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Synthesis and Metal Chelate Stability of *N,N'*-Ethylenebis(aminomalonic) Acid

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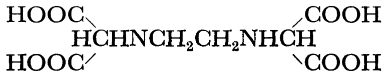
N,N'-Ethylenebis(aminomalonic) acid (EAMA) has been synthesized, and its acid dissociation constants and the stability constants of its alkaline earth metal complexes were determined potentiometrically at 25°C in a medium of ionic strength of 0.10 (KNO_3) with the following results: $pK_1=2.1$, $pK_2=2.72$, $pK_3=6.56$, $pK_4=9.69$; $\log K_{MY}$ and $\log M_{MHY}$ for Ca(II) respectively, 5.45 and 2.02; for Mg(II) respectively 4.93 and 1.80. The exact stability constants of Cu(II) and Ni(II) chelates of this ligand were not obtained on account of its decomposition in low pH solution, but the order of relative stability has been established. From a comparison of the stability of Ca(II) and Mg(II) chelates with those of the analogous complexane, the function of the malonate group in the chelate formation has been discussed. Zn(II) and Co(II) chelates of this ligand have been obtained and their probable structures are proposed.

Aminomalonic acid investigated by Schwarzenbach[1] as a chelating ligand has three functional groups in metal chelate formation. However, it is sterically impossible for these three groups to coordinate to the metal ion forming two chelate rings. The ligand functions as a bidentate ligand in which the amino nitrogen and one carboxylate participate in chelate formation. This was evidenced by the fact that the stability of the metal chelates of aminomalonic acid is lower than that of iminodiacetic acid which can act as a terdentate ligand to form two chelate rings with the metal ion.

N,N'-Ethylenebis(aminomalonic) acid (EAMA) (I) is a tetrabasic acid having six donor groups including two basic nitrogen atoms.



$$\begin{matrix}\mathrm{HOOC}\diagdown & & \diagup\mathrm{COOH}\\ & \mathrm{HCHNCH_2CH_2NHCH} & \\ \mathrm{HOOC}\diagup & & \diagdown\mathrm{COOH}\end{matrix} \qquad \text{(I)}$$

However, it is considered to act as a quadridentate ligand in metal chelate formation as in aminomalonic acid, being expected to exhibit behavior analogous to that of ethylenediamine-*N,N'*-diacetic acid.

This paper deals with the synthesis and chemical behavior of EAMA, the potentiometric determination of acid dissociation constants, and metal chelate stability. A discussion is given on the function of the

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[1] G. Schwarzenbach, E. Kampitsch, and R. Steiner, *Helv. Chim. Acta*, **28**, 1133 (1945).

malonate moieties in metal chelate formation and stability in comparison with analogous ligands such as ethylenediaminetetraacetic acid (EDTA), ethylenediamine-*N*,*N*′-diacetic acid (EDDA), and ethylenediamine-*N*,*N*′-di(α-propionic) acid (EDDMA). The structure of the insoluble chelates with Co(II) and Zn(II) ion has been determined by means of infrared spectroscopy.

Experimental

Material. N,N′-*Ethylenebis(aminomalonic) acid (EAMA)*: To a solution of 9.2 g (0.05 M) of bromomalonic acid dissolved in 30 ml of water and neutralized with 30% aqueous sodium hydroxide at 5°C was added 1.5 g (0.025 M) of 98% ethylenediamine and the mixture was heated at 70°C. The pH of the solution was kept at 9—11 for 1 hr by dropwise addition of 30% aqueous sodium hydroxide. On cooling, it was brought to 1—2 by careful addition of dilute hydrochloric acid and the resulting precipitates were filtered and washed with water and methanol. For purification, the crude product was dissolved in aqueous alkali, filtered and precipitated by adjusting the pH of the filtrate at nearly 1 with dilute hydrochloric acid. The procedure was repeated three times and a pure sample was dried over calcium chloride in a vacuum. The acid undergoes decarboxylation at 166—169°C and melts at 202—204°C with decomposition.

Found: C, 33.62; H, 5.33; N, 10.03%. Cacld for $C_8H_{12}N_2O_8 \cdot H_2O$: C, 34.05; H, 5.00; N, 9.93%.

Disodium Salt of EAMA: To a suspension of 6 g of free EAMA in 100 ml of water was added 30% aqueous sodium hydroxide until the pH of the solution reached 8 and the solution was filtered. The filtrate was diluted with 300 ml of ethanol and the resulting precipitates were filtered. The product was dissolved in a minimum amount of water, filtered, and precipitated by the addition of a large amount of ethanol. The procedure was repeated and the product was dried over calcium chloride in a vacuum.

Found: C, 28.14; H, 4.04; N, 8.55%. Calcd for $C_8H_{10}N_2O_8Na_2 \cdot 2H_2O$: C, 27.92; H, 4.10; N, 8.14%.

Decarboxylation of EAMA: A suspension of 6 g of free EAMA in 60 ml of water was refluxed for 2 hr, while the acid gradually dissolved into solution accompanied by evolution of carbon dioxide. The resulting clear solution was concentrated to 20 ml in a vacuum and diluted with 60 ml of ethanol. After being left overnight in a refrigerator, the resulting crystals were filtered. Recrystallization twice from dilute ethanol gave a pure sample of ethylenediamine-*N*,*N*′-diacetic acid, mp 210—211°C (decomp.).

Found: C, 40.56; H, 7.12; N, 15.84%. Calcd for $C_6H_{12}N_2O_4$: C, 40.91; H, 6.82; N, 15.90%.

The filtrate from which crude EDDA was obtained was evaporated to dryness and the residue was recrystallized three times from methanol. The compound was determined to be ethylenediamine-*N*,*N*′-diacetic acid lactam. It melts at 222°C with decomposition. IR (KBr) 1645 cm^{-1} (lactam C=O), 1586 cm^{-1} (COO$^-$).

Found: C, 44.02; H, 6.58; N, 17.29%. Calcd for $C_6H_{10}N_2O_3 \cdot 1/3\ H_2O$: C, 43.90; H, 6.55; N, 17.06%.

Co(II) Complex of EAMA: A 100 ml aqueous solution of 0.01 M disodium salt of EAMA was mixed with 90 ml of 0.01 M $Co(NO_3)_2$ aqueous solution, to which was added 20 ml of 0.1 N HNO_3. After being left overnight, the resulting precipitates were filtered and washed with water and methanol and dried over calcium chloride in a vacuum. Pink crystalline powder, mp>280°C.

Found: C, 25.43; H, 4.24; N, 7.77; Co, 15.85%. Calcd for $C_8H_{10}N_2O_8Co \cdot 3H_2O$: C, 25.61; H, 4.30; N, 7.47; Co, 15.72%.

Zn(II) Complex of EAMA: The procedure was the same as in the preparation of Co(II) complex except that zinc nitrate was used in place of cobalt nitrate. Colorless crystalline powder, mp>280°C.

Found: C, 25.18; H, 4.03; N, 7.48; Zn, 17.20%. Calcd for $C_8H_{10}N_2O_8Zn \cdot 3H_2O$: C, 25.18; H, 4.23; N, 7.34; Zn, 17.13%.

Measurements and Calculation. The method consists of potentiometric titration of the ligand in the absence of the metal ion for the acid dissociation constant and in the presence of the metal ion for the chelate stability. A carbonate free 0.1M KOH was used for the titration. All measurements were carried out at 25±0.1°C in a medium of ionic strength of 0.10 (KNO_3) with a Hitachi Horiba model F-5 pH meter.

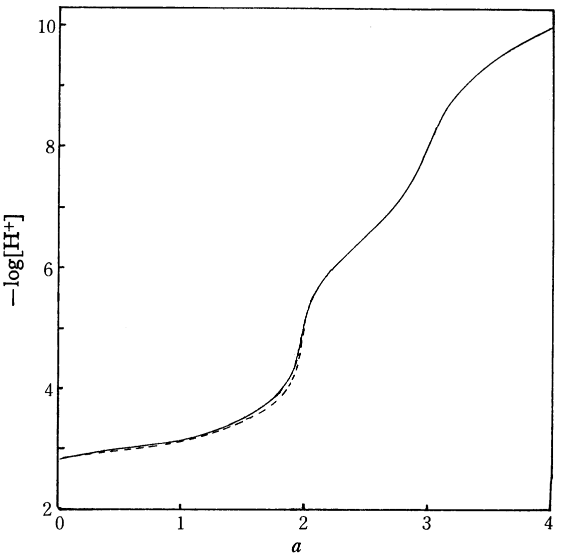

Fig. .1 Titration of EAMA and EAMA-2Na, ------ EAMA-2Na+0.1M HCl; —— EAMA+0.1M KOH (after the neutralization of EAMA-2Na). The concentration of the acid is 0.001 M.

It should be substantiated that no decomposition of the ligand occurs during the course of titration, since EAMA turns to decarboxylate in solution at low pH. Thus the solution of disodium salt of EAMA was titrated with 0.1M HCl until two equivalent of the acid had been added and the solution was retitrated with 0.1M KOH until four equivalent of the base had been added. As seen in Fig. 1, the titration curves coincide with each other within experimental error, provided that the effect of increasing volume is taken into consideration. Therefore, it has been proved that no decomposition occurred.

The acid dissociation constants were calculated by the method of Schwarzenbach and Ackermann.[2] Determination of the stability constants of the Ca(II) and Mg(II) chelates was also accomplished by the same method. For the determination of the stability of Ni(II) and Cu(II) chelates, attempts were made to apply the method of Anderegg used for measuring the stability constants of moderately stable chelates of complexanes.[3] However, the stability constants could not be calculated owing to possible partial decomposition of the ligand. Thus the calculation was made by Bjerrum's

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2) G. Schwarzenbach and H. Ackermann, *ibid.*, **31**, 1029 (1947).

3) F. L'Eplattenier and G. Anderegg, *ibid.*, **47**, 1792 (1964).

procedure on the assumption that EAMA would form 1:1 chelates with both metal ions almost exclusively. The procedure was applied by Chaberek and Martell[4] to measure the stability of transition metal chelates of ethylenediamine-*N*,*N*′-diacetic-*N*,*N*′-dipropionic acid. In the present case, the relative precision of the obtained data was very low.

The equilibrium constants are expressed as follows:

Acid dissociation constants,

$$K_n = [\mathrm{H^+}][\mathrm{H}_{4-n}\mathrm{Y}^{n-}]/[\mathrm{H}_{4-n+1}\mathrm{Y}^{(n-1)-}]$$

Stability constants,

$$K_{\mathrm{MHY}} = [\mathrm{MHY^-}]/[\mathrm{M^{2+}}][\mathrm{HY^{3-}}]$$

$$K_{\mathrm{MY}} = [\mathrm{MY^{2-}}]/[\mathrm{M^{2+}}][\mathrm{Y^{4-}}]$$

where H_4Y and M represent EAMA and metal ion, respectively.

Results and Discussion

Titration Curves. The titration curve of EAMA (Fig. 2) has buffer regions at about pH 4 and 7 followed by inflections at two equivalents and three equivalents of base respectively per mole of the amino acid. Thus the free acid, the divalent anion and the trivalent anion exist in a relatively pure state in solution, whereas the tetraalkali metal salt is extensively hydrolyzed.

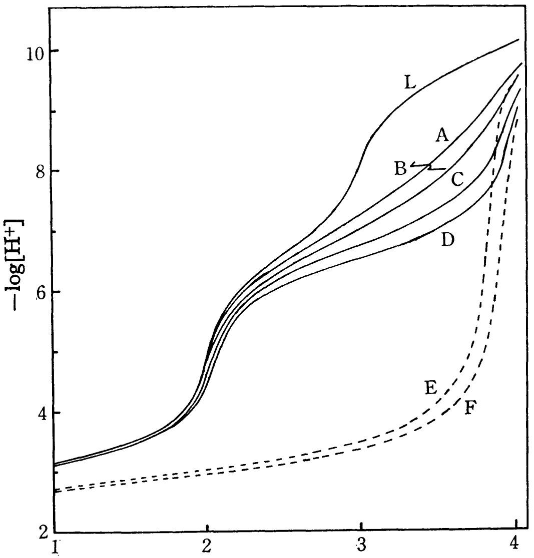


Fig. 2. Titration of EAMA with 0.1M KOH in the presence of metal ions. L, 0.001M free acid; A, B, E, and F, same as L with equimolar Mg(II), Ca(II), Ni(II), and Cu(II) respectively; C and D, with about ten times excess of Mg(II) and Ca(II) respectively. (All metal salts are the nitrate)

The titration curves in the presence of metal ions, shown in Fig. 2, indicate relatively weak chelate formation with alkaline earth metals but strong interaction with transition metals.

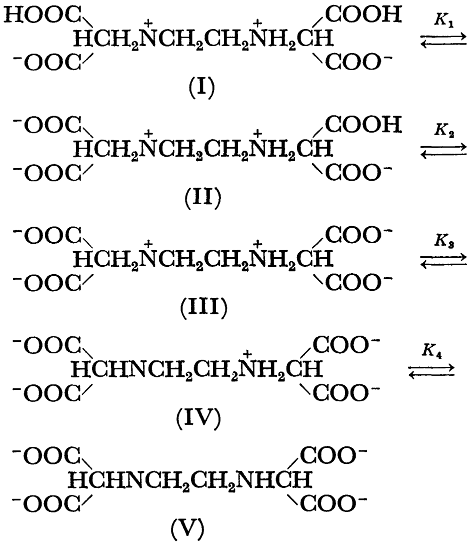
The free amino acid tends to decompose in acidic solution due to decarboxylation of the malonic acid moiety to yield ethylenediamine-*N*,*N*′-diacetic acid. In the absence and presence of alkaline earth metal ions, however, such decomposition process could not be observed during the course of titration. On the other hand, in the titration curves with Cu(II) and Ni(II) ions, the inflection deviates from the exact stoichiometry at $a=4$ indicating the decomposition of the ligand.

Table 1. Acid dissociation constants
$t=25°\mathrm{C}$; $\mu=0.10$ ($\mathrm{KNO_3}$)

	pK_1	pK_2	pK_3	pK_4
EAMA	2.1	2.72	6.56	9.69
EDTA[6]	2.0	2.67	6.16	10.27
			pK_1	pK_2
EDDA[5]			6.48	9.57
EDDMA[7]			6.69[a]	9.58[a]

a) These were measured at 20°C, $\mu=0.10$(KCl)

Acid Dissociation and Metal Chelate Stability Constants. The first and second acid dissociation constants (pK_1 and pK_2) of EAMA, listed in Table 1 are almost the same as the corresponding values for EDTA, indicating that they are due to the dissociation of the free carboxylic acid in (I) and (II).



$$\begin{array}{l}\mathrm{HOOC}\diagdown \qquad\qquad\qquad \diagup\mathrm{COOH}\\ \quad\mathrm{HCH_2\overset{+}{N}CH_2CH_2\overset{+}{N}H_2CH}\\ {}^-\mathrm{OOC}\diagup \qquad\qquad\qquad \diagdown\mathrm{COO^-}\end{array} \overset{K_1}{\rightleftarrows}$$

(I)

$$\begin{array}{l}{}^-\mathrm{OOC}\diagdown \qquad\qquad\qquad \diagup\mathrm{COOH}\\ \quad\mathrm{HCH_2\overset{+}{N}CH_2CH_2\overset{+}{N}H_2CH}\\ {}^-\mathrm{OOC}\diagup \qquad\qquad\qquad \diagdown\mathrm{COO^-}\end{array} \overset{K_2}{\rightleftarrows}$$

(II)

$$\begin{array}{l}{}^-\mathrm{OOC}\diagdown \qquad\qquad\qquad \diagup\mathrm{COO^-}\\ \quad\mathrm{HCH_2\overset{+}{N}CH_2CH_2\overset{+}{N}H_2CH}\\ {}^-\mathrm{OOC}\diagup \qquad\qquad\qquad \diagdown\mathrm{COO^-}\end{array} \overset{K_3}{\rightleftarrows}$$

(III)

$$\begin{array}{l}{}^-\mathrm{OOC}\diagdown \qquad\qquad\qquad \diagup\mathrm{COO^-}\\ \quad\mathrm{HCHNCH_2CH_2\overset{+}{N}H_2CH}\\ {}^-\mathrm{OOC}\diagup \qquad\qquad\qquad \diagdown\mathrm{COO^-}\end{array} \overset{K_4}{\rightleftarrows}$$

(IV)

$$\begin{array}{l}{}^-\mathrm{OOC}\diagdown \qquad\qquad\qquad \diagup\mathrm{COO^-}\\ \quad\mathrm{HCHNCH_2CH_2NHCH}\\ {}^-\mathrm{OOC}\diagup \qquad\qquad\qquad \diagdown\mathrm{COO^-}\end{array}$$

(V)

The third dissociation of a proton is the liberation from the $-\overset{+}{\mathrm{N}}\mathrm{H_2}-$ in (III). It is greatly influenced by positive charge of the adjacent ammonium group. The pK_3 value is higher than that of EDTA by 0.4 log unit and almost comparable to that of EDDA as seen in Table 1.

The difference between the acidity of the last proton to dissociate from (IV) and that of corresponding anion of EDTA may be explained on the basis of the relative electrostatic effects in these anions. The pK_4 value of EAMA is lower than that of EDTA by *ca.* 0.6 log unit. We see that the inductive effect of two carboxylate anions through one −CH< group in EAMA is smaller than that of the two carboxylate anions through each $-\mathrm{CH_2}-$ group in EDTA. However, a larger inductive effect of the malonate anion than that of single acetate

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[4] S. Chaberek, Jr., and A. E. Martell, *J. Amer. Chem. Soc.*, **74**, 6228 (1952).

[5] L. C. Thompson, *J. Inorg. Nucl. Chem.*, **24**, 1083 (1962).

[6] R. Skochdopole and S. Chaberek, Jr., *ibid.*, **11**, 222 (1959).

[7] H. Irving, R. Shelton, and R. Evans, *J. Chem. Soc.*, **1958**, 3540.

Table 2. Stability constants of EAMA and some related chelates (μ=0.10)

	$\log K_{MY}$ for				$\log K_{MHY}$ for		Temp. (°C)	Medium
	Ca (II)	Mg(II)	Cu(II)	Ni (II)	Ca (II)	Mg(II)		
EAMA	5.45	4.93	(13)	(12)	2.02	1.80	25	KNO_3
EDTA	10.59	8.69	18.3	18.4	3.51	2.28	20	KCl
EDDA[4]		3.9	16.2	13.5			30	KCl
EDDMA[7]		2.8	15.2	12.2			20	KCl

group is observed in comparing the pK_4 value with pK_2 value in EDDA.

The stability constants of EAMA with alkaline earth metal ions are much lower than those with EDTA as seen in Table 2. Although EAMA carries six coordination sites in the molecule, it will be sterically impossible for the two carboxylate groups in each malonate moiety to coordinate to the metal ion at the same time. Since the presence of the binuclear chelate is not observed from titration in the presence of large excess of the metal ion ($\log K_{M_2Y}\approx 0$), the most probable structure of the alkaline earth metal chelates will be one in which a carboxylate group in each malonate moiety is free and the remaining coordination sites are occupied by water molecules as shown in Fig. 3.

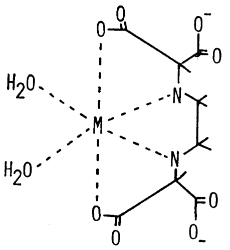

Fig. 3. Probable structure of the alkaline earth metal chelate.

We see from a comparison of $\log K_{MY}$ of Mg(II) chelate of EAMA with that of EDDA that the stability for the former is higher by one log unit. This may be partly due to higher basicity of the nitrogen atoms. However, the main contribution lies on the entropy effect of the two malonate groups, which results from an increase of the probability of attaining a spatial orientation required for chelation with the central metal ion. This is also evidenced by the comparison with EDDMA in which one carboxylate of both malonate groups in EAMA is replaced by a methyl group. Although the basicities of the two nitrogen atoms are comparable to those of EAMA (Table 1), the stability of Mg(II) chelate is lower than that of EAMA and even that of EDDA (Table 2). The methyl groups functioned only as a bulky group to exert a steric hindrance to the chelate formation.

A strong interaction of EAMA with Cu(II) and Ni(II) ions is observed from the titration curves. However, the chelate formation with these ions is accompanied by decomposition of the ligand, and the stability constants obtained suggest only a relative order of their magnitude. Considering the above chelate effect the true stability constants might assume any values between those of EDDA and EDTA provided the structures of these chelates are the same as those of the alkaline earth chelates. Decomposition will be due to a lowering of pH by the chelate formation and the metal ion in the chelate also may catalyze the decomposition.

Structure of Co(II) and Zn(II) Chelates. Titration of EAMA with Co(II) and Zn(II) ions was impossible because they formed insoluble precipitates before titration. It was found that the lower pH was favorable for the formation of precipitates. The metal-ligand composition is exactly 1 : 1 for both compounds as suggested by elementary analysis.

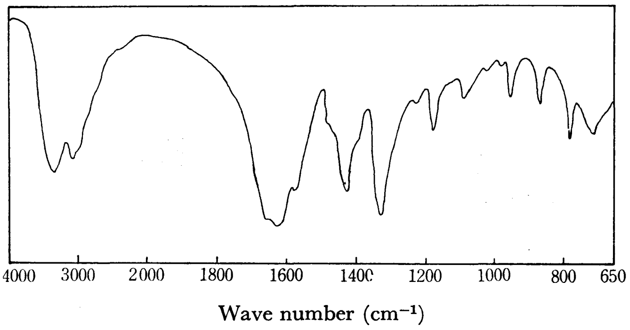

Fig. 4. Infrared spectrum of Zn(II) chelate.

Infrared spectra of both compounds are superimposal (Fig. 4). A very strong and broad band was observed around 1640 cm^{-1}, due to a symmetric stretching vibration of the carboxylate group. A stretching vibration of ammonium group appears around 3000—2500 cm^{-1}. In the free ligand, the carboxylate absorption is at the same position, but the carbonyl vibration of the free carboxylic acid is observed as a sharp absorption at 1754 cm^{-1}. Thus the compound might be a neutral metal chelate polymer in which the ligand molecules are bridged together with the metal ion at the terminal malonate groups and all imino nitrogens are protonated (Fig. 5).

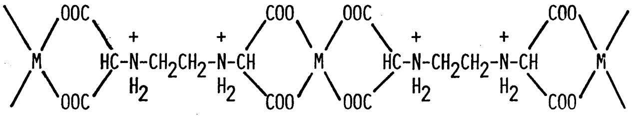

Fig. 5. Structure of Co(II) and Zn(II) chelates.

The chelate polymer is insoluble in water and soluble in alkaline solution. This can be explained by the positive charges on the ammonium nitrogens being neutralized by the hydroxide anion and the unit molecule carring —2 charge.