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Synthesis of Chelating Agents. VI.*[1] Chelating Behavior of 1,2,3-Triaminopropanehexaacetic Acid with Divalent Metal Ions*[2]

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The chelate stability constants of 1,2,3-triaminopropanehexaacetic acid (TAPHA) with alkaline earth metals, cobalt(II), nickel(II), copper(II), zinc(II) and cadmium(II) were determined at 25°C and an ionic strength of 0.1 (KNO_3). The stability constants of monoprotonated mono nuclear-, dinuclear- and mixed metal dinuclear chelates as well as normal mononuclear chelate were determined. The structure and chelating behavior of TAPHA in an aqueous solution were discussed by refering to those of the other complexanes of related structure. The crystalline metal chelates of TAPHA were also prepared and their structures were proposed on basis of the results of elementary analyses and infrared spectra.

1,2,3-Triaminopropane-*N,N,N',N',N'',N''*-hexaacetic acid (TAPHA) is a nonadentate ligand, having three nitrilodiacetic acid groups pending from each carbon atom of propane. As easily understood from the structure, these three nitrilodiacetate groups can not coordinate to a metal ion simultaneously. If the neighboring two nitrilodiacetate groups coordinate to a metal ion, leaving the remaining nitrilodiacetate group uncoordianted, then the coordinating structure of TAPHA resembles EDTA chelate. If the terminal two nitrilodiacetate groups coordinate to a metal ion, leaving the central nitrilodiacetate group uncoordinated, then the structure of TAPHA chelate resembles TMDTA (trimethylenediamine-*N,N,N',N'*-tetraacetic acid) chelate. It is of great interest to investigate the structure of TAPHA metal chelate from this standpoint of view.

Following to the previous paper,[1] in which the acid dissociation scheme of TAPHA was investigated, this paper is to report on the chelating behavior of TAPHA with divalent cations, such as magnesium(II), calcium(II), strontium(II), barium(II), cobalt(II), nickel(II), copper(II), zinc(II) and cadmium(II) in an aqueous solution as well as in a solid state.

The stability constants of normal mononuclear chelates, monoprotonated mononuclear chelates, diprotonated mononucelar chelates, dinuclear chelates and mixed dinuclear chelates have been determined. By comparing their values with those of other complexanes of related structure, a possible structure of TAPHA chelates in aqueous solution is proposed.

Experimental

The pH measurement was carried out at 25±0.1°C in aqueous solution of ionic strength with $\mu=0.1$ by KNO_3. The same apparatus as described in our previous paper was employed.[2] The procedure for the determination of chelate stability constants with

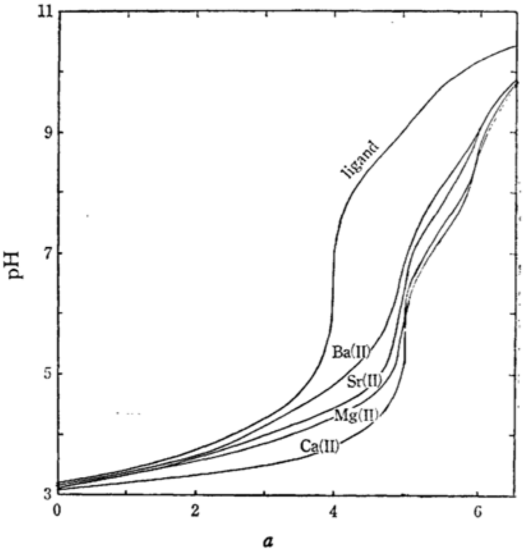

Fig. 1. Potentiometric titration curves of alkaline earth metals-TAPHA chelates at 25°C in 0.1 M KNO_3 with molar ratio of metal ion to ligand, 10 : 1.
Concentration of TAPHA: 4.66×10^{-4} M

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*[1] Paper V; M. Miyazaki, Y. Moriguchi and K. Ueno, This Bulletin, **41**, 838 (1968).

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1) M. Miyazaki, Y. Moriguchi and K. Ueno, This Bulletin, **41**, 838 (1968).

2) T. Ando, *ibid.*, **36**, 1593 (1963).

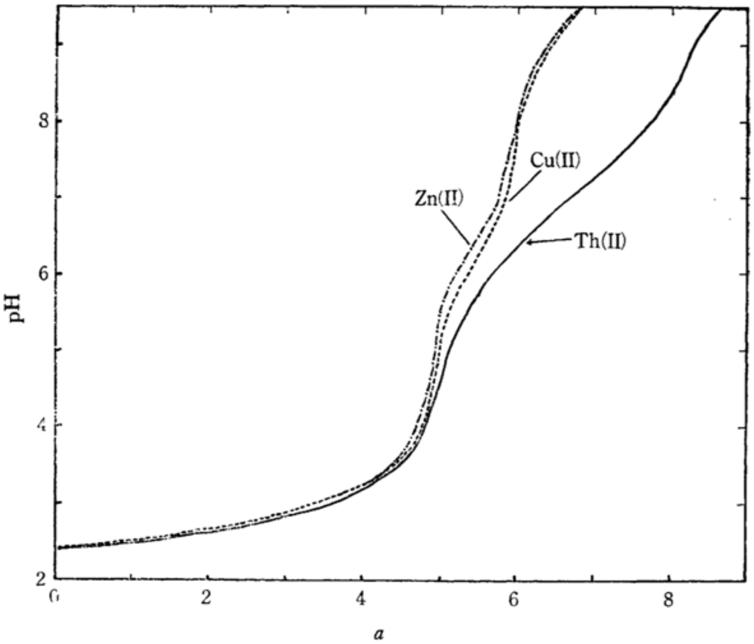

Fig. 2. Potentiometric titration curves of some heavy metals-TAPHA chelates at 25°C in 0.1 M KNO_3 with molar ratio of metal ion to ligand, 1 : 1. Concentration of TAPHA: 4.66×10^{-4} M

TABLE 1. COMPOSITIONS OF CRYSTALLINE CHELATES OF TAPHA

		C(%)	H(%)	N(%)	M(%)[a]	Na(%)[b]	H_2O(%)
$Na_4MgL\cdot3H_2O$	Found	30.13	4.50	6.87	3.98	15.2	8.82
	Calcd	29.95	3.85	6.98	4.04	15.3	8.98
$Na_4CaL\cdot3.5H_2O$	Found	29.90	4.34	6.49	6.35	14.4	9.20
	Calcd	28.76	3.86	6.71	6.40	14.7	10.1
$Na_4SrL\cdot3.5H_2O$	Found	27.64	3.98	6.21	12.7	13.6	8.75
	Calcd	26.73	3.59	6.23	13.0	13.6	9.36
$MgH_4L\cdot3H_2O$	Found	35.45	5.61	8.05	4.98		10.4
	Calcd	35.07	5.30	8.18	4.73		10.5
$CaH_4L\cdot2H_2O$	Found	34.86	4.99	7.89	7.85		6.45
	Calcd	35.23	4.93	8.22	7.84		7.04
$SrH_4L\cdot2H_2O$	Found	30.62	4.56	7.81	15.9		5.41
	Calcd	32.23	4.51	7.52	15.7		6.45
$CoH_4L\cdot2.5H_2O$	Found	33.69	5.27	7.86	10.7		8.00
	Calcd	33.41	4.86	7.79	10.9		8.35
$NiH_4L\cdot2.5H_2O$	Found	33.98	5.39	7.99	10.2		8.76
	Calcd	33.42	4.86	7.79	10.9		8.35
$CuH_4L\cdot1.5H_2O$	Found	34.45	4.94	8.10	11.7		5.20
	Calcd	34.24	4.60	8.01	12.2		5.34
$Mg_2H_2L\cdot4H_2O$	Found	32.62	5.19	7.50	8.51		12.8
	Calcd	32.52	4.91	7.58	8.78		13.0
$Ca_2H_2L\cdot3H_2O$	Found	31.79	4.84	7.31	13.6		8.90
	Calcd	31.75	4.44	7.40	14.1		9.52
$Cu_2H_2L\cdot4H_2O$	Found	28.35	4.53	6.81	20.0		11.6
	Calcd	28.49	4.30	6.64	20.1		11.4

a) Metal content was determined by EDTA titration after wet digestion of the metal chelate with nitric acid and hydrogen peroxide. Y. Tsuchitani, Y. Tomita and K. Ueno, *Talanta*, **9**, 1023 (1962).

b) Sodium was determined by precipitating as zinc sodium uranyl acetate from acid digested solution, followed by EDTA titration of zinc in the precipitate.

alkaline earth metals involved the direct pH titration of 200 m*l* of 5×10^{-4} M ligand solution in 1 : 1 and 10—24 : 1 molar ratios of metal nitrate to ligand. The typical pH titration curves are shown in Figs. 1 and 2.

As for transition metal ions, the chelate stability constants were determined by the competitive reaction using triaminotriethylamine (tren)[*4] and calcium ion as an auxiliary ligand and a metal ion respectively.[3] The measurements were carried out on the five solutions containing equimolar amounts of TAPHA (4×10^{-4} M), tren and metal ion, ten fold excess of calcium ion to TAPHA and different amounts of 1×10^{-1} N potassium hydroxide solution. The pH values of each soluiotn were measured until constant readings were obtained. They were usually attained within a week.

The acid dissociation constants of monoprotonated mononuclear chelates and the stability constants of dinuclear chelates were determined by the direct pH titration method as described above in the presence of equimolar amounts of TAPHA and metal ion and in the presence of 10—24 fold excess of metal ion to TAPHA respectively. The pH meter used and the method of calibration were those reported previously.[2]

Preparation of Crystalline Metal Chelates. TAPHA chelates of selected divalent metal ions were prepared in crystalline form by the procedures described below. Of the possible compositions of the chelates from the nonadentate hexa-basic ligand (H_6L) and divalent cations (M), three types of the chelates, $Na_4ML\cdot xH_2O$, $H_4ML\cdot xH_2O$ and $H_2M_2L\cdot xH_2O$, were isolated as well difined crystalline materials. The compositions of the chelates were determined by elementary analyses (C, H and N) as well as metal determinations. Hydrated water was determined from the weight loss after drying the sample in vacuum over phosphorus pentoxide at 100°C until it became constant weight. The results are summarized in Table 1.

$Na_4M^{II}L\cdot xH_2O$. Two millimoles (911 mg) of TAPHA ($H_6L\cdot H_2O$) and equimolar amount of metal carbonate in 80 m*l* of hot water was heated on a water bath. After complete dissolution, twice equivalent amounts of sodium carbonate (424 mg) were added, and the total volume of the solution was concentrated to 15 m*l*, to which 200—250 m*l* of ethanol was added to precipitate the sirupy product. After washing the precipitate by decantation with ethanol for several times, the crude chelate was dissolved into a small amount of water, and reprecipitated by adding a large amount of ethanol. The chelate was dried in vacuum over silica gel overnight at room temperature.

$H_2M_2^{II}L\cdot xH_2O$. An equimolar mixture of TAPHA and metal carbonate in hot water was heated on a water bath in a same scale as described above, and the solution was concentrated to 10—15 m*l*. To this solution, ethanol was added until the solution became slightly cloudy, and the mixture was kept in a refrigerator to precipitate the chelate. The crude chelate was recrystallized several times from 70—80% aqueous ethanol. The chelate was dried by the same fashion as described above.

$H_2M_2^{II}L\cdot xH_2O$. The chelate was prepared by the similar procedure as in the case of 1 : 1 hydrogen chelates, but twice molar equivalent of metal carbonate was used.

Besides the chelates listed in Table 1, which were obtained as well defined crystalline product, the chelates of manganese (II), cadmium(II) and lead(II) were prepared. However, manganese gave a sirupy chelate and cadmium and lead gave no products with consistent analytical results, so that the further purifications of these chelates were given up.

Infrared Spectra. The measurements were made with a Nippon Bunko Model DS 301 double-beam infrared spectrophotometer equipped with sodium chloride optics. The spectra were studied in Nujol mull.

Calculation of Chelate Stability Constants

Equilibrium Constants Involving Alkaline Earth Metal Ions. Definitions of equilibrium constants discussed in this paper, are summarized in Table 2.

TABLE 2. DEFINITIONS OF EQUILIBRIUM CONSTANTS

1) Acid dissociation constants of TAPHA
$K_1=[H_5L^{1-}][H^+]/[H_6L]$
$K_2=[H_4L^{2-}][H^+]/[H_5L^{1-}]$
$K_3=[H_3L^{3-}][H^+]/[H_4L^{2-}]$
$K_4=[H_2L^{4-}][H^+]/[H_3L^{3-}]$
$K_5=[HL^{5-}][H^+]/[H_2L^{4-}]$
$K_6=[L^{6-}][H^+]/[HL^{5-}]$

2) Composite acid dissociation constants[4,5]
$K_4'=[H^+]([H_2L^{4-}]+[MH_2L^{2-}])/[H_3L^{3-}]$
$K_5'=[H^+]([HL^{5-}]+[MHL^{3-}])/([H_2L^{4-}]+[MH_2L^{2-}])$
$K_6'=[H^+]([L^{6-}]+[ML^{4-}]+[M_2L^{2-}])/([HL^{5-}]+[MHL^{3-}])$

3) Acid dissociation constants of triaminotriethylamine trihydrochloride (H_3 tren)
${}^tK_1=[H_2\ tren^{2+}][H^+]/[H_3\ tren^{3+}]$
${}^tK_2=[H\ tren^{1+}][H^+]/[H_2\ tren^{2+}]$
${}^tK_3=[tren][H^+]/[H\ tren^{1+}]$

4) Acid dissociation constant of monoprotonated mononuclear chelate
$K^{H}_{MHL}=[H^+][ML^{4-}]/[MHL^{3-}]$

5) Chelate stability constants of TAPHA
$K_{MH_2L}=[MH_2L^{2-}]/[M^{2+}][H_2L^{4-}]$
$K_{MHL}=[MHL^{3-}]/[M^{2+}][HL^{5-}]$
$K_{ML}=[ML^{4-}]/[M^{2+}][L^{6-}]$
$K^{M}_{M_2L}=[M_2L^{2-}]/[M^{2+}][ML^{4-}]$
$K^{M'}_{MM'L}=[MM'L^{2-}]/[M'^{2+}][ML^{4-}]$

6) Chelate stability constant of tren
$K_{Mtren}=[Mtren^{2+}]/[M^{2+}][tren]$

In the following discussion, however, the charges on the ions, such as those in Eqs. (5)—(12) and (14)—(19), were omitted for the purpose of simplicity. The procedure of Schwarzenbach modified by Grims[4]

[*4] Triaminotriethylamine trihydrochloride was synthesized by Mr. Y. Toyota in our laboratory.

[3] G. Schwarzenbach and E. Freitag, *Helv. Chim. Acta*, **34**, 1492, 1503 (1951).

[4] J. H. Grimes, A. J. Huggard and S. P. Wilford, *J. Inorg. Nucl. Chem.*, **25**, 1225 (1963).

was followed to determine the chelate stability constants of alkaline earth metals. The outline of this procedure is as follows. By an analogus treatment to the determination of acid dissociation constants of the free ligand,[1] the composite acid dissociation constants, K'_4, K'_5, K'_6 are obtained by the direct pH titration method in the presence of excess metal ions to ligand.[5] Then, the stability constants of mono- and diprotonated mononuclear chelates, K_{MH_2L}, K_{MHL}, can be calculated from the composite and the simple acid dissociation constants with an aid of Eqs. (1) and (2).

The acid dissociation constants of monoprotonated mononuclear chelates, K^{H}_{MHL}, can be determined by the direct pH titration method in the presence of equimolar amounts of metal and ligand, in a similar manner to the determination of simple acid dissociation constants.

Now, the stability constants of mononuclear chelates, K_{ML} and that of dinuclear chelates, $K^{M}_{M_2L}$ can be obtained from Eqs. (3) and (4) respectively, as the equilibrium constants on the right hand side are known, and [M] can be approximated as M_t, a total concentration of the metal ion, if a large excess of metal ions to ligand is present.

$$K_{MH_2L} = \frac{K'_4}{K_4[M]} - \frac{1}{[M]} \tag{1}$$

$$K_{MHL} = \frac{K'_4K'_5}{K_4K_5[M]} - \frac{1}{[M]} \tag{2}$$

$$K_{ML} = \frac{K^{H}_{MHL}K_{MHL}}{K_6} \tag{3}$$

$$K^{M}_{M_2L} = \frac{1}{K_{ML}[M]}\left(\frac{K_4'K'_5K'_6}{[M]K_4K_5K_6} - \frac{1}{[M]} - K_{ML}\right) \tag{4}$$

Equilibrium Constants Involving Transition Metal Ions. The stability constants of mononuclear chelates of nickel(II), cobalt(II), copper(II), zinc(II) and cadmium(II) were determined by extending Schwarzenbach's procedure[3] using the competitive reaction with an auxiliary ligand (tren) and a metal ion (calcium). In the case of thorium(IV) ion, the stability constant K_{ML} could not be obtained because of the precipitate formation. The final equations for the transition metal chelates are as follows:

$$M_t = c = [ML]\cdot(1 + [H]/K^{H}_{MHL}) + [Mtren] \tag{5}$$

$$tren_t = c = [Mtren] + \beta[H_3tren] \tag{6}$$

$$L_t = c = [ML]\cdot(1 + [H]/K^{H}_{MHL}) + [CaL]\cdot(1 + [H]/K^{H}_{CaHL}) \tag{7}$$

$$9c - [KOH] = [H] - [OH] + [ML][H]/K^{H}_{MHL} + [CaL][H]/K^{H}_{CaHL} + \gamma[H_3tren] \tag{8}$$

$$\beta = 1 + \frac{{}^{t}K_1}{[H]} + \frac{{}^{t}K_1{}^{t}K_2}{[H]^2} + \frac{{}^{t}K_1{}^{t}K_2{}^{t}K_3}{[H]^3} \tag{9}$$

$$\gamma = 3 + \frac{2{}^{t}K_1}{[H]} + \frac{{}^{t}K_1{}^{t}K_2}{[H]^2} \tag{10}$$

$$K_{ML} = \frac{{}^{t}K_1{}^{t}K_2{}^{t}K_3K_{CaL}K_{Mtren}}{K_C} \tag{11}$$

$$K_C = \frac{[H]^3[CaL][Mtren]}{[ML][H_3tren][Ca]} \tag{12}$$

The acid dissociation constants, K^{H}_{MHL}, of monoprotonated mononuclear chelates of transition metals and thorium(IV) were determined according to Anderegg[6] by the direct pH titration in the presence of equimolar amounts of metal and ligand. Then, the stability constants of monoprotonated mononuclear chelates, K_{MHL}, can be calculated from the known values, K_6, K^{H}_{MHL} and K_{ML}[*5].

Mixed Metal Dinuclear Chelates.[6] The formation of dinuclear chelate could be considered by the two step process. The first step is the formation of 1 : 1 mononuclear chelate. The second step is the formation of 1 : 2 dinuclear chelate from mononuclear chelate and the second metal ion. When the first and the second metal ions are same, a homo-dinuclear chelate is formed. When these two metal ions are different, and the stability constant with the first metal ion (K_{ML}) is considerablly larger than that with the second metal ($K_{M'L}$), the stability constants of the mixed metal dinuclear chelates ($K^{M'}_{MM'L}$) could be obtained from Eq. (14) by the direct pH titration in the presence of an equimolar amount of the first metal ion (M) to the ligand, and in the presence of large excess of the second metal ion (M′) to the first metal ion.

$$MHL^{3-} + M'^{2+} \overset{K_m}{\rightleftharpoons} MM'L^{2-} + H^+ \tag{13}$$

$$K^{M'}_{MM'L} = \frac{[H][MM'L]}{[M'][MHL]}\cdot\frac{[MHL]}{[H][ML]} = \frac{K_m}{K^{H}_{MHL}} \tag{14}$$

$$[MHL] = p\cdot L_t \tag{15}$$

$$[MM'L] = L_t(1 - \alpha p) \tag{16}$$

$$[M'] = M_t' - L_t(2 - \alpha p) \tag{17}$$

$$\alpha = 1 + K^{H}_{MHL}/[H] \tag{18}$$

$$p = 6 - \frac{[KOH] - [H] - [OH]}{L_t} \tag{19}$$

In the treatment of the mixed metal dinuclear chelates, it is assumed that a mononuclear chelate with the first metal ion is formed in the first step ($a \leqq 5$), then it reacts with a second metal ion to form a mixed metal dinuclear chelate in the second step ($5 < a \leqq 6$).

In the case of alkaline earth meatl ions, the stability constants of homo-dinuclear chelates were obtained as described previously. However, in the cases where the second metal ions are transition metals, the stability constants of homo-dinuclear or mixed metal dinuclear chelates could not be obtained, because the formation of precipitate was observed even at the earlier stage of pH titration in the presence of excess amount of transition metal ion to the ligand.

However, the pH titration was carried out successfully when the transition metals and calcium were chosen as the first and the second metal ions respectively, and the stability constants for the transition metal-calcium TAPHA chelates (K^{Ca}_{MCaL}) were obtained from Eq. (14).

The various equilibrium constants thus obtained are summarized in Tables 3—8.

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[5] G. Schwarzenbach and H. Ackermann, *Helv. Chim. Acta*, **31**, 1029 (1948).

[*5] $\log K_{MHL} = -pK_6 + \log K_{ML} + pK^{H}_{MHL}$.

[6] G. Anderegg, P. Nägeli, F. Müller and G. Schwarzenbach, *Helv. Chim. Acta.*, **42**, 827 (1959).

Results and Discussion

Crystalline Chelates. The infrared spectra of alkaline earth metal chelates and some transition metal chelates are shown in Fig. 3. These spectra were interpreted with an aid of our knowledge on nitrilotriacetate chelates.⁷⁾ As for sodium salt of alkaline earth metal chelates ($Na_4ML \cdot xH_2O$), the absorption peak of –COOM and that of $\rangle\overset{+}{N}HCH_2COO^-$ appear in a similar region and become a single peak at around 1600 cm^{-1}. This peak shifts to lower frequency with the increase of ionic radius of metal ion. On the other hand, in the case of protonated chelate ($MH_4L \cdot xH_2O$), the two absorption peaks appear at around 1600 cm^{-1} and 1720 cm^{-1} respectively, and they are assigned to –COOM and –COOH groups respectively.⁷⁾ Therefore, if the ratio of –COOM to –COOH is estimated from the relative intensity of the two peaks, it is possible to presume the structure of $MH_4L \cdot xH_2O$. In order to make this estimation, the peak intensities were measured by the base-line method⁸⁾ and it is assumed that the values of molar extinction coefficient on EDTA chelates in aqueous solution can be adopted to TAPHA chelates, that is the molar extinction coefficient of –COOM is nearly equal to that of $-COO^-$, and the values for –COOH and –COOM are 240 and 705 mol·cm^{-1} respectively.⁹⁾ The latter assumption seems to be rather critical, since the absorption data in solution are employed in the interpretation of solid state spectra. However, the result may be still useful for the meaningful discussion of the structure, because the ratio of the band intensities of –COOM to –COOH will not differ appreciablly between the states in solid and in solution. The result shows that the ratio of –COOM to –COOH is approximately 1 : 1 in the case of protonated chelate ($MH_4L \cdot xH_2O$), and the structure of these chelates is presumed as shown in Fig. 4A or 4B.

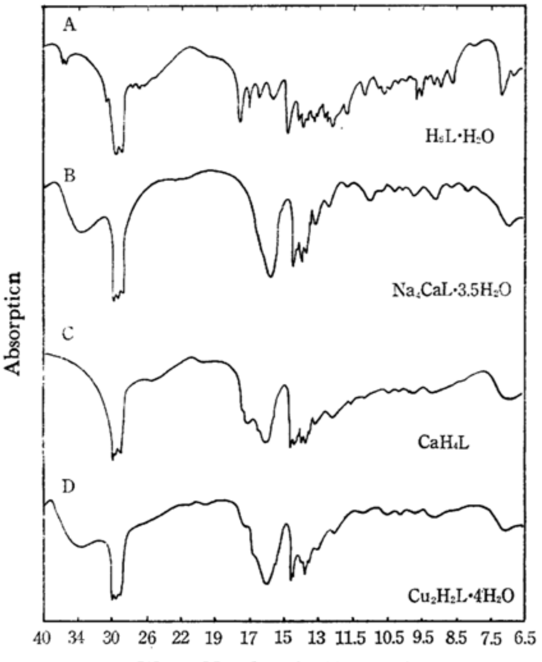
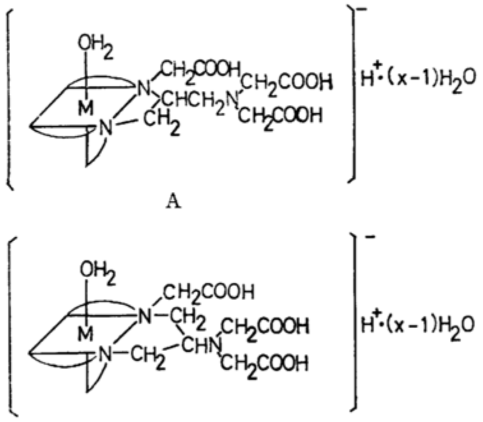


Fig. 3. Infrared spectra of crystalline TAPHA chelates in Nujol mull.

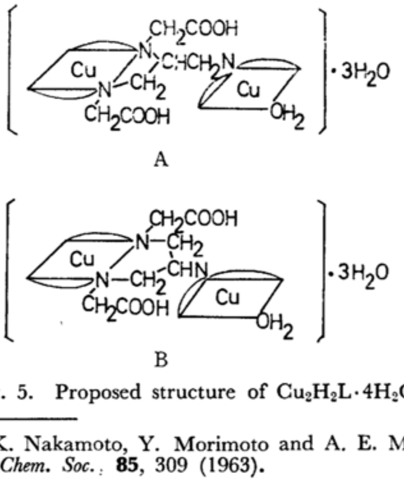


A

B

Fig. 4. Proposed structure of $MH_4L \cdot xH_2O$.

As for copper(II) dinuclear chelate ($Cu_2H_2L \cdot 4H_2O$), a peak at 1578 cm^{-1} and a shoulder at 1728 cm^{-1} are assigned to –COOM and –COOH groups respectively. The presence of two protons which is supported by the elementary analysis, suggests the existence of two uncoordinated carboxylic acid groups. Although the structures proposed in Fig. 5A or 5B may satisfy such requirment,



A

B

Fig. 5. Proposed structure of $Cu_2H_2L \cdot 4H_2O$.

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7) Y. Tomita and K. Ueno, This Bulletin, **36**, 1069 (1963).

8) N. Wright, *Ind. Eng. Chem., Anal. Ed.*, **13**, 1 (1941). J. J. Heigl, M. F. Bell and J. U. White, *Anal. Chem.*, **19**, 293 (1947).

9) K. Nakamoto, Y. Morimoto and A. E. Martell, *J. Am. Chem. Soc.*, **85**, 309 (1963).

TABLE 3. STABILITY CONSTANTS ($\log K_{ML}$) OF MONONUCLEAR CHELATES OF TAPHA AND ITS RELATED COMPLEXANES

	Mg	Ca	Sr	Ba	Ref.	Co	Ni	Cu	Zn	Cd	Ref.
TAPHA	9.21 ±0.08	10.50 ±0.04	8.56 ±0.05	7.41 ±0.09		13.8 ±0.12	18.00 ±0.09	18.37 ±0.02	15.80 ±0.08	16.18 ±0.09	
EDTA*	8.9	10.7	8.7	7.9	10[a]	16.31	18.62	18.7	16.4	16.4	10[a]
TMDTA*	6.02	7.12	5.18	4.24	14[b]	15.55	18.15	18.92	15.26	13.90	11[b]
DTPA*	9.03	10.63	9.68	8.63	13[b]	19.27	20.22	21.53	18.55	19.31	6[b]
TTHA*	8.47	10.06	9.26	8.24	4[c]	20.6	18.8	20.3			12[a]

a) 25°C, $\mu=0.1$, b) 20°C, $\mu=0.1$, c) 30°C, $\mu=0.1$

* EDTA: ethylenediaminetetraacetic acid, TMDTA: trimethylenediaminetetraacetic acid
DTPA: diethylenetriaminepentaacetic acid, TTHA: triethylenetetraminehexaacetic acid

the relative absorption intensity of –COOH group against that of –COOM group is too weak to support the proposed structures, and more experimental results are needed to conclude the structure of this chelate.

Solution Equilibria. Mononuclear Chelates (ML). As shown in Table 3, the chelate stability order of TAPHA for alkaline earth and transition metal ions is same as that of other complexanes. In the case of alkaline earth metal chelates, it is noticed that the stability constants of TAPHA chelates are very close to those of EDTA chelates, but not to those of TMDTA chelates. This results may suggest that the ligand of mononuclear chelate (ML) will take a EDTA type coordination, but not a TMDTA type coordination, as far as the effect of uncoordinated nitrilodiacetate group on the chelate stability is assumed to be same order in either case.

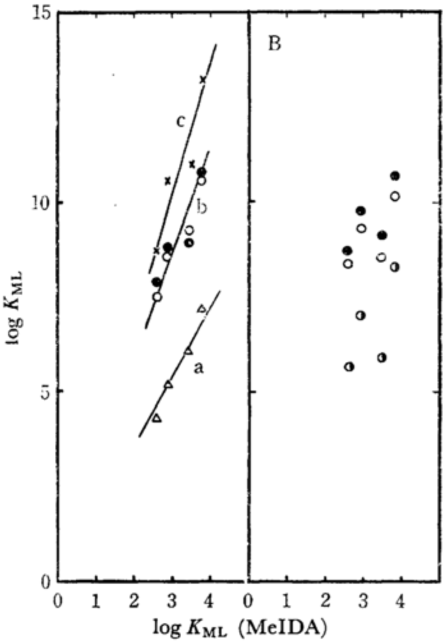

Fig. 6. Relationship between stability constant of alkaline earth metals - methyliminodiacetic acid chelates and stability constant of its related complexane chelates.

A ×: CyDTA, ○: EDTA, ●: TAPHA,
△: TMDTA
B ●: DTPA, ⊙: TTHA, ◑: HEDTA

Now, if one looks into the structure of complexanes under consideration, the coordinating groups of these ligands can be divided into two classes, *i. e.*, *N*-methyliminodiacetic acid (MeIDA) and *N,N*-dimethylglycine. Figure 6 shows a plot of the chelate stability constants of various complexanes for alkaline earth metals versus those of *N*-methyliminodiacetic acid. The plots for TMDTA, EDTA, CyDTA and TAPHA give straight lines which pass through the origin (Fig. 6A), but those for HEDTA, DTPA and TTHA do not give straight lines (Fig. 6B). The complexanes of the first family have only *N*-methyliminodiacetic acid groups as coordinating group, but those of the second family have both *N*-methyliminodiacetic acid groups and *N,N*-dimethylglycine groups within a ligand molecule. The fact that the plots for TAPHA fit on the same line as those of EDTA, is indicative that the chelating behavior of TAPHA for alkaline earth metal ions is very similar to that of EDTA, since the slope of straight lines in Fig. 6A seems to be related with the nature and size of the chelate ring.

In the case of transition metal chelates, the stabilities of EDTA and TMDTA chelates are so close to those of TAPHA chelates that it is not so easy to discuss the coordinating structure of the chelates by comparing stability data of mononuclear chelate alone. In spite of the general concept that the chelate stability increases with increasing number of coordinating groups in the ligand, a nonadentate TAPHA chelate is less stable than an octadentate DTPA chelate. The result may be explained by the number of nitrogen

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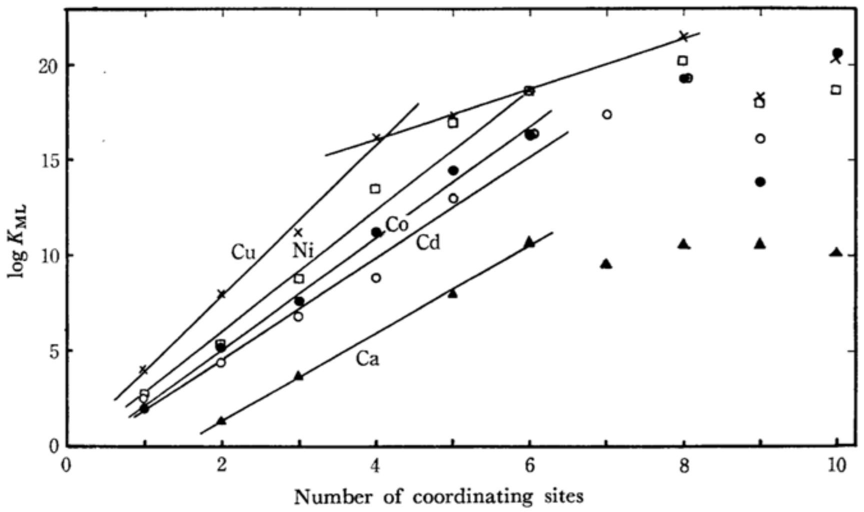

Fig. 7. Relationship between stability constant of complexanes chelates and number of coordinating sites.
Coordinating sites 1: NH_3, 2: *N*-methylglycine or glycine, 3: MeIDA or IDA, 4: EDDA, 5: HEDTA, 6: EDTA, 7: bis-[di(carboxylmethyl)aminoethyl]-methylamine, 8: DTPA, 9: TAPHA, 10: TTHA.
× Cu(II), □ Ni(II), ● Co(II), ○ Cd(II), ▲ Ca(II)

TABLE 4. STABILITY CONSTANTS (log K_{MHL}) OF MONOPROTONATED MONONUCLEAR CHELATES OF TAPHA AND ITS RELATED COMPLEXANS

	Mg	Ca	Sr	Ba	Ref.	Co	Ni	Cu	Zn	Cd	Ref.
TAPHA	6.46 ±0.07	8.03 ±0.05	6.32 ±0.05	5.42 ±0.09		10.5 ±0.13	14.6 ±0.10	14.93 ±0.03	12.7 ±0.10	13.1 ±0.11	
EDTA	2.28	3.51	2.30	2.07	15b)	9.15	11.56	11.54	9.0	9.1	11b)
TMDTA	2.91	3.07	2.39	2.11	16b)	7.4	9.9	10.7	7.3	6.5	11b)
DTPA	5.59	6.17	4.78	3.77	13b)	13.43	15.26	15.69	13.40	12.79	6b)
TTHA	7.39	8.07	6.71	5.55	4c)	18.4	17.7	18.1			

* $\log K_{MHL} = -pK_6 + \log K_{ML} + pK^{H}_{MHL}$
b) 20°C, $\mu=0.1$. c) 30°C, $\mu=0.1$

TABLE 5. STABILITY CONSTANTS (log K_{MH_2L}) OF DIPROTONATED MONONUCLEAR CHELATES OF TAPHA AND TTHA

	Mg	Ca	Sr	Ba	Ref.
TAPHA	2.8	2.9	1.7	1.4	
TTHA	1.9	2.4	1.6	1.7	4c)

c) 30°C, $\mu=0.1$

atoms which are involved in the coordination. In the case of DTPA chelate, all three nitrogens can coordinate to a metal ion, whereas, in the case of TAPHA, only two of three nitrogens can coordinate to a metal ion. Since the nitrogen atom has a larger affinity with transition metals than with alkaline earth metals, the number of coordinating nitrogens mainly affects the stability of transition metal chelates. Therefore, the values of the stability constant among EDTA, TMDTA and TAPHA chelates resemble each other.

An availability of only two nitrilodiacetate groups in the chelate formation of TAPHA, may also be proved by the following discussion. The dependence of the chelate stability of complexanes on the number of coordinating sites of the ligands can be clearly shown in Fig. 7, in which log K_{ML} values for selected metal ions are plotted against number of coordinating sites of the ligands form unidentate ammonia to multidentate complexanes.

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TABLE 6. ACID DISSOCIATION CONSTANTS (pK^{H}_{MHL}) OF MONOPROTONATED MONONUCLEAR CHELATES OF TAPHA AND ITS RELATED COMPLEXANS

	Mg	Ca	Sr	Ba	Ref.	Co	Ni	Cu	Zn	Cd	Th	Ref.
TAPHA	7.13 ±0.03	7.40 ±0.02	7.64 ±0.02	7.89 ±0.03		6.52 ±0.01	6.45 ±0.01	6.44 ±0.01	6.75 ±0.02	6.81 ±0.02	5.99 ±0.09	
EDTA	3.9	3.1			11[b]	3.0	3.2	3.0	3.0	2.9		11[b]
TMDTA	7.3	6.34			11[b]	2.4	2.2	2.2	2.5	3.06		11[b]
DTPA	7.09	5.99	5.69	5.55	13[b]	4.81	5.59	4.79	5.46	4.09		13[b]
TTHA	9.25	8.34	7.78	7.66	4[c]	7.97	9.11	7.96				12[a]

a) 25°C, $\mu=0.1$. b) 20°C, $\mu=0.1$. c) 30°C, $\mu=0.1$

It is noticed that the chelate stability increases linearly with increasing number of coordinating sites until the coordination number of metal ion is filled up. However, the values for the chelates of TAPHA which is a nonadentate ligand, is almost same as those of EDTA which is a sexadentate ligand. This result is indicative that only six of nine coordinating site of TAPHA, or in other word, two of three nitrilodiacetate groups, are involved in the formation of mononuclear chelate.

Protonated Chelates (MHL and MH_2L). As TAPHA is a hexabasic acid, protonated chelates are formed more easily than in the case of tetrabasic EDTA. The stability constants of monoprotonated mononuclear chelates (MHL) and diprotonated mononuclear chelates (MH_2L) of TAPHA are shown in Tables 4 and 5 along with the corresponding values of other complexanes of related structure. It is seen from Table 4 that, in the case of transition metal ions, the values of stability constant of TAPHA lie in between those of EDTA and of DTPA, while, in the case of alkaline earth metal ions, the values of stability constant of TAPHA are comparable with those of TTHA which is a decadentate hexabasic ligand. It is also noticed that the stability constants of diprotonated TAPHA chelates for alkaline earth metal ions are comparable with those of TTHA chelates.

The acid dissociation constants of monoprotonated TAPHA chelates were also determined and their values are listed in Table 6 along with the corresponding values of other complexanes. The acidity of protonated chelate is found to decrease with increasing the number of coordination sites in the ligands.

In contrast with the stability constants of normal chelates as well as protonated chelates which are very much dependent upon the kind of metal ions, the difference of acid dissociation constants of protonated chelates among alkaline earth metal ions as well as transition metal ions is very small in TAPHA chelates. The average value of pK^{H}_{MHL} is 7.52±0.25 for alkaline earth metal ions and 6.54±0.14 for transition metal ions. Thus, although the acidity of free monoprotonated ligand (HL) is increased by metal chelation, the influence of the kind of metal ion on the acid dissociation constant of protonated chelate is found to be not so significant. The result may suggest that the bonding site of proton is so remote from the site of metal coordination, that the acidity is not so sensitive with the kind of metal ion within each group of metals. Therefore, the most reasonable structure for monoprotonated TAPHA chelate may be an EDTA type chelate in which a terminal uncoordinated group is protonated (Fig. 8). This coordination structure, in its deprotonated form, may also be true in the case of normal mononuclear chelate of transition metal ions, whose coordination structure was not concluded in the foregoing discussion.

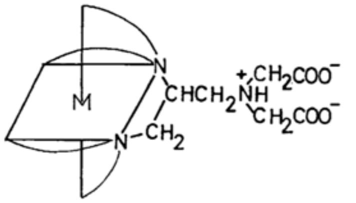

Fig. 8. Monohydrogen mononuclear chelate, MHL^{3-}.

Dinuclear Chelates (M_2L and MM'L). The formation of polynuclear chelates becomes easier when the number of coordination sites of the ligand is increased beyond the coordination number of the metal ion to be complexed. Thus, the formation of dinuclear chelates and di- and trinuclear chelates have been reported for DTPA and TTHA respectively.[6,12] The stability constants of polynuclear chelates have to be determined in the presence of large excess of metal ion. In the case of TAPHA, the formation of dinuclear chelate was observed for alkaline earth metals except magnesium. However, in the case of transition metals and magnesium, no satisfiable result could be obtained because of the formation of precipitation as the pH titration proceeded.

The stability constants of the dinuclear TAPHA chelate (M_2L) are shown in Table 7, together with those of TTHA. The values of $\log M^{M}_{M_2L}$ are

Table 7. Stability constants ($\log K^{M}_{M_2L}$) of alkaline earth metal-dinuclear chelates of TAPHA and TTHA

	Mg	Ca	Sr	Ba	Ref.
TAPHA		2.3	1.4	1.6	
TTHA	5.94	4.10	3.44	3.41	4c)

c) 30°C, $\mu=0.1$

considerably lower than those of $\log K_{ML}$ and are same order as those of 1 : 1 iminodiacetic acid chelates. This result suggests that the second metal ion may be chelated by the uncoordinated terminal nitrilodiacetate group of normal mononuclear TAPHA chelate. The structure of dinuclear chelate is proposed in Fig. 9.

It is also noticed that the values of the stability constant of dinuclear TAPHA chelate are apparently lower than those of TTHA. The magnitude of $\log K^{M}_{M_2L}$ for TTHA is comparable with those of quadridentate or quinquedentate complexanes, and this result can easily be understood if one consider the structure of mononuclear TTHA chelate, which can chelate the second metal ion by more coordination sites than does TAPHA.

As described in the experimental part, the stability constants of mixed dinuclear chelate (MM'L) were also determined by choosing transition metals and calcium as the first and the second metal ions respectively. The values of $\log K^{Ca}_{MCaL}$ can be understood as the dinuclear chelate formation constants when calcium ion is bound by a mononuclear TAPHA chelate of transition metal. The observed values are listed in Table 8. It is seen from the table that the stability constants of MCaL chelates are same order as that of Ca_2L chelate and that the values of $\log K^{Ca}_{MCaL}$ are not sensitive to the kind of the first metal ions as in the case of pK^{H}_{MHL}. These results may also support the structure of dinuclear TAPHA chelate which is shown in Fig. 9.

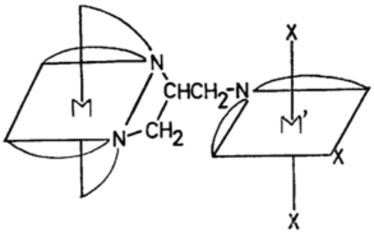

Fig. 9. Dinuclear chelate, $MM'L^{2-}$.

Table 8. Stability constants ($\log K^{Ca}_{MCaL}$) of mixed metal dinuclear chelate of TAPHA

Co	Ni	Cu	Zn	Cd
2.05 ±0.01	2.08 ±0.01	2.08 ±0.03	2.62 ±0.01	2.19 ±0.01

Th(IV)-TAPHA System. Titration of TAPHA in the presence of excess of thorium to ligand could not be carried out because of the precipitate formation. Titration of 1 : 1 mixture was successful only in the lower pH region, where no precipitate was formed and no pH drift was observed. From the data of pH titration, the acid dissociation constant of monoprotonated chelate (ThHL) was calculated as shown in Table 6. In the higher pH region, however, the hydrolyses of aquo and chelated species as well as the polymerization through olation may take place to result in a complicated system.

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