[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY, CLARK UNIVERSITY]

Stability of Metal Chelates. II. β-Hydroxyethyliminodiacetic Acid

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The acid dissociation constants of β-hydroxyethyliminodiacetic acid and its chelate stability constants with divalent Ca, Mg, Mn, Pb, Cd, Zn, Co, Ni and Cu ions are reported at 30° and ionic strength of 0.1. Approximate hydrolysis constants of divalent Mg, Mn, Cd, Zn, Co, Ni and Cu ions are also given. The relative values for the first chelate formation constant are: Cu > Ni > Pb > Zn > Co > Cd > Mn > Ca, while the corresponding values of the second formation constant in the order of decreasing stability are: Ni, Cd > Co > Cu > Pb > Zn > Mn.

Investigation of the stability of metal chelates of β-hydroxyethyliminodiacetic acid makes possible an interesting comparison with chelation tendencies of nitrilotriacetic acid and iminodiacetic acid. Schwarzenbach has demonstrated the high affinity of nitrilotriacetate ions for alkaline earth ions[2a] and transition metal ions.[2b] The affinity of iminodiacetate ions for metal ions has been shown to be much weaker both for the alkaline earths[3] and transition metals.[4] Although hydroxyethyliminodiacetic acid has been prepared previously,[5] its ionic equilibria with hydrogen ions and various metal ions have never been investigated. The chelate formation constants reported in the present paper were studied in order to determine the relative effects of the hydroxyethyl and acetate groups on the affinity for metal ions in aqueous solution.

Experimental

The experimental method employed in the study of dissociation and metal ion affinity of β-hydroxyethyliminodiacetic acid is the same as that described in a previous publication.[4] The only deviation from this procedure was the use of a hydrogen atmosphere in runs involving Mn^{+2} ions, and the fact that the metal ion concentration was 3.5×10^{-3} M in runs for which the ratio of metal ion to amino acid concentration was 1:1, while the metal ion concentration was 1.25×10^{-3} M in runs where the ratio was 1:2. The β-hydroxyethyliminodiacetic acid was synthesized by a method which will be described in a subsequent publication.[6] It was purified by repeated recrystallization from hot water.

Experimental Results.—The potentiometric titration data for β-hydroxyethyliminodiacetic acid in the presence of, and in the absence of, an equivalent concentration of metal ion are given in graphic form in Fig. 1. The pH values were corrected in the manner previously described. Similar data are presented in Fig. 2 for a 2:1 ratio of amino acid to metal ion. The significance of these curves is given in the discussion.

Calculations.—The calculations were carried out in the same manner as has been described in the first paper in this series.[4] The acid dissociation constants were calculated both by an algebraic method and by a modification of Bjerrum's method. The 1:1 metal chelate titration curves were used for the calculation of stability constants by both methods, and the 2:1 curves were used as a basis for the graphical Bjerrum method only.

Calculation of Hydrolysis Constants.—Although all titrations of the divalent metal ions were carried out in regions where no precipitation of metal hydroxide takes place, it was thought that the formation of the monohydroxo complexes of these ions in aqueous solution might have some influence on the equilibria being studied. Therefore, the metals being investigated were also checked for hydrolysis by titration with hydroxide ion under the same conditions as those employed in the presence of the amino acid. The potentiometric data for these calculations are presented graphically in Fig. 3. Experimentally, the curves were obtained by acidifying the solution of the metal ion with 0.1 M HCl and titrating with 0.1 M KOH. The metal ion concentration was about 0.01 molar in each case, and the ionic strength was maintained at 0.1 by the use of potassium chloride solution as a diluent. In the flat portion of the curves of Fig. 3 precipitation occurred and equilibrium was reached very slowly, a number of hours being required to reach equilibrium at each point in this region of the curve.

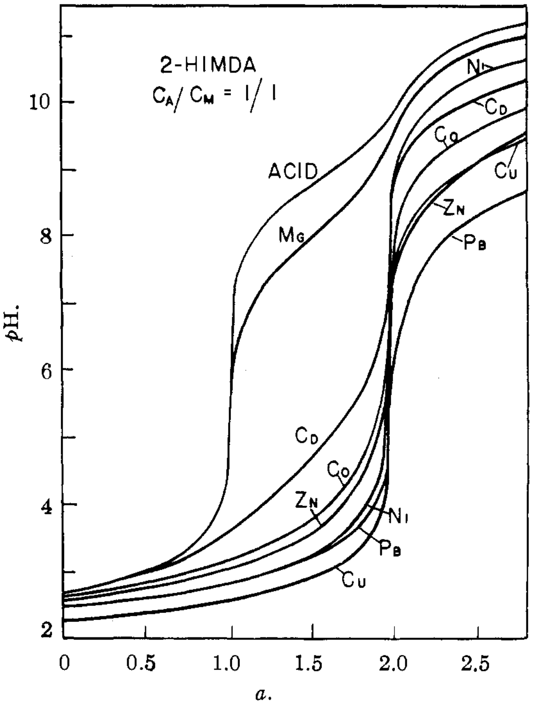

Fig. 1.—Titration curves of β-hydroxyethyliminodiacetic acid (2-HIMDA): C_A and C_M are total molar concentrations of amino acid and metal species, respectively; a = moles of base added per mole of acid.

Approximate values of the first hydrolysis constants of the metal ions were calculated on the alkaline side of the titration curve in the region indicated by Fig. 4. The two curves shown in Fig. 4 represent the titration of the same quantities of hydrochloric acid with a standard KOH solution, the only difference being the addition of a metal salt to one of the solutions. The ionic strength of each solution was maintained at a value of 0.1 by the addition of potassium chloride. The same is also true of the titration curves shown in Fig. 3. The calculation was carried out using pairs of points (A + B of Fig. 4) chosen at the same total volume. The equations involved in the first hydrolysis are

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

[2] (a) G. Schwarzenbach, H. Ackermann and P. Ruckstuhl, *Helv. Chim. Acta*, **32**, 1175 (1949); (b) G. Schwarzenbach and E. Freitag, *ibid.*, **34**, 1492 (1951).

[3] G. Schwarzenbach, E. Kampitsch and R. Steiner, *ibid.*, **28**, 1133 (1945).

[4] S. Chaberek, Jr., and A. E. Martell, THIS JOURNAL, **74**, 5052 (1952).

[5] Kiprianow, *Ukr. Chemic. Z.*, **4**, 239 (1929); *Chem. Zentr.*, **100**, II, 2880 (1929).

[6] S. Chaberek, Jr., F. C. Bersworth and A. E. Martell, unpublished work.

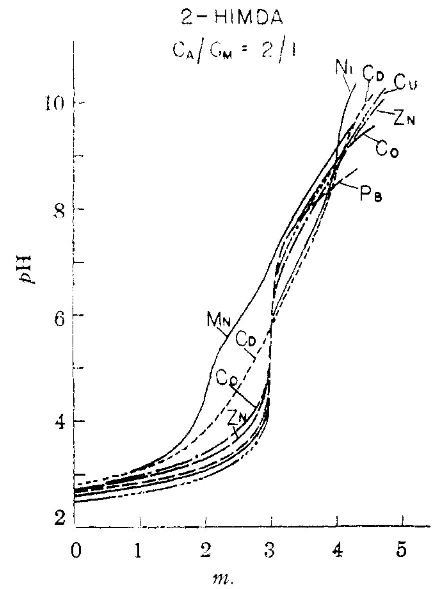


Fig. 2.—Titration curves of β-hydroxyethyliminodiacetic acid (2-HIMDA): C_A and C_M are total molar concentrations of amino acid and metal species, respectively; m = moles of base added per mole of metal ion.

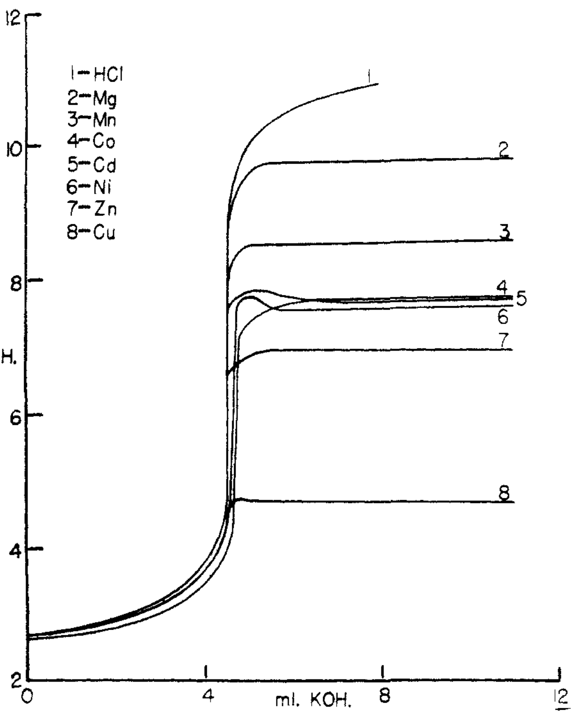


Fig. 3.—Hydrolysis curves of metal ions.

$$M(H_2O)_n^{+2} \rightleftharpoons H^+ + [M(H_2O)_{n-1}OH]^+$$

$$K = \frac{(H^+)(M(H_2O)_{n-1}\,OH^+)}{M(H_2O)_n^{+2}}$$

$$\text{or } k = \frac{(MOH^+)K_w}{(M^{+2})(OH^-)}$$

where ( ) signify molar concentration and other terms have their usual significance. Since

$$(MOH^+) = (H^+)_B - (H^+)_A$$

and

$$C_M = (M^{+2}) + (MOH^{+1})$$

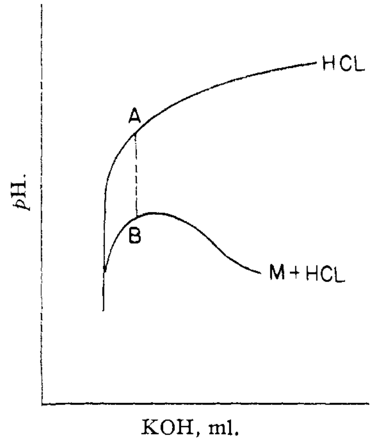


Fig. 4.—Calculation of metal hydrolysis.

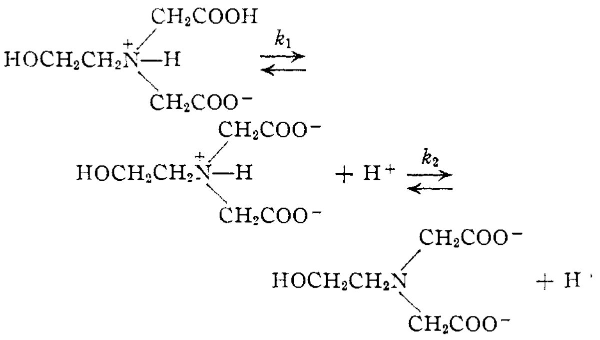
it follows that

$$k = \frac{[(H^+)_B - (H^+)_A]K_w}{[C_M - (H^+)_B + (H^+_A)](OH^-)}$$

The hydrolysis constants thus calculated were considered to be concentration constants applying at 0.1 ionic strength and 30.0°.

Discussion of Results

The potentiometric titration of β-hydroxyethyliminodiacetic acid given in Fig. 1 indicates one strongly acid carboxyl group and a weakly acid substituted ammonium group. Thus the ionization takes place in two steps



$$HOCH_2CH_2\overset{+}{N}H(CH_2COOH)(CH_2COO^-) \underset{}{\overset{k_1}{\rightleftharpoons}} HOCH_2CH_2\overset{+}{N}H(CH_2COO^-)_2 + H^+ \overset{k_2}{\rightleftharpoons} HOCH_2CH_2N(CH_2COO^-)_2 + H^+$$

There is no evidence in the titration curves for the ionization of the hydroxyl group in the absence of heavy metal ions.

The metal titrations shown in Fig. 1 have a definite inflection at two moles of base per mole of metal ion, indicating that the 1:1 chelate of the divalent anion is a stable entity with stability extending over an appreciable pH range. Thus, the curves show that all the metals investigated react with the monovalent anion according to the equation

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

The positions of the metal curves also indicate all the chelates to be quite stable with the exception of the magnesium compound which is relatively weak, and the cadmium chelate, which has intermediate stability. The Co, Zn, Ni, Pb and Cu chelates are apparently so stable that they form even in the strongly acid solution where the undissociated form of the amino acid predominates. Hence we may write

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

for these metals.

An important aspect of the titration curves of Fig. 1 is the fact that the less basic metals show pronounced buffer regions beyond two moles of base per mole of metal ion. The less basic the metal the lower this buffer region seems to be. Thus while copper forms the most stable chelate, and lead and nickel form chelates which are only slightly less stable, the lead chelate is the most strongly hydrolyzed in alkaline solutions, whereas the more basic nickel ion is not appreciably affected. There are two alternative interpretations of the further interaction of the chelates with base. One involves the formation of a hydroxo complex of the chelate as a result of dissociation of a proton from one of the metal-bound water molecules, while the other involves the dissociation of a proton from the hydroxyethyl group. This question is discussed below in connection with the question of structure of these chelates.

The 2:1 titration curves illustrated in Fig. 2 show a strong inflection point at three moles of base per mole of metal ion except in the case of Cd^{++} and Mn^{++} ions. This indicates that the 1:1 chelate is formed as a separate and stable compound in solutions with no appreciable formation of the 2:1 chelate. At higher *p*H all metals react with an additional mole of base and produce the 2:1 chelate. Thus the titration curves may be explained by the reactions

First inflection point at $M = 3$ $\quad H_2A + M^{+2} + 2OH^- \longrightarrow MA + 2H_2O$

$H_2A + OH^- \longrightarrow HA^- + H_2O$

Second inflection point at $M = 4$ $\quad MA + HA^- + OH^- \longrightarrow MA_2^{-2} + H_2O$

It may be noted that the 2:1 curves of Fig. 2 show little tendency for the 2:1 chelates to react further with base (except possibly in the case of lead) in the high *p*H region. This is probably due in part to the fact that the metals are coördinately saturated in these compounds, whereas this is not the case for the 1:1 chelates.

The 2:1 titration curves for Mn and Cd show long sloping buffer regions between two and four moles of base per mole of metal ion, showing that the formations of the 1:1 and 2:1 chelates overlap. This is indicated very clearly by the plot of the formation functions of the metal chelates in Fig. 5. It is apparent that overlapping is greatest with cadmium and almost as complete with Mn. All the other metal chelates shown have moderately large separation factors except for Ca, which is not given in Figs. 1 and 2. The same would probably be true of Mg, which is not shown in Figs. 2 and 5. The relative positions of the formation curves indicate the relative values of K_1 for the various 1:1 chelates to be: Pb, Ni > Zn > Co > Cd > Mn > Ca, Mg?, while the relative values of K_2 decrease in the order: Ni, Cd > Co > Cu, Pb, Zn > Mn > Ca?, Mg?.

Hydrolysis Constants.—The hydrolysis constants calculated as described above for the various metal ions titrated according to Fig. 3 are listed in Table I. The calculations involve the assumption that the reaction goes as indicated.

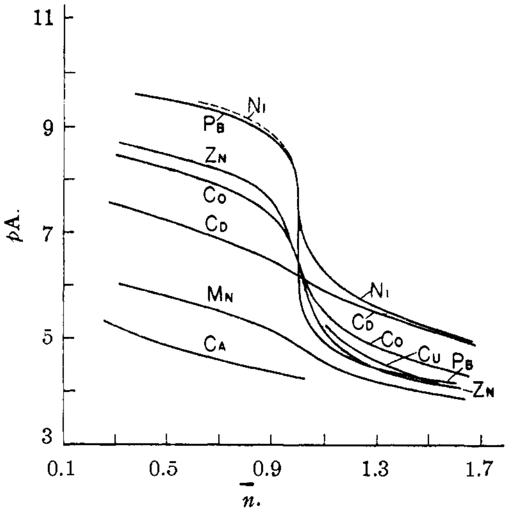


Fig. 5.—Formation functions of β-hydroxyethyliminodiacetic acid (2-HIMDA): $\bar{n}$ = average number of ligands bound per mole of metal ion; *p*A = negative logarithm of anion, A^{-2}, concentration.

TABLE I

FIRST HYDROLYSIS CONSTANTS OF VARIOUS METALS

$T = 30°, \mu = 0.1$

M	*pk*	*k*
Cu^{+2}	6.8	2×10^{-7}
Ni^{+2}	9.4	4×10^{-10}
Co^{+2}	8.9	1×10^{-9}
Zn^{+2}	8.7	2×10^{-9}
Cd^{+2}	11.6	2×10^{-12}
Mn^{+2}	10.6	2×10^{-11}
Mg^{+2}	12.8	1×10^{-13}

There may be some uncertainty in the case of the cupric ion, because of its known tendency to form chloro complexes. At best the values of *k* listed are reliable to only one significant figure. However, these hydrolysis studies served the important purpose for which they were undertaken: to determine the possible effects of hydrolysis on the calculation of the chelate stability constants for these ions. Calculation of the effect of hydrolysis on the concentration of metal ions in the region of the titration curves employed for the calculation of equilibrium constants showed that hydrolysis has no effect within the experimental error. The relative values of the constants listed are in agreement with the order of basicity of these metal ions, and the relative order of stability of these metals with other ligands. Note, for example, the rough agreement with the first hydrolysis constants listed by Bjerrum.[7]

Acid Dissociation Constants.—The first and second acid dissociation constants of β-hydroxyethyliminodiacetic acid are listed in Table II. The first constant (pk_1 = 1.96) corresponds to a strongly acidic carboxyl group, and is characteristic of the grouping  $R_2\overset{\overset{\displaystyle H}{|}}{N}{}^+CH_2COOH$. This value is comparable to that of the analogous compound iminodiacetic acid (pk_1 = 2.54) reported by Chaberek and Martell[4] and has practically the same value as the dissociation constant of nitrilotriacetic acid (pk_1 = 1.89) reported by Schwarzenbach and Freitag.[2b]

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[7] J. Bjerrum, "Metal Ammine Formation in Aqueous Solutions," P. Haase & Son, Copenhagen, 1941, p. 75.

It is interesting to note that the amino group of β-hydroxyethyliminodiacetic acid is less basic (pk_2 = 8.78) than the corresponding values for iminodiacetic acid (9.12[4]) and much less basic than the amino nitrogen of nitrilotriacetic acid (9.73[2]). This would tend to decrease the affinity of the hydroxyethyl derivative for metal ions in comparison with the more basic complexing agents.

TABLE II

EQUILIBRIUM CONSTANTS

$\gamma_{H^+} = 0.78$, $T = 30.0°$, $\mu = 0.1$, $pk_1 = 1.96$, $pk_2 = 8.78$

Metal	Bjerrum method log K_1	Bjerrum method log K_2	Algebraic method log K_1
Cu^{++}	..	4.23	>10
Ni^{++}		5.15	9.54
Pb^{++}	9.40[a]	4.17	9.50
Zn^{++}	8.57	4.10	
Co^{++}	8.27	1.44	
Cd^{++}	7.12	5.12	
Mn^{++}	5.65	3.93	
Mg^{++}	3.54		
Ca^{++}	4.83		

[a] $\bar{n}$ extrapolated to 0.5.

The results of the calculations of chelate stability constants by both methods given in Table II seem to be in good agreement within the experimental error, which is at least 0.1 log K unit for the higher constants, but much less than this for the lower constants. In this case a number of K_1 values were determined by the Bjerrum graphical method, as indicated. In the case of Cu and Ni the Bjerrum method could not be used since even in the most acid solutions the degree of dissociation was considerably less than 50% and hence no value of (A^{-2}) was available for $\bar{n} = 0.5$. This was also true of the Pb chelate. However, in this case an additional run was made in a more dilute solution and the Bjerrum formation function approached closely enough to 0.5 to allow extrapolation with a fair degree of certainty. The constant for Ni, and a better constant for Pb were obtained by the algebraic method previously described. However, in the case of Cu, the stability of the chelate is sufficiently high, and the pH of the solution is sufficiently low, so that it was not possible to calculate the stability constant even by the algebraic method. However, it was possible to calculate the second stability constant (log K_2) of the copper chelate by the Bjerrum method.

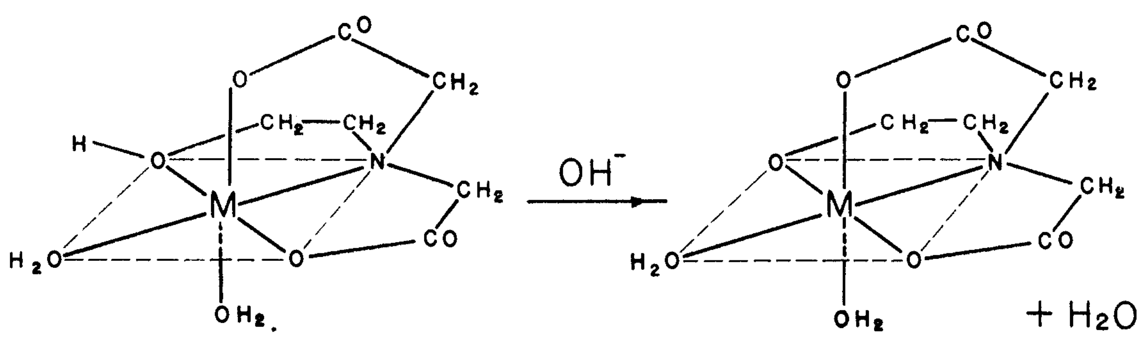
A comparison of the 1:1 chelate stability constants of various metals with nitrilotriacetic acid (NTA), β-hydroxyethyliminodiacetic acid (2-HIMDA), and iminodiacetic acid (IMDA) is given in Table III. The most obvious and striking fact is that in all cases the stabilities of the metal chelates of iminodiacetic acid are greatly increased when an amino hydrogen atom is replaced by the hydroxyethyl group. Also, the stability constants of 2-HIMDA have values which in all cases are very nearly two log K units below the corresponding values for nitrilotriacetic acid. These two sets of observations, taken together, demonstrate that the hydroxyethyl group definitely takes part in chelate formation, but that the hydroxyl oxygen has much less affinity for metal ions than a carboxylate oxygen. Thus we may represent an octahedral metal chelate of 2-HIMDA as having a tetradentate structure (formula I). This structure, in which the hydroxyl oxygen is directly bound to the metal ion suggests a probable explanation of the further reaction of the 1:1 chelates with base, as is indicated in Fig. 1. It seems that the acidity of the hydroxyl hydrogen would be increased sufficiently to cause dissociation in alkaline solution to give a chelate structure involving the ethoxide group (formula II). This would not, of course, preclude further hydrolytic reactions involving bound water molecules. Probably both types of reactions occur simultaneously.

TABLE III

COMPARISON OF CHELATION TENDENCIES OF NTA, 2-HIMDA AND IMDA

Metal ion	log K_1 NTA[a]	log K_1 2-HIMDA[b]	log K_1 IMDA
Cu	12.7	>10	10.6[c]
Ni	11.3	9.5	8.3[c]
Co	10.6	8.3	7.0[c]
Mn	7.4	5.6	
Zn	10.4	8.6	7.0[c]
Cd	9.5	7.1	5.3[c]
Pb	11.8	9.5	
Mg	5.4	3.5	3.6[d]
Ca	6.4	4.8	3.4[d]

[a] Determined by Schwarzenbach, *et al.*[2] [b] Reported in this publication. [c] Reported by Chaberek and Martell.[4] [d] Reported by Schwarzenbach, *et al.*[3]



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