

# New Multidentate Ligands. VI. Chelating Tendencies of N,N'-Di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic Acid<sup>1</sup>

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**Abstract:** The synthesis and study of a new multidentate ligand, N,N'-di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic acid (HBED), is described. Acid dissociation constants and metal chelate stability constants are determined by potentiometric and spectrophotometric methods. The new ligand is found to be highly selective for Fe(III), the corresponding chelate having the highest stability ( $10^{39.68}$ ) of any 1:1 ferric chelate of a multidentate ligand thus far reported. The binding of the ligand donor groups to divalent metal ions frequently takes place in a stepwise fashion. The order in which each phenolate group becomes coordinated to metal ions, and the structures of the intermediate complexes, are deduced by correlating absorption spectra with potentiometric data. Ligand donor group reactivities are compared with those of the analogous ligands N,N'-ethylenediaminediacetic acid and N,N'-ethylenebis[2-(*o*-hydroxyphenyl)]glycine (EHPG), and structural comparisons are made. The stability constant of the Fe(III)-HBED chelate is nearly  $10^6$  times greater than that of the most stable ferric chelate (Fe(III)-EHPG) previously known.

Recent investigations<sup>3,4</sup> have shown the usually high stability of the Fe(III) chelate N,N'-ethylenebis[2-(*o*-hydroxyphenyl)]glycine (EHPG) to be due to the high affinity of Fe(III) for the two phenolate groups present in the ionized ligand and to orientation of these groups so as to permit participation in chelate ring formation. The structure of EHPG is such, however, that steric hindrance may interfere somewhat with participation of all six donor groups (two basic nitrogens, two carboxylate groups, and the two phenolate groups) in simultaneous coordination at the six most favorable positions about an octahedral metal ion. For this reason attempts have been made by several investigators to synthesize a new chelating agent, N,N'-di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic acid (HBED), with a more favorable arrangement of the same donor groups. This is the first report of a successful synthesis of this compound (by I. M.), the determination of its protonation constants, and its stability constants with various divalent and trivalent metal ions.

## Experimental Section

**Apparatus and Procedure.** The interaction of HBED with metal ions was measured potentiometrically and spectrophotometrically. A Radiometer pH meter (Type PMH4), fitted with glass and calomel extension electrodes, was used for measuring the free hydrogen ion concentration. The ionic strength was maintained constant at 0.10 *M* by adding an adequate amount of potassium nitrate. Since HBED is a sexadentate ligand, only 1:1 complexes are expected; therefore only 1:1 ratios of ligand to metal were investigated, except for the weakly bound Ca(II) and Mg(II) ions. For chelates of these metal ions, the calculation of the stability constants was simplified by measuring solutions containing both excess (10:1) and equivalent (1:1) molar ratios of metal ion to ligand. During all the titrations the temperature was maintained

constant at 25° and a stream of CO<sub>2</sub>-free nitrogen gas was passed through the titration flask.

The visible and ultraviolet absorption spectra of the ligand and metal chelate solutions were determined with a Cary Model 14 recording spectrophotometer.

**Materials.** The standard metal salt solutions, having a concentration of about 10<sup>-2</sup> *M*, were prepared from reagent grade nitrates and chlorides and were standardized by direct titration with ethylenediaminetetraacetic acid in the presence of a suitable indicator.<sup>5</sup> Carbonate-free potassium hydroxide was used in all titrations.

**N,N'-Di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic Acid (HBED).** To 1.8 g (0.010 mole) of ethylenediamine-N,N'-diacetic acid, which was neutralized with 0.80 g of sodium hydroxide in 10 ml of water and diluted with 25 ml of ethanol, 4.6 g (0.020 mole) of *o*-acetoxybenzyl bromide was added. The clear solution was maintained at 35–40° while 1.0 g of sodium hydroxide as a 30% aqueous solution was added with stirring at such a rate as to maintain a pH corresponding to the blue-violet color of a phenolphthalein-thymolphthalein mixed indicator. The reaction mixture was then heated at 60° for 1 hr, a second addition of 1.0 g of sodium hydroxide as a 30% aqueous solution was made, and the solution was further heated at 70° for 2 hr. Ethanol was removed by distillation under reduced pressure and the residue was diluted to 70 ml with water. The pH of the solution was brought to 1–1.5 by the addition of concentrated hydrochloric acid; the solution was filtered and allowed to stand at ice-bath temperature overnight. The product, N,N'-di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic acid, was obtained as the crystalline dihydrochloride and was recrystallized from boiling water. The yield of purified material was 2.4 g. The recrystallized product sintered at 130–134° and melted at 139° with decomposition.

*Anal.* Calcd for C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>·2HCl·2H<sub>2</sub>O: C, 48.3; H, 6.04; N, 5.64. Found: C, 48.16; H, 5.94; N, 5.73.

This material is slightly soluble in water, and a 2.0 × 10<sup>-3</sup> *M* solution may be prepared at room temperature; however, the velocity of dissolution is very slow.

## Results

**Determination of Protonation Constants.** Since there is no overlapping of the buffer regions for the third and fourth association constants of the ligand, the log *K* values were calculated separately from potentiometric data. The first two association reactions occur only above pH 10, where potentiometric measurements become inaccurate. The first two association steps of the ligand were measured spectrophotometrically, since they involve the combination of protons with the

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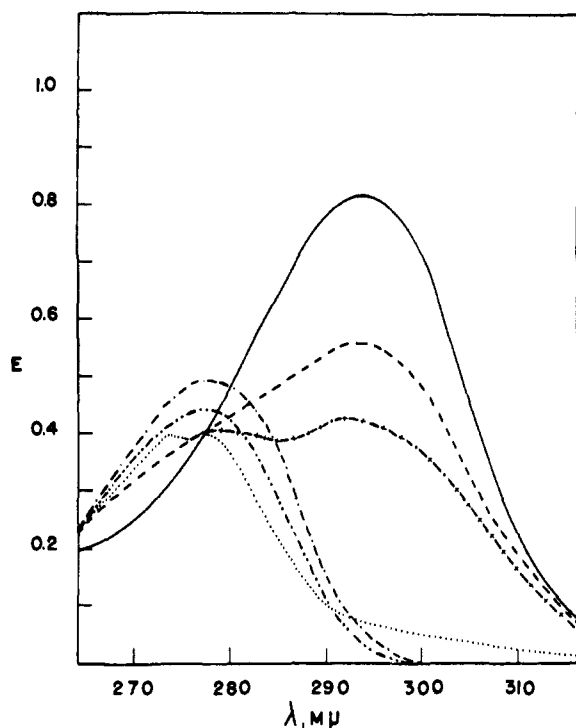


Figure 1. Ultraviolet spectra of HBED as a function of pH: ----, pH 2.68; - · - · - ·, pH 4.71; · · · · ·, pH 8.29; - - - - - + - + - +, pH 11.99; - - - - - - - - - -, pH 12.47; ———, pH 13.95;  $[\text{HBED}]_t = 1.00 \times 10^{-4} M$ ;  $\mu = 0.10 M (\text{KNO}_3)$ ; 1.00-cm cell,  $25^\circ$ .

phenolic groups and are therefore accompanied by extensive changes in the absorption spectra.

The absorption spectra of HBED, measured over a wide pH range, are shown in Figure 1. The measured extinction  $E$  is the sum of the products of the molar extinction coefficient  $\epsilon_{H_p L}$  ( $p = 0, 1, 2, 3$ , and  $4$ ) and the concentrations of the corresponding species,  $H_p L$ .

$$E = \sum_0^4 \epsilon_{H_p L} [H_p L] \quad (1)$$

$E$  and  $\epsilon_{H_p L}$  must correspond to the same wavelength. The total ligand concentration is also known.

$$L_t = \sum_0^4 [H_p L] = \sum_0^4 K_p^H [H^+]^p [L] \quad (2)$$

$$\beta_p^H = \frac{[H_p L]}{[H^+]^p [L]} \quad (3a)$$

also

$$K_p^H = \frac{[H_p L]}{[H^+]^p [H_{p-1} L]} \quad (3b)$$

With the aid of these relations, the first and second proton association constants ( $K_1^H$  and  $K_2^H$ , respectively) may be determined, as described below.

Application of the above equations to this ligand requires the determination of a set of five extinction coefficients and a set of four protonation constants, whose values should be such that (1) and (2) are satisfied for every point. Because of inevitable experimental errors there will always be some difference between the measured  $E$  and the sum calculated with eq 1. The unknown parameters are to be so chosen that this difference is minimized. The solution is simplified by the fact that some quantities are already known and

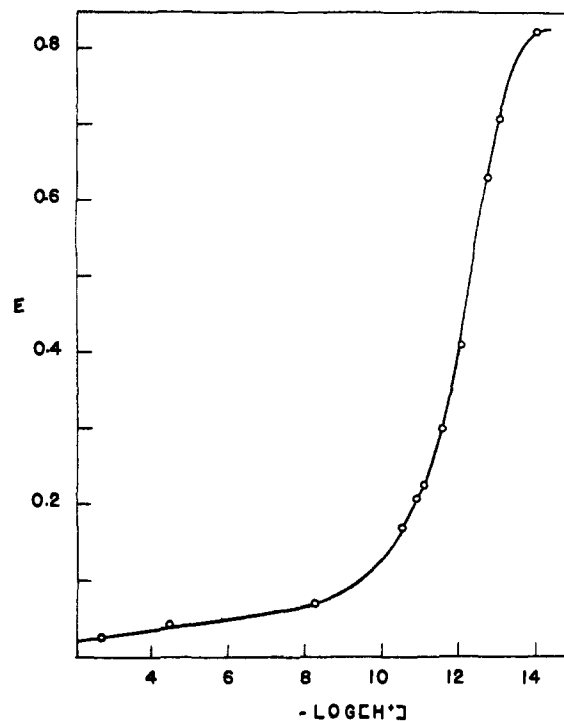


Figure 2. Variation of extinction coefficient at  $294 m\mu$  as a function of pH; the points are calculated values.  $[\text{HBED}]_t = 1.00 \times 10^{-4} M$ ;  $\mu = 0.10 M (\text{KNO}_3)$ ; 1.00-cm cell.

some others are readily obtained, since part of the transition  $H_4 L$  to  $L^{4-}$  takes place in separate steps. The calculation is therefore divided in the following way.

(a) Independent determination of  $K_4^H$  and  $K_3^H$  from the alkalimetric titration curve.

(b) Direct measurement of the extinction coefficients of certain species under conditions where all others are present in negligible amounts. The extinction coefficient of  $H_4 L$  is measured in the pH range 2–3, where the HBED solutions have a constant extinction, indicating the absence of ionized forms of the ligand. Similarly the extinction coefficient of  $L^{4-}$  was measured at pH 14 where the ligand is completely ionized.

(c) The extinction coefficients of  $H_3 L^-$  and  $H_2 L^{2-}$  were obtained from absorption spectra taken under pH 10, where the concentrations of  $HL^{3-}$  and  $L^{4-}$  are negligible. The spectra were measured at pH values which correspond approximately to the values of  $\log K_4^H$  and  $\log K_3^H$ .

(d) On the basis of the above, the only terms in eq 1 and 2 that are still unknown are  $\epsilon_{HL}$ ,  $K_1^H$ , and  $K_2^H$ . These parameters may then be determined by absorption measurements between pH 12.50 and 13.50, where only  $L^{4-}$  and  $HL^{3-}$  are present. A value for  $K_1^H$  is determined so as to give a constant value of  $\epsilon_{HL}$  for a given wavelength at different pH values within the specified range. In a similar manner, the value of  $K_2^H$  is determined in a lower pH range (*i.e.*, between pH 10.50 and 11.50). The values obtained for  $\epsilon_{HL}$ ,  $K_1^H$ , and  $K_2^H$  were then varied, until the differences between measured and calculated extinctions were minimized. The logarithms of the protonation constants thus obtained for  $\mu = 0.10 M (\text{KNO}_3)$ ,  $25^\circ$ , are  $K_1^H = 12.46$ ,  $K_2^H = 11.00$ ,  $K_3^H = 8.32$ , and  $K_4^H = 4.64$ .

Figure 2 illustrates the measured extinction at  $294 m\mu$ , the wavelength at the maximum of the phenolate

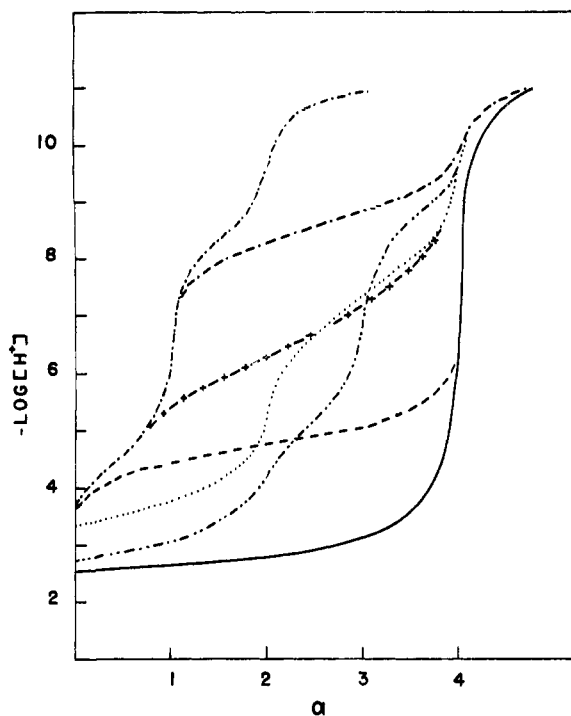
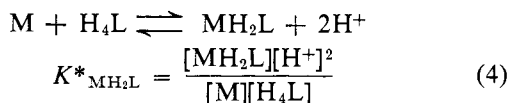


Figure 3. Potentiometric titration of various metal nitrates in the presence of equivalent quantities of HBED; abscissa  $a$  represents moles of base added per mole of ligand present; ---, ligand; - - - - -,  $\text{Ca}^{2+}$ ; - + - + - +,  $\text{Mn}^{2+}$ ; ·····,  $\text{Cd}^{2+}$ ; - - - - -,  $\text{Lu}^{3+}$ ; - ·····,  $\text{Cu}^{2+}$ ; ———,  $\text{Fe}^{3+}$ ;  $\mu = 0.10 \text{ M} (\text{KNO}_3)$ ,  $25^\circ$ .

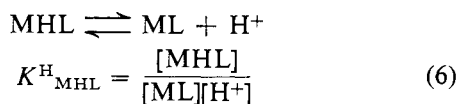
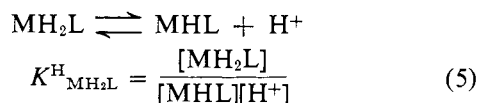
absorption band (Figure 1), as a function of pH. The sharply rising part of the curve between pH 9 and 14 may be considered a measure of the degree of association of the two phenolic groups.

#### Potentiometric Determination of Stability Constants.

Sample potentiometric titration curves obtained in this investigation are shown in Figure 3. The shapes of the curves clearly show the different types of reactions observed, involving the formation of simple mononuclear chelates, as well as various protonated chelates. The most common initial reaction involving divalent transition metal ions is a two-proton displacement to form a dihydrogen complex.



This is generally followed by two subsequent dissociation reactions, in which 2 additional moles of base is required per metal chelate.



In the cases of  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ , and  $\text{Pb}^{2+}$ , the buffer regions of the above reactions do not overlap, so that each reaction step is apparent in the titration curves, and equilibrium constants for each step may be calculated separately. In the case of  $\text{Cd}^{2+}$ , the last

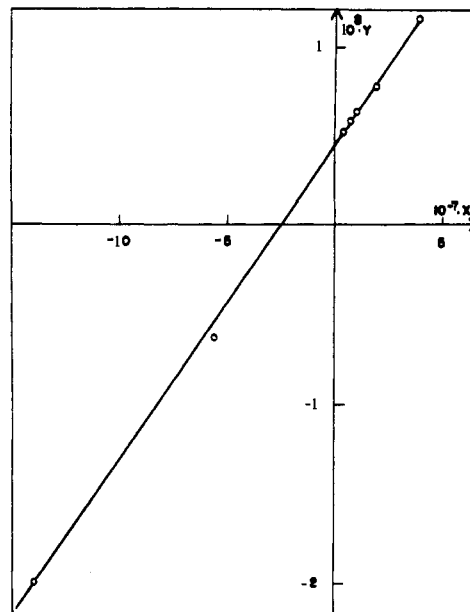
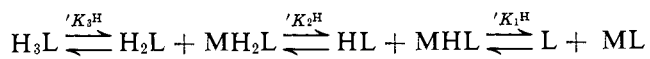


Figure 4. Graphic determination of the proton association constants  $K^{\text{H}}_{\text{MH}_2\text{L}}$  and  $K^{\text{H}}_{\text{MHL}}$  of HBED in the presence of an equivalent amount of  $\text{Mn}^{2+}$ . The equation plotted,  $y = mx + p$ , is:  $\bar{p}/(1 - \bar{p})[\text{H}^+] = \{(\bar{p} - 2)/(\bar{p} - 1)\}[\text{H}^+][K^{\text{H}}_{\text{MHL}}K^{\text{H}}_{\text{MH}_2\text{L}} + K^{\text{H}}_{\text{MHL}}]$  ( $\bar{p}$  is the average number of protons bound per ligand);  $m = K^{\text{H}}_{\text{MHL}}K^{\text{H}}_{\text{MH}_2\text{L}} = 1.76 \times 10^{14}$ ;  $p = K^{\text{H}}_{\text{MHL}} = 4.60 \times 10^7$ ;  $\mu = 0.10 \text{ M} (\text{KNO}_3)$ ,  $25^\circ$ .

two dissociation steps overlap to give a single sloping buffer region.

With  $\text{Mn}^{2+}$  and  $\text{Lu}^{3+}$  the reactions become somewhat more complicated, apparently because of weaker binding of these metal ions by the ligand, so that neutralization reactions of the ligand and of the partially formed metal chelate occur simultaneously. The equilibrium constants  $K^*_{\text{MH}_2\text{L}}$  were calculated in the region between 0.5 and 1.5 moles of base per mole of ligand, for those metal ions having a suitable buffer region in this range of neutralization values (e.g.,  $\text{Cu}^{2+}$  and  $\text{Cd}^{2+}$  of Figure 3). The data between  $a = 2.5$  and  $a = 4.0$  (Figure 3) were similarly employed for the evaluation of  $K^{\text{H}}_{\text{MHL}}$  and  $K^{\text{H}}_{\text{MH}_2\text{L}}$ . With  $\text{Lu}^{3+}$ , however, the transition,  $\text{LuH}_2\text{L}^+ \rightarrow \text{LuL}^-$ , occurs in one step, a fact that is easily seen from the slope of the titration curve between  $a = 2$  and  $a = 4$  (Figure 3), and therefore  $[\text{MHL}]$  does not appear in measurable concentration during the potentiometric titration. For this reason only the over-all equilibrium constant,  $K^{\text{H}}_{\text{MHL}}K^{\text{H}}_{\text{MH}_2\text{L}}$ , could be calculated. These overlapping constants, and the over-all constant for  $\text{Lu}^{3+}$ , were determined graphically in order to obtain the best possible values. An example of this graphical determination is illustrated in Figure 4 for  $\text{Mn}^{2+}$ .

With  $\text{Ca}(\text{II})$  and  $\text{Mg}(\text{II})$ , 10:1 excess curves were taken and the assumption made that  $\text{Ca}(\text{II})$  and  $\text{Mg}(\text{II})$  are not effectively bound until at least two protons are displaced from the ligand (as may be readily observed from the titration curve). Since the metal ion concentration remains relatively constant, the excess curves may be considered as three successive overlapping dissociation steps.



In the presence of excess metal ion the ratio of con-

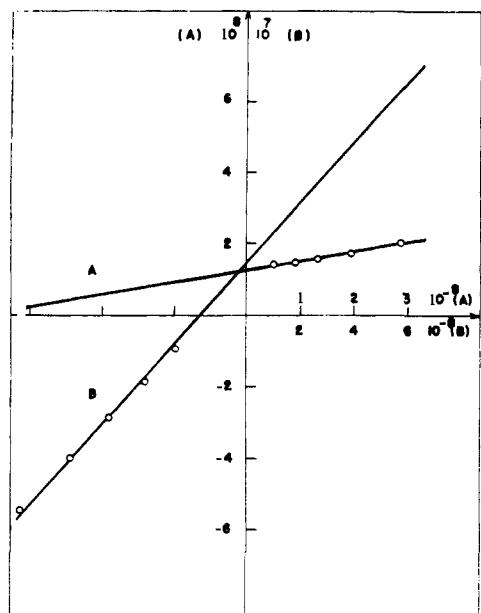


Figure 5. (A) Graphic determination of the apparent proton association constants  $'K_1^H$  and  $'K_2^H$  of HBED in the presence of excess  $Mg^{2+}$ . The equation plotted,  $y = mx + p$ , is  $\bar{p}/(1 - \bar{p})[H^+] = \{(\bar{p} - 2)/(\bar{p} - 1)\}[H^+]'K_1^H/K_2^H + 'K_1^H$  ( $\bar{p}$  is the average number of protons bound per ligand;  $m = 'K_1^H/K_2^H = 2.60 \times 10^{15}$ ;  $p = 'K_1^H = 1.40 \times 10^8$ ;  $\mu = 0.10 M (KNO_3)$ ,  $25^\circ$ ). (B) Graphic determination of the apparent proton association constants  $'K_2^H$  and  $'K_3^H$  of HBED in the presence of an excess amount of  $Mg^{2+}$ ;  $m = 'K_2^H/K_3^H = 1.19 \times 10^{16}$ ;  $p = 'K_2^H = 1.47 \times 10^7$ ;  $\mu = 0.10 M (KNO_3)$ ,  $25^\circ$ .

concentrations of a protonated ligand species and its corresponding metal chelate (e.g.,  $H_2L$  and  $MH_2L$ ) is always the same, so that the following equilibrium constants may be written

$$'K_1^H = \frac{[HL] + [MHL]}{([L] + [ML])[H^+]} \quad (7)$$

$$'K_2^H = \frac{[H_2L] + [MH_2L]}{([HL] + [MHL])[H^+]} \quad (8)$$

$$'K_3^H = \frac{[H_3L]}{([H_2L] + [MH_2L])[H^+]} \quad (9)$$

These apparent dissociation constants  $'K_n^H$  are related to the metal chelate formation constants and the normal protonation constants  $K_n^H$  by the following relationships

$$'K_1^H = K_1^H \frac{(1 + K_{MHL}^M[M])}{(1 + K_{ML}^M[M])} \quad (10)$$

$$'K_2^H = K_2^H \frac{(1 + K_{MH_2L}^M[M])}{(1 + K_{MHL}^M[M])} \quad (11)$$

$$'K_3^H = K_3^H(1 + K_{MH_3L}^M[M]) \quad (12)$$

where

$$K_{MH_pL}^M = \frac{[MH_pL]}{[M][H_pL]} \quad (13)$$

Because of the constant concentration of the free metal ion, we may describe the excess curves by the following protonation function

$$\bar{p} + (\bar{p} - 1)[H^+]'K_1^H + (\bar{p} - 2)[H^+]^2'K_1^H/K_2^H + (\bar{p} - 3)[H^+]^3'K_1^H/K_2^H/K_3^H = 0 \quad (14)$$

where  $\bar{p}$  is the average number of protons bound per ligand.

In order to avoid a three-dimensional graphic solution, it was assumed that, in the range of  $a$  values between 3 and 4, the pH was high enough that no appreciable amount of triprotonated ligand,  $H_3L$ , was present. Experimental points in this range were used for the graphic solution for  $'K_1^H$  and  $'K_2^H$  with the following equation

$$\frac{\bar{p}}{(1 - \bar{p})[H^+]} = \frac{\bar{p} - 2}{\bar{p} - 1} [H^+]'K_1^H/K_2^H + 'K_1^H \quad (15)$$

The graphical solution of this equation is illustrated in Figure 5. Similarly in the range of  $a$  values between 1.0 and 2.0, neglecting the amount of completely dissociated ligand  $L^{4-}$  and metal chelate,  $ML^{2-}$ , values for  $'K_3^H$  and  $'K_2^H$  can be obtained. The validity of these determinations was checked by comparing the two values obtained for  $'K_2^H$ . The difference was quite reasonable and within experimental error.

In the case of Fe(II) a titration curve could not be obtained because of irreversible oxidation to Fe(III) in the presence of the ligand. Oxidation takes place in acid solution, before the addition of base, and even in the absence of oxygen.

The values obtained for the stability constants calculated by the methods described above are shown in Table I.

Table I. Stability Constants of Metal Complexes of N,N'-Di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic Acid (HBED)<sup>a</sup> ( $\mu = 0.10 M (KNO_3)$ ,  $25^\circ$ )

Cations	Log $K_{MH_2L}^M$	Log $K_{MHL}^M$	Log $K_{ML}^M$	Log $K_{MH_2L}^H$	Log $K_{MHL}^H$
Mg <sup>2+</sup>	2.21	6.20	10.51	7.01	8.15
Ca <sup>2+</sup>	2.02	5.52	9.29	7.50	8.69
Mn <sup>2+</sup>	5.56	9.98	14.78	6.58	7.66
Co <sup>2+</sup>	9.76	15.20	19.89	5.56	7.77
Ni <sup>2+</sup>	10.81	15.36	19.31	6.45	8.51
Cu <sup>2+</sup>	11.73	17.55	21.38	5.18	8.63
Zn <sup>2+</sup>	9.17	14.18	18.37	5.99	8.27
Cd <sup>2+</sup>	8.85	13.17	17.52	6.68	8.11
Pb <sup>2+</sup>	10.38	14.76	18.24	6.62	8.98
Lu <sup>3+</sup>	7.06	...	20.38	...	10.14 <sup>b</sup>
Fe <sup>3+</sup>	...	...	39.68	...	...

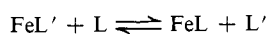
<sup>a</sup> Proton association constants of HBED are  $K_1^H = 12.46$ ,  $K_2^H = 11.00$ ,  $K_3^H = 8.32$ ,  $K_4^H = 4.64$ . <sup>b</sup> This value represents the sum of  $\log K_{MH_2L}^H$  and  $\log K_{MHL}^H$ .

**Stability Constant of the Fe(III) Chelate.** The alkalimetric titration of a 1:1 mixture of HBED and iron(III) nitrate (Figure 3) gives a curve which corresponds to the titration of a strong acid with a concentration  $4[L]_t$ , indicating that the following equilibrium is displaced completely to the right, even before the addition of base



The Fe(III)-HBED complex is so stable that neither hydrogen nor hydroxo complexes are present in the pH range between 2.5 and 11.0, as is clearly indicated by the potentiometric titration curve in Figure 3. Since this complex has an intense red color (the extinction at  $\lambda_{max}$  of 485 m $\mu$ ,  $\epsilon_{FeL}$ , is 3935) the distribution of iron(III) between some aminopolycarboxylic acids and

HBED is easily measured spectrophotometrically.<sup>4,6</sup> The displacement equilibrium for this reaction is



In this case L' is the polydentate anion of EDTA, which will naturally participate in the above equilibrium as protonated species H<sub>p</sub>L'. The same is true for L. Protonated metal chelate species, FeH<sub>p</sub>L and FeH<sub>p</sub>L', may, however, be neglected. The following equations are obtained for the total concentrations, M<sub>t</sub>, L<sub>t</sub>, and L<sub>t</sub>'.

$$M_t = [\text{FeL}] + [\text{FeL}'] \quad (16)$$

$$L_t = \sum_{p=0}^4 [\text{H}_p\text{L}] + [\text{FeL}] = \alpha_L[\text{L}] + [\text{FeL}] \quad (17)$$

$$L_t' = \sum_{p=0}^4 [\text{H}_p\text{L}'] + [\text{FeL}'] = \alpha_{L'}[\text{L}'] + [\text{FeL}'] \quad (18)$$

Since the extinction was measured at 485 mμ and FeL' does not absorb at this wavelength, the measured extinction for 1-cm cells is equal to

$$E = \epsilon_{\text{FeL}}[\text{FeL}] \quad (19)$$

Since the proton dissociation constants of the ligands, the amounts of reagents added, the hydrogen ion concentration, and the concentration of FeL are all known, the equilibrium constant K<sub>X</sub> may be calculated.

$$K_X = \frac{[\text{FeL}][\text{L}']}{[\text{FeL}'][\text{L}]} = \frac{K_{\text{ML}}}{K_{\text{ML}'}} \quad (20)$$

Equilibrium conditions were obtained by approach from both directions when thermostated experimental solutions were allowed to stand for 2 days. In one case HBED was added to the iron(III) solution and then EDTA was added; in the other case the EDTA-Fe(III) chelate was formed before addition of the HBED. The experimental values of K<sub>X</sub> and K<sub>ML</sub> thus obtained are presented in Table II. With log K<sub>FeL'</sub> =

Table II. Determination of the Displacement Constant K<sub>X</sub> (μ = 0.1 M (KNO<sub>3</sub>), 25°)

10 <sup>4</sup> L <sub>t</sub>	10 <sup>4</sup> L <sub>t</sub> '	10 <sup>4</sup> M <sub>t</sub>	-Log [H <sup>+</sup> ]	10 <sup>4</sup> [FeL]	Log K <sub>X</sub> <sup>a</sup>
2.00	2.00	2.00	2.74	1.188	14.566
2.00	2.00	2.00	2.75	1.210	14.602
Average					14.584

<sup>a</sup> For the calculation of α<sub>L'</sub>, the following protonation constants were used (log K<sub>p</sub><sup>H</sup> values): K<sub>4</sub><sup>H</sup> = 1.99, K<sub>3</sub><sup>H</sup> = 2.67, K<sub>2</sub><sup>H</sup> = 6.16, K<sub>1</sub><sup>H</sup> = 10.23.

25.10,<sup>7</sup> the following value of K<sub>FeL</sub> was obtained.

$$K_{\text{FeL}} = K_X K_{\text{FeL}'} = 10^{14.58} 10^{25.10} = 10^{39.68}$$

## Discussion

**Proton Association Constants.** A comparison of the proton association constants of HBED and EHPG (Table III) with those of ethylenediaminediacetic acid (EDDA) shows clearly that K<sub>3</sub><sup>H</sup> and K<sub>4</sub><sup>H</sup> of EHPG and HBED correspond to association of protons with the

(6) G. Anderegg, L. L'Eplattenier, and G. Schwarzenbach, *Helv. Chim. Acta*, **46**, 1409 (1963).

(7) A. E. Martell and L. G. Sillén, "Tables of Stability Constants of Metal Complexes," 2nd ed, Chemical Society Monograph, London, 1965.

basic amino groups, as is indicated by I, II, and III. The value of log K<sub>2</sub><sup>H</sup> of EDDA is very nearly equivalent to log K<sub>4</sub><sup>H</sup> of EHPG. On the other hand log K<sub>4</sub><sup>H</sup> of HBED has a much lower value than that of EDDA (and of EHPG). A similar situation exists for the relative values of K<sub>3</sub><sup>H</sup> of HBED and EHPG, that of the latter being lower than the corresponding value of EDDA, while the proton affinity of the diprotonated form of HBED is still lower by a significant amount.

Table III. Comparison of Proton Association Constants (Log K<sub>n</sub><sup>H</sup>)

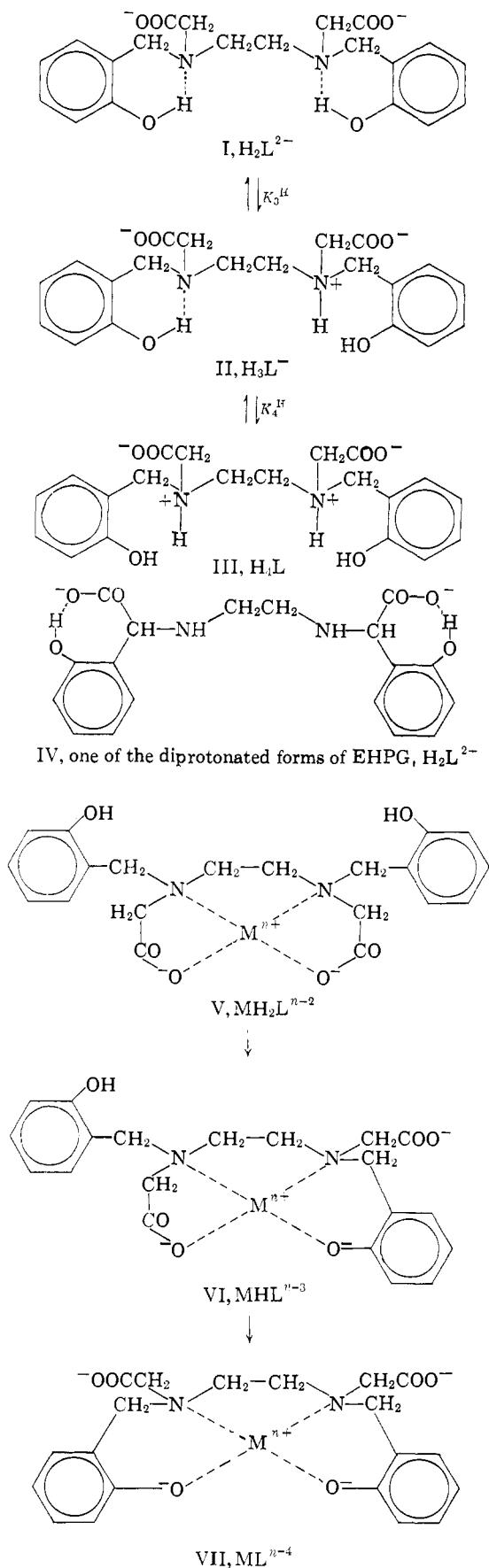
EDDA <sup>a</sup>	EHPG <sup>b</sup>	HBED <sup>c</sup>
K <sub>2</sub> <sup>H</sup> = 6.42	K <sub>4</sub> <sup>H</sup> = 6.39	K <sub>4</sub> <sup>H</sup> = 4.64
K <sub>1</sub> <sup>H</sup> = 9.46	K <sub>3</sub> <sup>H</sup> = 8.78	K <sub>3</sub> <sup>H</sup> = 8.32
	K <sub>2</sub> <sup>H</sup> = 10.56	K <sub>2</sub> <sup>H</sup> = 11.00
	K <sub>1</sub> <sup>H</sup> = 11.85	K <sub>1</sub> <sup>H</sup> = 12.46

<sup>a</sup> μ = 0.1 M (KCl), 30°. S. Chaberek and A. E. Martell, *J. Am. Chem. Soc.*, **74**, 6228 (1952). <sup>b</sup> μ = 0.1 M (KNO<sub>3</sub>), 20°. <sup>c</sup> This investigation, μ = 0.1 M (KNO<sub>3</sub>), 25°.

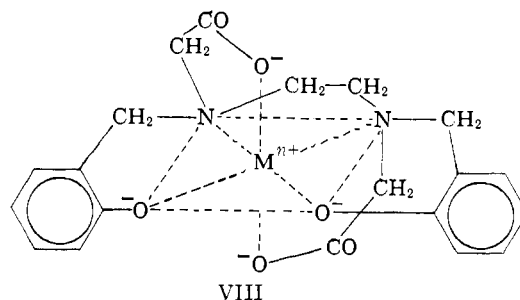
The reason for these differences is not obvious from a simple comparison of probable structures of the ligand anions in solution. Further inspection, however, shows that partially and completely protonated species of EHPG can exist in hydrogen-bonded configurations such as IV, in which the basic amino group would be more reactive toward protonation than would HBED. An attempt to write similar structures of HBED shows that they involve relatively less stable eight-membered rings (not counting the proton). Thus the abnormally low proton affinities of the di- and triprotonated forms of HBED are probably due to the stability of the hydrogen-bonded rings in I and II and the fact that they cannot be replaced by alternate stable hydrogen-bonded structures such as is possible in EHPG, indicated by IV.

The extensive change of the absorption spectra in alkaline solutions supports the conclusion, implied in the above discussion, that the two most basic groups in the ligand are phenolate groups. The ultraviolet spectra given in Figure 1 show that at low pH only one band is observed, with maximum absorption at 277 mμ, which is assigned to the undissociated phenolic groups. Not until the solution is quite alkaline does a longer wavelength band appear (λ<sub>max</sub> 294 mμ) corresponding to the formation of negative phenolate groups. At very high pH (above -log [H<sup>+</sup>] = 13) only the band at 294 mμ remains. The longer wavelength of the phenolate absorption band is in accord with its greater negative charge, which would be expected to result in the observed bathochromic shift.

**Stability Constants of the Metal Complexes.** The probable arrangements of ligand donor groups and coordinate bonds of metal chelates of HBED, and of their mono- and diprotonated forms, are given by formulas V, VI, and VII, respectively. The initial two-proton displacement to form the diprotonated metal chelate MH<sub>2</sub>L involves the displacement of a proton from each of the less basic tertiary amino groups. The metal ion thus is able to form a complex having three chelate rings with the tetradentate diprotonated ligand, similar to those formed by ethylenediaminediacetic acid, EDDA.



With increasing pH the metal ion begins to compete successfully with the protons for the phenolate groups, and appreciable amounts of complexes MHL and ML (VIII) form in solution. Depending on the coordination



number of the metal ion, the carboxylate functions may or may not remain coordinated to the metal ion. For  $CuL^{2-}$ , there is probably strong coordination of the metal ion with the amino nitrogens and phenolate oxygens in approximately coplanar positions, and weaker coordination with the carboxylate oxygens in the fifth and sixth positions above and below the plane. The conversion  $CuH_2L \rightarrow CuL$  is accompanied by a strong color change in the solution (Figure 6). Below pH 5 the  $Cu(II)$ -HBED complex has the typical blue color normally associated with  $Cu(II)$ -amino acid chelates, characterized by a broad absorption band with a maximum at about  $655 m\mu$ . The  $CuH_2L$  complex is probably a distorted octahedron, with weakly bonded water molecules in the fifth and sixth positions. The asymmetry of the observed absorption band indicates overlapping of at least two, and very probably three, absorption bands, since tetragonal distortion splits the  $e_g$  and  $t_{2g}$  levels of  $Cu^{2+}$  to give three d-d transitions. As the pH is increased above 4 a new, much stronger, band appears at about  $385 m\mu$ , the intensity of which increases with increasing pH and remains constant above pH 10.50, where the formation of  $CuL$  is complete. This new band is certainly associated with the formation of metal-phenolate linkages and is probably caused by charge transfer. The tailing off of this new band in the visible results in increased blue absorption and a shift in color of the complex from blue to green.<sup>3</sup>

If the diprotonated complexes of HBED,  $MH_2L$ , formula V, are compared with the analogous chelates of EDDA, a decrease of the stability constants is observed (Table IV). Although this comparison is

Table IV. Stability Constants of Analogous EDDA and HBED Chelates

$M^{n+}$	EDDA <sup>a</sup> Log $K_{ML}^{M}$	HBED <sup>b</sup> Log $K_{MH_2L}^{M}$	$\Delta$ Log $K$
Mg <sup>2+</sup>	4.53	2.21	2.32
Ca <sup>2+</sup>	4.63	2.02	2.61
Mn <sup>2+</sup>	7.71	5.56	2.15
Co <sup>2+</sup>	11.78	9.76	2.02
Ni <sup>2+</sup>	13.73	10.81	2.92
Cu <sup>2+</sup>	15.90	11.73	4.17
Zn <sup>2+</sup>	11.93	9.17	2.76
Cd <sup>2+</sup>	10.58	8.85	1.73
Pb <sup>2+</sup>	12.22	10.38	1.84
Lu <sup>3+</sup>	9.09	7.06	2.03

<sup>a</sup>  $\mu = 0.10 M$  (KCl), 20°.<sup>7</sup> <sup>b</sup> This investigation,  $\mu = 0.10 M$  (KNO<sub>3</sub>), 25°.

slightly influenced by the difference of conditions, the lower stabilities of the diprotonated HBED chelates are unmistakable and significant. This change in

stability correlates well with the lower basicities of the amino groups ( $K_3^H$  and  $K_4^H$ ) compared to the values of  $K_1^H$  and  $K_2^H$  of EDDA. The lower affinities of the donor groups of HBED are due to the fact that coordination of the metal ion with the ethylenediamine diacetate moiety is accompanied by the breaking up of hydrogen bonds of the type shown in I and II, a condition which does not apply to the coordination of a metal ion by the dianion of EDDA. The Irving-Williams order is followed for these diprotonated complexes,  $MH_2L$ .

A comparison between the stabilities of the normal or nonprotonated complexes,  $ML^{n-4}$  (VIII), and those reported in the literature for EHPG<sup>3,4</sup> is given in Table V. The variation of  $\Delta \log K$ , the increment of stability

Table V. Comparison of Stability Constants of HBED and EHPG Chelates

$M^{n+}$	HBED <sup>a</sup> Log $K_{ML}^{M}$	EHPG <sup>b</sup> Log $K_{ML}^{M}$	$\Delta \log K$
Mg <sup>2+</sup>	10.51	8.00	2.51
Ca <sup>2+</sup>	9.29	7.20	2.09
Ni <sup>2+</sup>	19.31	19.66	-0.35
Cu <sup>2+</sup>	21.38	23.90	-2.52
Zn <sup>2+</sup>	18.37	16.80	1.57
Cd <sup>2+</sup>	17.52	13.13	4.39
Fe <sup>3+</sup>	39.68	33.91 <sup>c</sup>	5.77

<sup>a</sup> This investigation,  $\mu = 0.1 M$  ( $KNO_3$ ), 25°. <sup>b</sup>  $\mu = 0.1 M$  ( $KNO_3$ ), 25°. <sup>c</sup>  $\mu = 0.1 M$  ( $KNO_3$ ), 20°.

of the HBED over the EHPG chelate, is seen to be roughly a measure of the importance of the contributions of the carboxylate groups in the stabilities of the chelate compounds formed. Thus the relatively basic ions Ca<sup>2+</sup> and Mg<sup>2+</sup>, which require all six polar groups for high stability in order to produce a "cage" of ionic and polar groups, form much more stable chelates with HBED, reflecting the more favorable steric arrangement of the carboxylate groups. Similarly the other metal ions of higher coordination number (e.g., Cd<sup>2+</sup> and especially Fe<sup>3+</sup>) show a large increment of stability for the HBED chelate. On the other hand, a smaller increment is observed for metal ions with lower coordination requirements (e.g., Zn<sup>2+</sup>). In the case of Cu(II), which has only four (square-planar) strong coordinate bonds, the lack of importance of carboxylate binding results in a much lower stability of the HBED chelate, in accord with the generally lower basicity of the HBED anion (compared to EHPG), and especially of the basic amino groups. The decrease in the value of  $\Delta \log K$  observed for Ni(II) probably indicates that

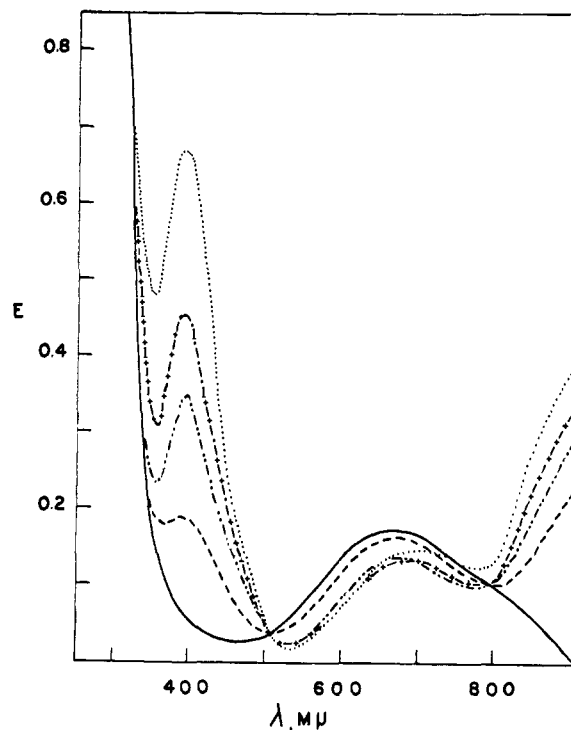


Figure 6. Visible absorption spectra of the HBED-Cu(II) chelate as a function of pH: —, pH 2.57; ---, pH 4.95; - · - · - ·, pH 7.16; - + - + - +, pH 8.53; · · · · ·, pH 11.96.  $[Cu]_t = [HBED]_t = 1.00 \times 10^{-4} M$ ;  $\mu = 0.10 M$  ( $KNO_3$ ); 1.00-cm cell; 25°.

in this case also the four strongest coordinate bonds are planar and that the six coordinate bonds around Ni<sup>2+</sup> are arranged in a tetragonal, rather than in a regular octahedral, fashion.

All experimental data indicate that the Fe(III) chelate of HBED is truly an unusual and extremely stable compound. The Fe(III) titration curve is unique in that four protons are displaced from the ligand in a single step, and no formation of hydrogen or hydroxo complexes is apparent from pH 2.5 to 11. Only the sideramines<sup>6</sup> and EHPG<sup>4</sup> show such behavior. Most of the other 1:1 complexes with polydentate ligands are unstable in alkaline medium and form hydroxo complexes or dissociate to give ferric hydroxide. As with EHPG, the high stability of the iron(III) complex may be rationalized on the basis of the high affinity of Fe<sup>3+</sup> for phenolate groups. The fact that the Fe(III)-HBED chelate is much more stable than that of EHPG is probably due to the sterically more favorable arrangement of bonds when all six donor groups of the ligand are involved in coordination of the metal ion.