Acta*, 31, 339 (1948).

[8] L. A. Jones and A. E. Martell, unpublished work.

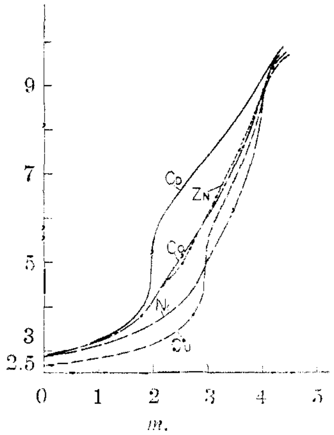

Fig. 3.—Titration curves of iminodiacetic acid (IMDA) $C_A/C_M = 2/1$: m = moles of base added per mole of metal ion.

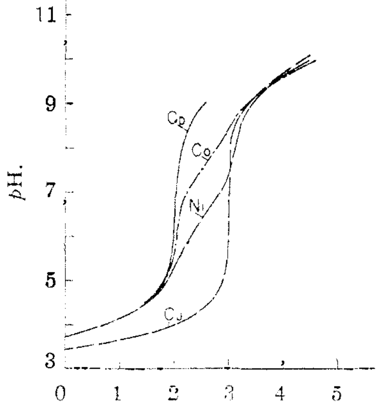

Fig. 4.—Titration curves of iminodipropionic acid (IMDP) $C_A/C_M = 2/1$: m = moles of base added per mole of metal ion

form (H_2A) of the amino acid may be neglected, and equations (3) and (4) become

$$C_A = (HA^-) + (A^{-2}) \qquad (6)$$

$$(a - 1)C_A - (OH^-) = (A^{-2}) \qquad (7)$$

Under these conditions k_2 is expressed by

$$k_2 = \frac{(H^+)[(a - 1)C_A - (OH^-)]}{C_A - [(a - 1)C_A - (OH)^-]} \qquad (8)$$

This method of calculation was checked by employing the Bjerrum[9] approach to the determination of step equilibria, in which the hydrogen ion is considered the ligand and the amino acid anion, (A^{-2}), is considered the central ion. Thus $\bar{n}$, the number of moles of ligand bound per mole of central ion becomes

$$\bar{n} = \frac{(HA^-) + 2(H_2A)}{C_A} \qquad (9)$$

The calculated values of $\bar{n}$ are plotted *vs.* pH. The values of pH at $\bar{n} = 0.5$ and $\bar{n} = 1.5$ are equal to pk_2 and pk_1, respectively.

Calculation of Chelate Stability Constants.—The first and second chelate formation constants were calculated from 2:1 titration curves (Figs. 3 and 4) by an adaptation of Bjerrum's method. The data obtained from the 1:1 titrations (Figs. 1 and 2) were employed in the calculation of the first metal chelate formation constant by a direct algebraic method.

The equilibria involved in chelate formation may be expressed as

$$M^{+2} + A^{-2} \rightleftarrows MA \quad K_1 = (MA)/(M^{+2})(A^{-2}) \quad (10)$$

$$MA + A^{-2} \rightleftarrows MA_2^{-2} \quad K_2 = (MA_2^{-2})/(MA)(A^{-2}) \quad (11)$$

where M^{+2} represents any of the divalent metal ions employed, and the other symbols have the same meaning as before. If C_M represents the total concentrations of metal ion species, the following relationships hold for solutions of amino acid and metal ion

$$C_A = (H_2A) + (HA^-) + (A^{-2}) + (MA) + 2(MA_2^{-2}) \qquad (12)$$

$$C_M = (M^{+2}) + (MA) + (MA_2^{-2}) \qquad (13)$$

$$aC_A + (H^+) - (OH^-) = (HA^-) + 2(A^{-2}) + 2(MA) + 4(MA_2^{-2}) \qquad (14)$$

In order to calculate (A^{-2}), equation (14) is subtracted from equation (12). From the resulting equation the values of (H_2A) and (HA^-) are eliminated by employing equations (1) and (2). The resulting expression is

$$(A^{-2}) = \frac{(2 - a)C_A - (H^+) + (OH^-)}{\frac{2(H^+)^2}{k_1k_2} + \frac{(H^+)}{k_2}} \qquad (15)$$

The average number of moles of ligand, A^{-2}, bound per mole of metal ion present is designated by $\bar{n}$, and is given by the expression

$$\bar{n} = [(MA) + 2(MA_2^{-2})]/C_M \qquad (16)$$

The quantity $(MA) + 2(MA_2^{-2})$ may be evaluated by combining equation (12) with equations (1) and (2), giving rise to the relationship for $\bar{n}$

$$\bar{n} = \frac{1}{C_M}\left(C_A - \left[\frac{(H^+)^2}{k_1k_2} + \frac{(H^+)}{k_2} + 1\right](A^{-2})\right) \qquad (17)$$

Values of $\bar{n}$ obtained from equation (17) are plotted *vs.* pA, the logarithm of $(A^{-2})^{-1}$. The value of pA at $n = 0.5$ is equal to log K_1, and the value of pA at $n = 1.5$ is taken as equivalent to log K_2. The values of K_1 and K_2 thus obtained are only approximate if they do not differ greatly in magnitude. Such approximate values may be used to calculate the exact values by successive approximations.

In the case of the 1:1 titration curves it may be assumed that at about $a = 1.5$, the amount of MA_2^{-2} at equilibrium is negligible. Calculation indicates the value of (MA_2^{-2}) to be always less than 1% of (MA) under these conditions and equations (12)-(14) are accordingly simplified. Equation (10) and simplified forms of equations (12) and (13) may be combined to give

$$K_1 = \frac{C_A - x(A^{-2})}{(A^{-2})[C_M + x(A^{-2}) - C_A]} \qquad (18)$$

where $x = \frac{(H^+)^2}{k_1k_2} + \frac{(H^+)}{k_2} + 1$. The combination of equations (18) and (15) allows a direct calculation of K_1.

Discussion of Results

Titration Curves.—The corrected potentiometric titration curves for the amino acids with and without an equivalent amount of the metal ion in the solution are given in Figs. 1 and 2. The titration curves for iminodiacetic acid and iminodipropionic acid are similar in shape, both having a strong inflection point corresponding to the monopotassium salt. The first dissociation constant is therefore much stronger than the second, and buffer regions are obtained at low and very high pH. Also, visual observation of the pure acid curves indicates that iminodiacetic acid is a stronger acid than iminodipropionic acid, since the acid buffer region occurs at a much lower pH level with the former.

The metal curves shown in Figs. 1 and 2 indicate that the second, or high, pH buffer region is greatly

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[9] J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.

lowered in the presence of metal ions, corresponding to the equilibrium

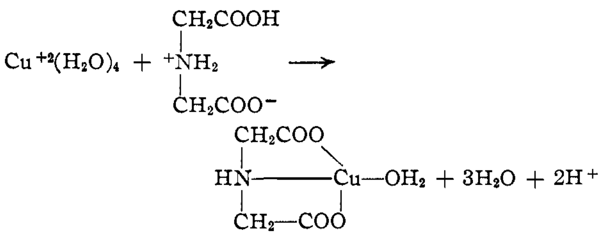
$$M^{+2} + HA^- \rightleftharpoons MA + H^+$$

where H_2A represents iminodiacetic and iminodipropionic acids. In the case of iminodiacetic acid the lowering is much greater, indicating a much higher stability for the metal complexes with this acid. In the case of cupric and nickelous ions, it is apparent that the first buffer region of iminodiacetic acid is also lowered appreciably. Hence, it is possible to write the displacement reaction

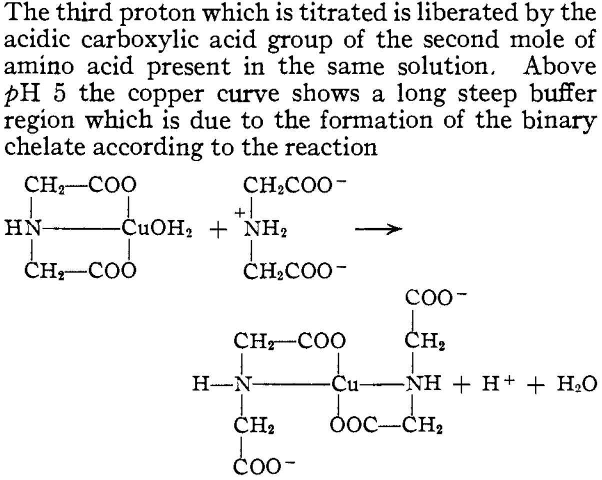
$$M^{+2} + H_2A \rightleftharpoons MA + 2H^+$$

for these metals. This is also true for the interaction of cupric ions with iminodipropionic acid. For both chelating agents the relative positions of the metal curves indicate the relative stabilities of the metal chelate to be: Cu > Ni > Co, Zn, > Cd, although in the case of iminodipropionic acid strong chelation apparently occurs only with the cupric ion.

The titration curves involving two moles of amino acid per mole of metal ion are somewhat more varied but offer much more indication of the chelation reactions involved. In the reaction between cupric ions and iminodiacetic acid, three hydrogen ions are liberated per mole of metal ion before the first rather pronounced inflection point occurs. This indicates that the first step in the reaction is probably

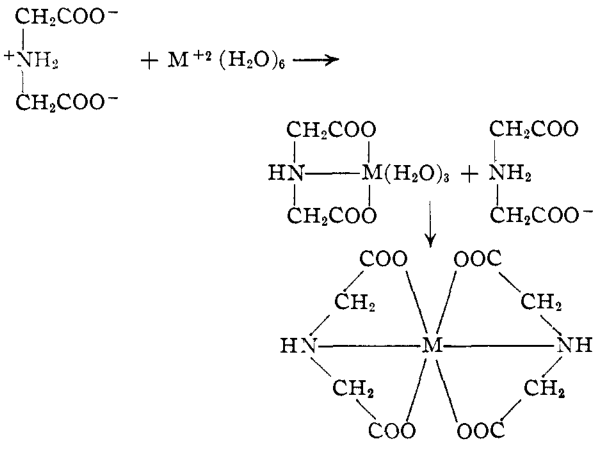


Thus two protons are liberated in the formation of the 1:1 chelate, as is also indicated by Fig. 1. The third proton which is titrated is liberated by the acidic carboxylic acid group of the second mole of amino acid present in the same solution. Above pH 5 the copper curve shows a long steep buffer region which is due to the formation of the binary chelate according to the reaction



Thus a fourth mole of base is required to complete the titration.

The remaining metal ions in Fig. 3 all show long sloping buffer regions involving the neutralization of the third and fourth protons. Chelate formation therefore occurs in two steps with considerable overlapping, and no definite inflection point at $m = 3$ is apparent for these ions. Since zinc normally has a coördination number of 4, the formulas of the 1:1 and 2:1 chelates may be represented in much the same manner as the structures given for copper, it being understood that the ligand donor groups are probably arranged tetrahedrally about the zinc ion and in a plane about the cupric ion. With Ni, Co and Cd ions the donors are probably arranged octahedrally about the central metal ion, corresponding to a coördination number of six in each case. Thus the overlapping reactions may be represented by



With the cadmium ion the formation of metal chelates apparently does not take place until the pH exceeds 5.5.

The 2:1 curves for iminodipropionic acid and cupric ion (Fig. 4) indicate a very strong pH increase at $m = 3$, indicating a still sharper demarcation between the 1:1 and 2:1 chelates. The remaining metals again show long sloping buffer regions in the range $m = 2$ to $m = 4$, with a weak inflection in the case of nickel. The structures of the chelates apparently may be formulated in the same manner as has been done for the iminodiacetic acid chelates, the main difference between the two groups of substances being the lower stability of the propionic acid derivatives. Further interpretation of the 2:1 curves for iminodipropionic acid is complicated by the fact that (1) zinc and cadmium hydroxides precipitate at high pH and (2) since the second mole of amino acid is very weakly bound the corresponding buffer region appears at such high pH values that it overlaps with hydrolysis effects in the solution.

Formation Functions.—The formation functions for iminodiacetic and iminodipropionic acid chelates, plotted in Figs. 5 and 6, respectively, give a clear indication of the relative stabilities of the 2:1 and 1:1 chelates. It is seen that the greatest difference exists between the successive chelates formed by cupric and iminodipropionate ions. This corresponds to a large value of the "spreading factor" described by Bjerrum.[9] It is interesting to note that the spreading factor is greater for the cupric iminodipropionates than for the corresponding iminodiacetates, in spite of the fact that the over-all stability is lower for the former ligand. This is also true of nickel, with a pronounced in-

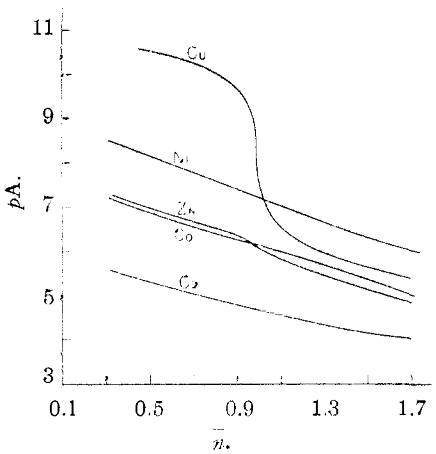


Fig. 5.—Formation functions of iminodiacetic acid (IMDA): $\bar{n}$ = average number of ligands bound per mole of metal ion; pA = negative logarithm of anion, A^{-2}, concentration.

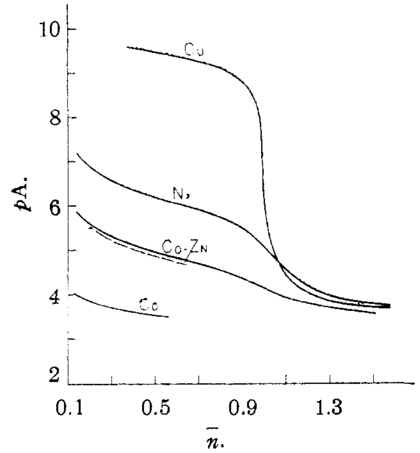


Fig. 6.—Formation functions of iminodipropionic acid (IMDP): $\bar{n}$ = average number of ligands bound per mole of metal ion; pA = negative logarithm of anion, A^{-2}, concentration.

flection in the formation function curve of Fig. 6. The remaining curves, however, show little or no break at $\bar{n} = 1$, indicating relatively small differences between the successive chelate stability constants.

Equilibrium Constants.—The acid dissociation constants and chelate stability constants, calculated by the methods outlined in the Experimental part, are summarized in Table I.[10]

Table I

Equilibrium Constants

$\gamma_{H^+} = 0.78$, $T = 30°$, $\mu = 0.1$

IMDA Iminodiacetic acid $pk_1 = 2.54$, $pk_2 = 9.12$				IMDP Iminodipropionic acid $pk_1 = 4.11$, $pk_2 = 9.61$			
	Bjerrum method		Algebraic method				From 1:1 curves
M^{+2}	log K_1	log K_2	log K_1	M^{+2}	log K_1	log K_2	log K_1
Cu^{+2}	..	5.65	10.55	Cu^{+2}	9.36	3.68	9.50
Ni^{+2}	8.21	6.35	8.30	Ni^{+2}	6.14	3.77	6.18
Co^{+2}	6.95	5.34	7.01	Co^{+2}	4.92	3.26	4.95
Zn^{+2}	7.03	5.14	7.02	Zn^{+2}	4.95[a]	..	..
Cd^{+2}	5.35	4.18	5.30	Cd^{+2}	3.51[a]	..	3.60

[a] Extrapolated to 0.5, some precipitation for greater $\bar{n}$ values.

All the acid dissociation constants were calculated by both methods described with the exception that pK_1 for iminodiacetic acid was calculated by the algebraic method only, from data (Fig. 1) in the vicinity of $a = 0.5$. It was not possible to extrapolate the corresponding formation function to $\bar{n} = 0.5$.

The 1:1 copper–iminodiacetate stability constant could not be calculated by the Bjerrum method from the 2:1 titration curve. This constant was calculated from the 1:1 titration curve by the algebraic method described.

In the case of iminodipropionic acid the precipitation of zinc and cadmium at high pH allowed calculation of the formation function only at low values. Hence, only K_1 could be calculated by Bjerrum's graphical method. For the 1:1 curves, the titration curve for zinc followed that of the amino acid up to the point where precipitation occurred. Hence, this particular curve is omitted from Fig. 2. The value of K_1 for the Cd–iminodipropionate chelate was calculated algebraically from points along the buffer region below the point of precipitation. The value thus obtained checked well with that obtained by the Bjerrum method.

In general, the stability constants calculated by the two methods employed agree reasonably well. The relative values of the constants for the various metal ions with a particular chelating anion correlate with the behavior observed by others: Co < Ni < Cu > Zn > Cd. Also, it is apparent that converting the α-amino acid grouping to a β-amino acid reduces the stability of the 1:1 and 2:1 chelates by about 10^2, except for the 1:1 Cu chelate, for which the effect is much less pronounced. The reasons for this, together with explanation of the variations observed in the spreading factors, must await further studies with analogous chelate compounds.

Acknowledgment.—The authors are indebted to the Berworth Chelate Research Organization for financial support.

Worcester, Massachusetts

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(10) Shortly after this paper was submitted for publication, metal stability constants were reported for this amino acid by Suder (J. K. Suder, Symposium on Chelate Compounds, Polytechnic Institute of Brooklyn, April 26, 1952). Since his work was carried out under somewhat different conditions no direct comparisons could be made. In general, the differences observed seemed to be in the right direction if the differences in the measurements are taken into consideration.