

## THE STABILITIES OF THE ALKALINE EARTH CHELATES OF SOME POLYAMINOPOLYCARBOXYLIC ACIDS

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**Abstract**—Interactions of the alkaline earth metals with some polyaminopolycarboxylic acids have been investigated by the potentiometric titration method for aqueous solutions of ionic strength approximately 0.1 at 30°. Metal chelate formation constants have been calculated, and the effects of ligand structure on chelate stability are discussed.

THE alkaline earth metals are well known to form strong complexes with compounds containing iminodiacetic acid groups. The stabilities of these complexes can be correlated with a number of ionic properties,<sup>(1)</sup> and for calcium, strontium and barium, stability constants with the same ligand are invariably found to be in the order  $K_{CaL} > K_{SrL} > K_{BaL}$  (i.e. in the inverse order to that of the ionic radii). For calcium and magnesium, the order predicted from ionic properties ( $K_{MgL} > K_{CaL}$ ) is frequently reversed, particularly with the polyaminopolycarboxylic acids. This is generally attributed to the overcrowding of donor groups round the metal ion, resulting in mutual repulsion. In the particular case of the magnesium ion and EDTA, HUGHES and MARTELL<sup>(2)</sup> have suggested that overcrowding prevents some of the donor groups from displacing water molecules from the solvent sheath of the ion, so that fewer are displaced into solution than are from the calcium ion. However, calorimetric data<sup>(3)</sup> indicate that the enthalpy change, unlike the entropy change, is higher for calcium, from which it may be deduced that the spatial configuration of EDTA is such that the calcium ion co-ordinates in all six positions with less strain. This deduction is supported by infra-red spectroscopic data on the solid alkaline earth EDTA chelates.<sup>(4)</sup>

A large number of iminodiacetic acid derivatives is now known, and it is therefore possible to study the influence of electronic and steric variation on the order and degree of complex stability with a closely related group of metals. A detailed analysis of this nature has been made by SCHWARZENBACH *et al.*,<sup>(5)</sup> who studied the effect of various functional groups as partners to a single iminodiacetic acid residue. The results were interpreted using the correlation between acid dissociation constant and metal stability constant—this relationship between ligand basicity and chelate stability has been well discussed in the literature.

In this paper this method of interpretation is used in the study of some other ligands.

<sup>(1)</sup> A. E. MARTELL and M. CALVIN, *Chemistry of the chelate compounds*, Prentice-Hall, Englewood Cliffs (1956).

<sup>(2)</sup> V. L. HUGHES and A. E. MARTELL, *J. Amer. Chem. Soc.* **78**, 1319 (1956).

<sup>(3)</sup> R. A. CARE and L. A. K. STAVELEY, *J. Chem. Soc.* 4571 (1956).

<sup>(4)</sup> D. T. SAWYER and P. J. PAULSEN, *J. Amer. Chem. Soc.* **80**, 1597 (1958).

<sup>(5)</sup> G. SCHWARZENBACH, G. ANDEREGG, W. SCHNEIDER and H. SENN, *Helv. Chim. Acta*, **38**, 1147 (1955).

## EXPERIMENTAL

*Materials*

The following ligands were studied:

- 1,2-diaminopropane-NNN'N'-tetra-acetic acid\* (C-Me-EDTA) H<sub>4</sub>L  
 ethylenediamine-NN'-diacetic acid-NN'-di-2-propionic acid\* (EDDADP) H<sub>4</sub>L  
 NN'-bis(aminoethyl)ethylenediamine-NN'N''N'''-hexa-acetic  
 acid\* (TTHA) H<sub>6</sub>L  
 2-hydroxy-1,3-diaminopropane-NNN'N'-tetra-acetic acid† (HPDPA) H<sub>4</sub>L  
 o-phenylenediamine-NNN'N'-tetra-acetic acid (o-PDPA) H<sub>4</sub>L  
 1,3,5-triaminocyclohexane-NNN'N''N'''-hexa-acetic acid (CTHA) H<sub>6</sub>L

Analyses of the commercially obtained ligands, after water washing and drying to constant elemental analysis, showed that they could be used without further purification (in some cases hydrates were obtained). These analyses were: C-Me-EDTA (Found: C, 43.2; H, 6.2; N, 9.15. Calc. for C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>8</sub>: C, 43.1; H, 5.9; N, 9.15%). EDDADP (Found: C, 42.6; H, 6.9; N, 8.4. Calc. for C<sub>12</sub>H<sub>20</sub>N<sub>2</sub>O<sub>8</sub>·H<sub>2</sub>O: C, 42.6; H, 6.6; N, 8.3%). TTHA (Found: C, 43.6; H, 6.1; N, 11.2. Calc. for C<sub>18</sub>H<sub>30</sub>N<sub>4</sub>O<sub>12</sub>: C, 43.7; H, 6.1; N, 11.3%). HPDPA (Found: C, 35.1; H, 6.1; N, 7.7. Calc. for C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>9</sub>·3H<sub>2</sub>O: C, 35.1; H, 6.4; N, 7.4%).

o-phenylenediamine-NNN'N'-tetra-acetic acid (o-PDPA) was prepared by the method of OTOZAI and KATO<sup>(6)</sup> (Found: C, 49.5; H, 4.9; N, 8.2; equivalent weight 86.1. Calculated for C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>8</sub>: C, 49.4; H, 4.7; N, 8.2%; equivalent weight 85.0). Solutions of o-PDPA deteriorate with time, this effect being enhanced by ultra-violet light, and maximum stability was obtained by keeping the solid in a dry state in the absence of light.

1,3,5-triaminocyclohexane-NNN'N''N'''-hexa-acetic acid (CTHA) was prepared using phloroglucinol as the starting material.

Phloroglucinol trioxime was prepared from phloroglucinol (A.R. grade, Messrs. B.D.H. Ltd.) by a procedure based on Baeyer's method.<sup>(7)</sup> Phloroglucinol dihydrate (81 g, 0.5 mole) was added to an ice-cold mixture of hydroxylamine hydrochloride (121.5 g, 1.75 moles) and potassium carbonate (121.5 g, 0.88 mole) in 3.5 l. of water. The reaction mixture was placed in a darkened polythene container and stored in a refrigerator (-5°). After 12 hr the mixture was filtered to remove undissolved materials, necessary precautions being taken to exclude light. The filtrate was replaced in the darkened container and left in the refrigerator for seven days. The mixture was then filtered and the precipitate obtained leached twice with boiling ethanol. The crude phloroglucinol trioxime, so obtained, was purified by recrystallization from methanol, giving the pure trioxime in 65 per cent yield, m.p. 155°(d). (Found: C, 42.4; H, 5.5; N, 23.9. Calc. for C<sub>6</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>: C, 42.1; H, 5.3; N, 24.6%).

Phloroglucinol trioxime was reduced to cyclohexane 1,3,5-triamine (eee) by the method of LIONS and MARTIN.<sup>(8)</sup> The triamine was obtained in 46 per cent yield as a clear liquid, b.p. 103°/2 mm, and was characterized as the tri-hydrochloride monohydrate, m.p. 320°. LIONS and MARTIN cite 110°/2.7 mm and 320° respectively.

CTHA was prepared by adding a solution of potassium chloroacetate (Prepared using "Analar" reagents. 12.5 g in the minimum amount of water.) to a solution of cyclohexane-1,3,5-triamine (2.6 g in the minimum amount of water). A yellow colour developed in the mixture. Over a period of 3 hr a concentrated aqueous solution of potassium hydroxide (11 g) was added, whilst the mixture was stirred and heated at 85°. The temperature was maintained for a further seventy hours and then, after cooling, concentrated hydrochloric acid was added until the pH was about 2. The mixture (20 ml) was poured into methanol (300 ml) and left standing for about eighteen hours at 0°. The precipitate which was formed was collected by filtration and twice purified by precipitation from water/methanol to give a white solid, m.p. 200°, which elemental analysis showed to be cyclohexane-1,3,5-triamine-NNN'N''N'''-hexa-acetic acid tri-hydrate with 0.05 molar proportions of ionizable

\* The Geigy Company Ltd.

† Aldrich Chemical Co., Inc.

<sup>(6)</sup> K. OTOZAI and I. KATO, *Japan Analyst* **8**, 259 (1959).

<sup>(7)</sup> A. BAEYER, *Ber. Dtsch. Chem. Ges.* **19**, 159 (1886).

<sup>(8)</sup> F. LIONS and K. V. MARTIN, *J. Amer. Chem. Soc.* **79**, 1572 (1957).

hydrogen replaced by potassium. (Found: C, 40.15; H, 5.7; N, 7.55; K (as ash), 2.0; Cl, <0.1; molecular weight 540.  $C_{18}H_{26.7}N_3O_{12}K_{0.3} \cdot 3H_2O$  requires: C, 39.8; H, 6.1; N, 7.7; K, 2.2%; molecular weight 543). A silver nitrate test indicated that chloride ion was absent. Titration confirmed partial neutralization by 0.05 molar proportions of base.

The concentrations of the ligand solutions used ( $\approx 1 \times 10^{-3}$  M) were determined by titration with a standard zinc solution using a metallochromic indicator.

Standard metal solutions and the carbonate free potassium hydroxide solution, used for titrations, were specially prepared by Messrs. B.D.H. Ltd.

In accordance with much published work,<sup>(9)</sup> all titrations were carried out in the presence of a constant concentration of inert salt (0.1 M potassium chloride). Background acid ( $1 \times 10^{-3}$  M perchloric acid) was present in those titrations where the stability constants were to be calculated after IRVING.<sup>(10)</sup> "Analar" water (Messrs. B.D.H. Ltd.) was used in the preparation of all solutions.

### Apparatus

Measurement of pH was made with an Electronic Instruments Ltd. direct reading pH meter (Model 23A) using a glass electrode (E.I.L. GHS23) and a reference electrode (E.I.L. RJ23 Calomel). The instrument was standardized before each titration with solutions prepared from Burroughs Wellcome buffer tablets (these conform to N.B.S. definition of pH). Measurements of pH were accurate to  $\pm 0.02$  pH units. Titrations were carried out at  $30.0^\circ \pm 0.2^\circ$  in a double-walled glass cell of total capacity 250 ml. Water from a thermostat circulated through the outer jacket. An "agla" micrometer syringe was used for alkali addition, a very fine polythene capillary being employed to prevent diffusion of alkali into the solution.

### Titration procedure

The appropriate solution (200 ml in all cases) was pipetted into the titration cell, the electrodes and stirrer placed in position, and oxygen-free nitrogen, presaturated with water vapour by passing through water at  $30^\circ$ , bubbled through the solution. When temperature equilibrium had been reached, the titration was carried out, time being allowed for equilibration after each addition of alkali; curves were plotted of pH versus ml of alkali added. For a particular ligand the following titration curves were plotted, according to the method of calculation employed (IRVING and ROSSOTTI<sup>(10)</sup> or SCHWARZENBACH and ACKERMANN<sup>(11)</sup>):

Irving: (a) Perchloric acid (b) perchloric acid + ligand (c) perchloric acid + ligand + metal; equal concentrations of ligand and metal.

Schwarzenbach: (a) ligand (b) ligand + metal; ten times excess of metal (c) ligand + metal; equal concentration of metal.

## CALCULATIONS AND RESULTS

It should be noted that all the values reported here are stoichiometric concentration constants, valid only for the conditions of solvent and ionic background under which they were obtained.

### Constants for C-Me-EDTA, HPDTA and EDDADP

The acid dissociation constants, and chelate stability constants with the alkaline earth metals, of C-Me-EDTA, HPDTA and EDDADP were calculated by the method of IRVING and ROSSOTTI.<sup>(10,12)</sup> A special feature of this method is that the formation curve of a system of metal-ligand complexes can be calculated directly from pH meter readings during a titration, without knowledge of the hydrogen ion concentration or

<sup>(9)</sup> J. BJERRUM, G. SCHWARZENBACH and L. G. SILLEN: *Stability Constants Part 1: Organic Ligands*. Chem. Soc., London (1956).

<sup>(10)</sup> H. M. IRVING and H. S. ROSSOTTI, *J. Chem. Soc.* 2904 (1954).

<sup>(11)</sup> G. SCHWARZENBACH and H. ACKERMANN, *Helv. Chim. Acta* 31, 1029 (1948).

<sup>(12)</sup> H. IRVING and H. S. ROSSOTTI, *J. Chem. Soc.* 3397 (1953).

activity. This method of calculation makes no allowance for the formation of protonated and/or binuclear complexes, but SCHWARZENBACH and ACKERMANN<sup>(13)</sup> have shown that for EDTA—an analogous compound—the protonated complex is an unstable intermediate never present to more than a few per cent, and that the binuclear complex is not formed under normal conditions. Also the presence of these additional complexes leads to unusual formation function curves which were not obtained for the above compounds. The results are given in Table 1, together with other authors' data relevant to the discussion.

TABLE 1

Compound	Acid dissociation constants				Chelate stability constants			
	pK <sub>1</sub>	pK <sub>2</sub>	pK <sub>3</sub>	pK <sub>4</sub>	log K <sub>Mg</sub>	log K <sub>Ca</sub>	log K <sub>Sr</sub>	log K <sub>Ba</sub>
(1) C-Me-EDTA	2.60	3.03	6.20	10.84	10.29	11.47	9.61	8.48
(2) HPDTA	~2	3.36	6.85	9.70	5.3	6.52	5.10	4.65
(3) EDDADP	2.29	2.91	6.82	10.60	9.41	10.74	8.68	6.86
(4) EDTA	2.4	2.86	6.22	10.25	—	10.59	8.80	—
(5) C-Me-EDTA <sup>(14)</sup>	—	—	—	—	8.8	10.4	10.7	8.1
(6) HPDTA <sup>(14)</sup>	—	—	—	—	5.3	6.0	5.1	4.7
(7) TMDTA <sup>(11)</sup>	2.0	2.67	7.91	10.27	6.02	7.12	5.18	4.24

(1), (2), (3), (4)—present authors. 30°, in 0.1 M KCl.

(5), (6)—ref. 14, no experimental details given.

(7)—ref. 11, trimethylenediamine-NNN'N'-tetra-acetic acid, 20°, in 0.1 M KCl.

#### Constants for TTHA, CTHA and o-PDTA

The appropriate constants for TTHA, CTHA and o-PDTA were calculated by an extension of the method of SCHWARZENBACH and ACKERMANN<sup>(11)</sup>; the previous method<sup>(10,12)</sup> was not used (except for o-PDTA *-v.i.*) because examination of the titration curves suggested that protonated metal chelates are stable species and this was confirmed by its application to TTHA, which resulted in abnormal formation function curves. The method used involved the conversion of pH meter readings into hydrogen ion concentrations. This problem has been considered by BATES<sup>(15)</sup> and FELDMAN.<sup>(16)</sup> BATES, in discussing the interpretation of pH values as measured on the NBS scale, considers that a measured pH may be expected to approach an experimental  $-\log f_{\text{H}^+} \cdot m_{\text{H}^+}$  provided that the test solution has an ionic strength within the same range as that of the standard buffer solution, namely between 0.01 and 0.1. Under these conditions  $[\text{H}^+]$  can be calculated with an error of not greater than  $\pm 0.01$

<sup>(13)</sup> G. SCHWARZENBACH and H. ACKERMANN, *Helv. Chim. Acta*, **30**, 1798 (1947).

<sup>(14)</sup> R. L. SMITH, *The sequestration of metals*, Chap. 5. Chapman and Hall, London (1959).

<sup>(15)</sup> R. G. BATES, *Electrometric pH determination*, Chap. 4. Wiley, New York (1954).

<sup>(16)</sup> I. FELDMAN, *Analyt. Chem.* **28**, 1859 (1956).

pH units, provided that  $f_{\text{H}^+}$  is calculated using the same expression as was used for the assignment of the pH values of the standard buffer solutions. This expression is;

$$-\log f_i = \frac{AZ_i^2\sqrt{\mu}}{1 + Ba_i\sqrt{\mu}} \quad (1)$$

$a_i$ ,  $A$  and  $B$  being assigned the values as used by the NBS. As the errors introduced by this are less than the experimental error, calibration against a hydrogen electrode was considered unnecessary.

Thus, from Equation (1) the following relationship was used to obtain hydrogen ion concentrations:

$$-\log_{10} [\text{H}^+] = \text{pH reading} - 0.11 \quad (2)$$

Equation (2) is calculated for an ionic strength of 0.1. Although the ionic strength varied slightly according to the concentrations of ligand and metal present, the effect of this can readily be shown to be negligible using Equation (1).

Dealing first with CTHA and TTHA, the acid dissociation constants of these compounds were calculated essentially by the method of SCHWARZENBACH *et al.*<sup>(17)</sup> except that an algebraic method of solution was used instead of a graphical one (acid dissociation constants are defined as follows: for an acid  $\text{H}_n\text{L}$ ,  $K_i = \frac{[\text{H}][\text{H}_{n-i}\text{L}]}{[\text{H}_{n-i+1}\text{L}]}$  and  $\text{p}K_i = -\log_{10} K_i$ ). The value of the ionization constant for water,  $K_w^0$  (i.e.  $\text{C}_{\text{H}^+} \cdot \text{C}_{\text{OH}^-}$ ), used in these calculations was  $2.35 \times 10^{-14}$ , this value being obtained from published data.<sup>(18)</sup>

Examination of the potentiometric titration curves for these compounds, alone and in the presence of metal ions, indicates that chelation commences when the species  $\text{H}_3\text{L}^{3-}$  is present. Thus, in titrations containing excess metal ion, the possible chelate species are  $\text{MH}_2\text{L}^{2-}$ ,  $\text{MHL}^{3-}$ ,  $\text{ML}^{4-}$  and  $\text{M}_2\text{L}^{2-}$ , their respective stability constants being

$$K_{\text{MH}_2\text{L}} = \frac{[\text{MH}_2\text{L}]}{[\text{M}][\text{H}_2\text{L}]} \quad (3) \quad K_{\text{MHL}} = \frac{[\text{MHL}]}{[\text{M}][\text{HL}]} \quad (4)$$

$$K_{\text{ML}} = \frac{[\text{ML}]}{[\text{M}][\text{L}]} \quad (5) \quad K_{\text{M}_2\text{L}} = \frac{[\text{M}_2\text{L}]}{[\text{M}][\text{ML}]} \quad (6)$$

The relative importance of these species can only be assessed from their respective stability constants, deductions from the shapes of the titration curves being misleading.

Using the approach of SCHWARZENBACH and ACKERMAN,<sup>(11)</sup> the titration curves when excess metal ion is present (Fig. 1. TTHA; Fig. 2. CTHA) may be defined in terms of the first three acid dissociation constants  $K_1$ ,  $K_2$  and  $K_3$ , and three new composite "acid" dissociation constants.

$$K_4' = \frac{[\text{H}](\text{[H}_2\text{L]} + \text{[MH}_2\text{L]})}{\text{[H}_3\text{L]}} \quad (7)$$

$$K_5' = \frac{[\text{H}](\text{[HL]} + \text{[MHL]})}{(\text{[H}_2\text{L]} + \text{[MH}_2\text{L]})} \quad (8)$$

$$K_6' = \frac{[\text{H}](\text{[L]} + \text{[ML]} + \text{[M}_2\text{L]})}{(\text{[HL]} + \text{[MHL]})} \quad (9)$$

<sup>(17)</sup> G. SCHWARZENBACH, A. WILLI and R. O. BACH, *Helv. Chim. Acta* **30**, 1303 (1947).

<sup>(18)</sup> H. S. HARNED and B. B. OWEN, *The physical chemistry of electrolytic solutions*. Chap. 15. Reinhold, New York (1958).

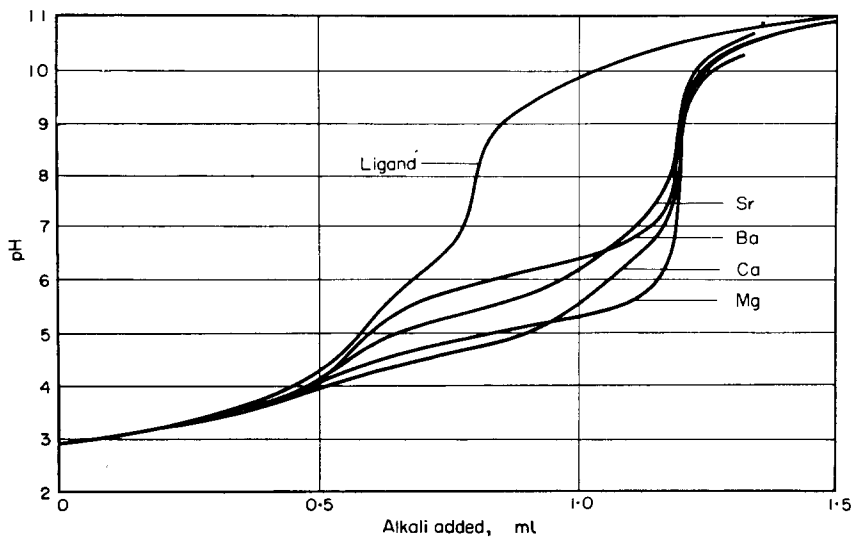


FIG. 1.—Titration of TTHA—metal.

Titration of TTHA in the absence and in the presence of ten times excess of alkaline earth ions.

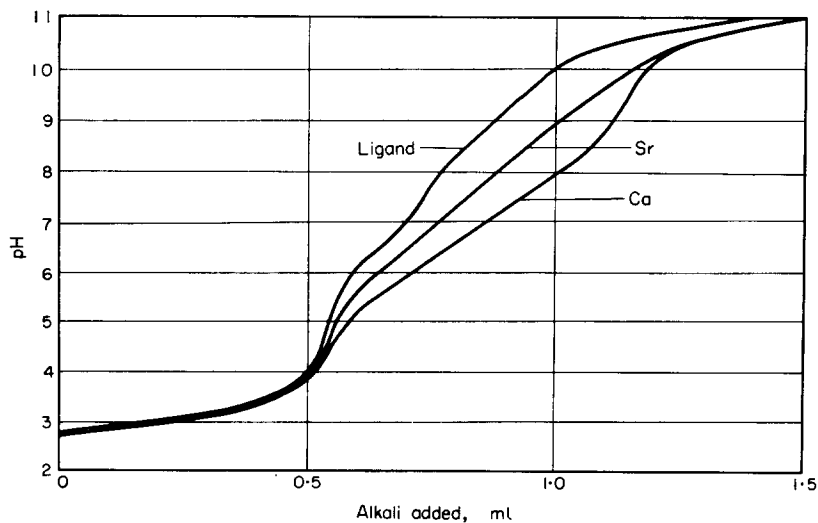


FIG. 2.—Titration of CTHA—metal.

Titration of CTHA in the absence and in the presence of ten times excess of calcium and of strontium ions.

The constants  $K_4'$ ,  $K_5'$  and  $K_6'$  are obtained by the usual algebraic process, by treating the excess metal curve as a simple dissociation curve. Using an essentially similar algebraic treatment to that of the above authors, the following equations may be obtained:

$$K_{\text{MH}_2\text{L}} = \frac{K_4'}{K_4 \text{Mt}} - \frac{1}{\text{Mt}} \quad (10)$$

$$K_{\text{MHL}} = \frac{K_5'(1 + \text{Mt} \cdot K_{\text{MH}_2\text{L}})}{K_5 \text{Mt}} - \frac{1}{\text{Mt}} \quad (11a)$$

$$= \frac{K_4' K_5'}{K_4 K_5 \cdot \text{Mt}} - \frac{1}{\text{Mt}} \quad (11b)$$

and

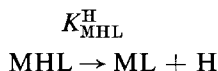
$$K_{\text{ML}} + K_{\text{ML}} \cdot K_{\text{M}_2\text{L}} \cdot \text{Mt} = \frac{K_6'(1 + \text{Mt} \cdot K_{\text{MHL}})}{K_6 \text{Mt}} - \frac{1}{\text{Mt}} \quad (12a)$$

$$= \frac{K_4' \cdot K_5' \cdot K_6'}{K_4 \cdot K_5 \cdot K_6 \cdot \text{Mt}} - \frac{1}{\text{Mt}} \quad (12b)$$

[N.B. Mt = concentration of metal ion, which is effectively constant, as it is present in large excess.]

Thus, values for  $K_{\text{MH}_2\text{L}}$  and  $K_{\text{MHL}}$  can be calculated and further, if it is assumed that the concentration of the binuclear complex is negligible, a value for  $K_{\text{ML}}$  can be obtained.

In the titrations of equimolar mixtures of ligand and metal ion (Fig. 3. TTHA; Fig. 4. CTHA) the presence of binuclear complexes may be disregarded. Since values for  $K_{\text{MH}_2\text{L}}$  and  $K_{\text{MHL}}$  are known, data from these titrations may be used to calculate values for  $K_{\text{ML}}$  which are not dependent on the assumption made above. The method of calculation used was the same as that outlined by SCHWARZENBACH and ACKERMAN, except in the cases of calcium and magnesium with TTHA. In these cases the titration curves have large inflexions at  $a = 5^*$ , indicating that the further release of a proton in the region  $a = 5$  to  $a = 6$  may be treated as a simple acid dissociation i.e.



The constant  $K_{\text{MHL}}^{\text{H}}$ , found by the standard method, is related to  $K_{\text{ML}}$  by

$$K_{\text{ML}} = \frac{K_{\text{MHL}}^{\text{H}} \cdot K_{\text{MHL}}}{K_6} \quad (13)$$

Substitution of the true value for  $K_{\text{ML}}$  into (12a) or (12b) allows the calculation of  $K_{\text{M}_2\text{L}}$ . The results for TTHA and CTHA are given in Table 2.

The acid dissociation constants and chelate stability constants of *o*-PDTA were obtained by two independent methods: SCHWARZENBACH'S<sup>(11,17)</sup> method of

\*  $a$  = no. of moles of alkali added per mole of ligand.

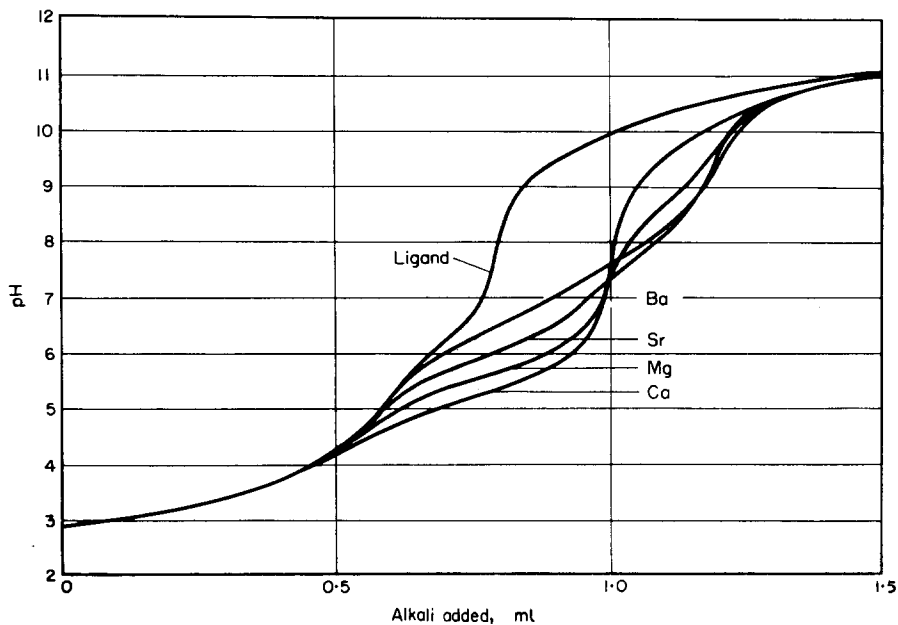


FIG. 3.—Titration of TTHA—metal.

Titration of TTHA in the absence and in the presence of equimolar alkaline earth ions.

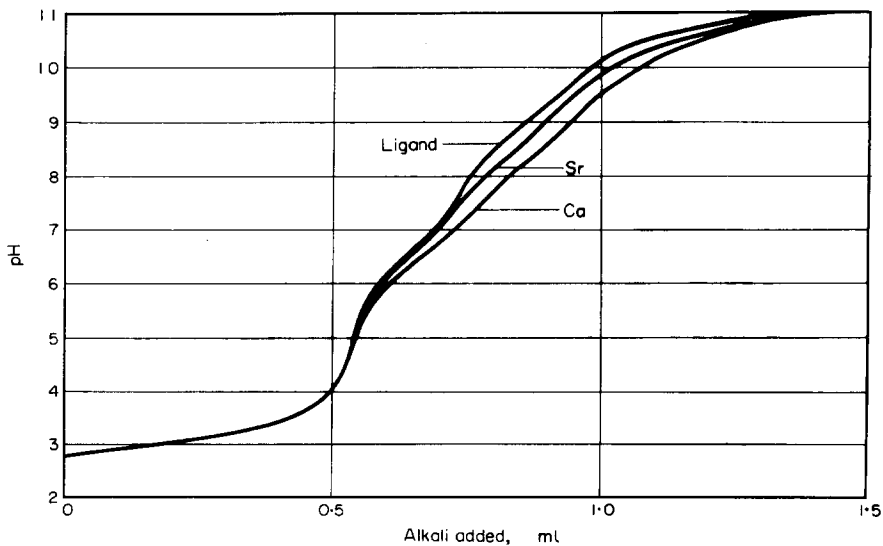


FIG. 4.—Titration of CTHA—metal.

Titration of CTHA in the absence and in the presence of equimolar calcium and strontium ions.



calculation was applied to the titration curves in Figs. 5 and 6 (excess and equimolar metal respectively), and IRVING'S<sup>(10,12)</sup> method was applied to the titration curves in Fig. 7.

Dealing first with SCHWARZENBACH'S<sup>(11,17)</sup> method, the calculation of acid dissociation constants, using an algebraic method of solution, was subject in this particular case to some inaccuracy due to arithmetical difficulties. Values of  $pK$ 's so obtained are therefore given to 0.1 log unit only. Since chelation begins before the species  $H_2L$

TABLE 2

Metal	Acid dissociation constants						Chelate stability constants			
	$pK_1$	$pK_2$	$pK_3$	$pK_4$	$pK_5$	$pK_6$	$\log K_{MH_2L}$	$\log K_{MHL}$	$\log K_{ML}$	$\log K_{M_2L}$
TTHA										
H	2.46	2.52	4.00	5.98	9.35	10.33				
Mg							1.9	7.39	8.47	5.94
Ca							2.4	8.07	10.06	4.10
Sr							1.6	6.71	9.26	3.44
Ba							1.7	5.55	8.22	3.41
CTHA										
H	$pK_1 + pK_2 + pK_3$									
	6.6		6.3	8.5	10.6					
Ca							2.9	4.7	5.5	3.6
Sr							2.3	3.5	4.5	2.1
<i>o</i> -PDTA										
Calculated after SCHWARZENBACH <sup>(11,17)</sup>										
H	2.9	3.7	4.8	6.7	—	—				
Mg							2.6	*	7.1	—
Ca							*	*	~9	—
Sr							1.3	3.0	6.2	—
Ba							1.6	2.3	4.8	—
Calculated after IRVING and ROSSOTTI <sup>(10,12)</sup>										
H	2.94	3.83	5.01	6.82	—	—				
Mg							—	—	7.3	—
Ca							—	—	8.1	—
Sr							—	—	6.4	—
Ba							—	—	4.8	—

\* These constants could not be calculated.

is present, the method used for the calculation of chelate stability constants from the excess metal curves was modified to include four "composite" dissociation constants, defined analogously to those shown previously. The flatness of the metal curves introduces considerable arithmetical uncertainties into the calculations, and, in some cases, values of individual "composite" constants and products thereof were either

doubtful or unobtainable. Consistent results were obtained for  $K_{ML}$  except in the case of calcium where values varied widely. With strontium and barium, where protonated chelate constants were obtained, it was possible to calculate  $K_{ML}$  from the equimolar metal curves and comparison of the results obtained with those from the excess metal curves indicates the absence of binuclear chelates. The results are shown in Table 2.

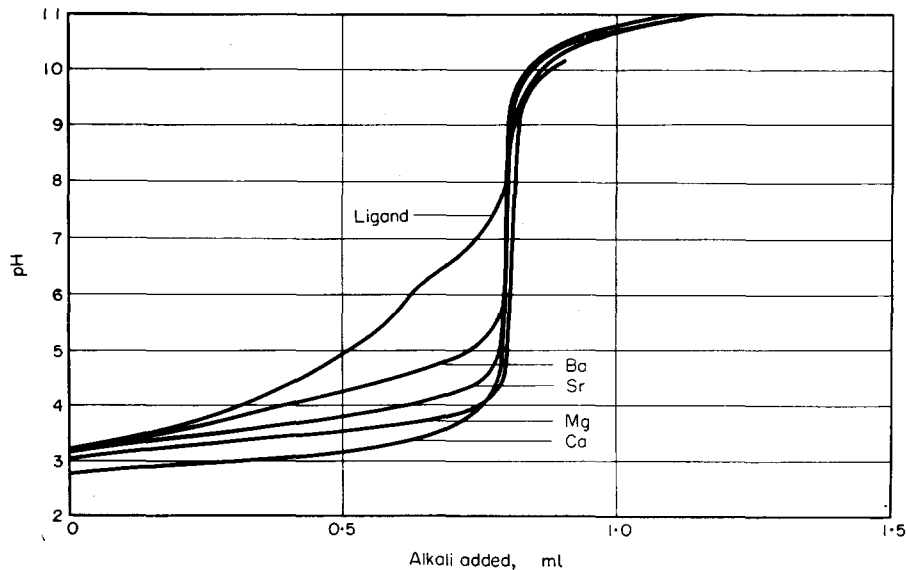


FIG. 5.—Titration of *o*-PDTA—metal.

Titration of *o*-PDTA in the absence and in the presence of ten times excess of alkaline earth ions.

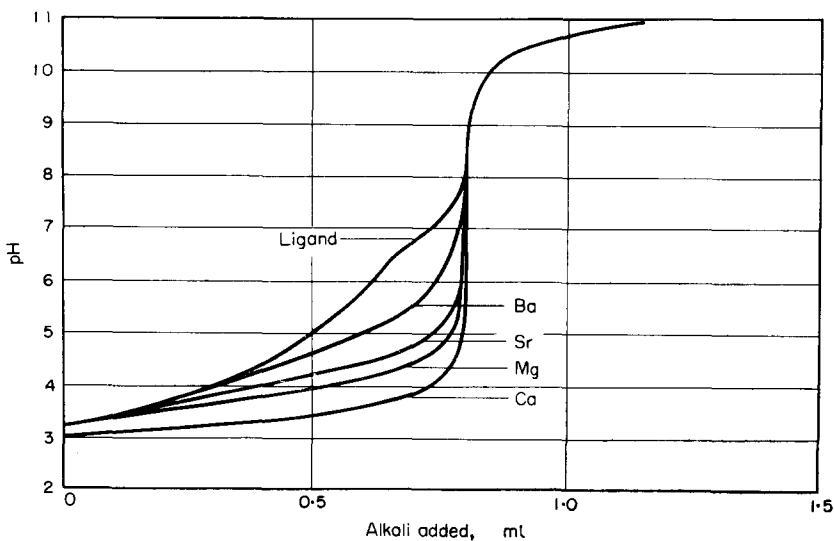


FIG. 6.—Titration of *o*-PDTA—metal.

Titration of *o*-PDTA in the absence and in the presence of equimolar alkaline earth ions.

The results obtained using IRVING and ROSSOTTI's<sup>(10,12)</sup> method are given in Table 2. The formation curves for the metal-ligand complexes are of normal shape but the results are given to 0.1 log unit only because protonated metal chelates can be shown to be stable intermediates from the data given in Table 2.

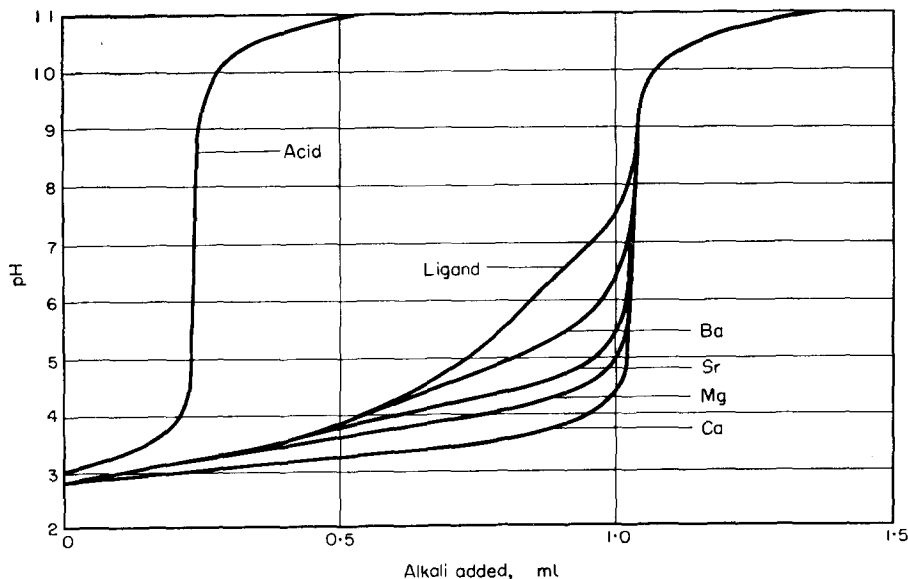


FIG. 7.—Titration of *o*-PDTA—metal.

Titration of *o*-PDTA, in perchloric acid solution ( $1 \times 10^{-3}$  M), in the absence and in the presence of equimolar alkaline earth ions.

For *o*-PDTA results obtained by the two methods agree well, except in the case of calcium, considering the difficulties encountered in calculating the figures in Table 2 and the fact that IRVING and ROSSOTTI's method does not take protonated metal chelates into account.

#### DISCUSSION

For the purpose of comparison, the values of the acid dissociation constants for EDTA, and its chelate stability constants with calcium and with strontium, were measured under the same experimental conditions. The values obtained are shown in Table 1.

Although there is some disagreement about the form of polyaminopolycarboxylic acids in solution<sup>(19,20,21)</sup> it has been assumed throughout that all the compounds studied exist initially in solution as completely betaine forms, as proposed by SCHWARZENBACH and ACKERMANN.<sup>(13)</sup>

<sup>(19)</sup> D. CHAPMAN, *J. Chem. Soc.* 1766 (1955).

<sup>(20)</sup> M. J. L. TILLOTSON and L. A. K. STAVELEY, *J. Chem. Soc.* 3613 (1958).

<sup>(21)</sup> D. C. OLSON and D. W. MARGERUM, *J. Amer. Chem. Soc.* **82**, 5602 (1960).



HPDTA and TMDTA, it can be seen that the introduction of a centrally attached hydroxyl group leads to reduced basicity of the nitrogen atoms. The two parent amines, 1:3 diaminopropane and 1:3 diaminopropane-2-ol, show a similar effect.<sup>(9)</sup> It is somewhat surprising that in HPDTA the effect is greater for  $K_3$  than for  $K_4$ . HPDTA is a weaker chelating agent than TMDTA, but the results are not strictly comparable, as values obtained apply to different temperatures, and our method of calculation takes no account of intermediate protonated metal chelates. (SCHWARZENBACH and ACKERMANN<sup>(11)</sup> have shown that, for tetra-acetic acids based on diamines with two carbon atoms in the main chain, this assumption is justifiable, but that when three carbon atoms interpose between the nitrogen atoms some protonated chelates are present.)

The greatly increased acidity of the nitrogen centres of *o*-PDTA compared with EDTA is expected from the presence of an aromatic ring. It may be shown empirically by plotting the logarithms of the chelate stability constants for a particular metal against the combined proton affinities of the nitrogen centres ( $pK_3 + pK_4$ ) for several 1,2-diamine tetra-acetic acids, that *o*-PDTA has exceptional chelating ability in relation to its basicity (see Fig. 8). This effect must be associated with the presence of a benzene ring, but the explanation is not clear.

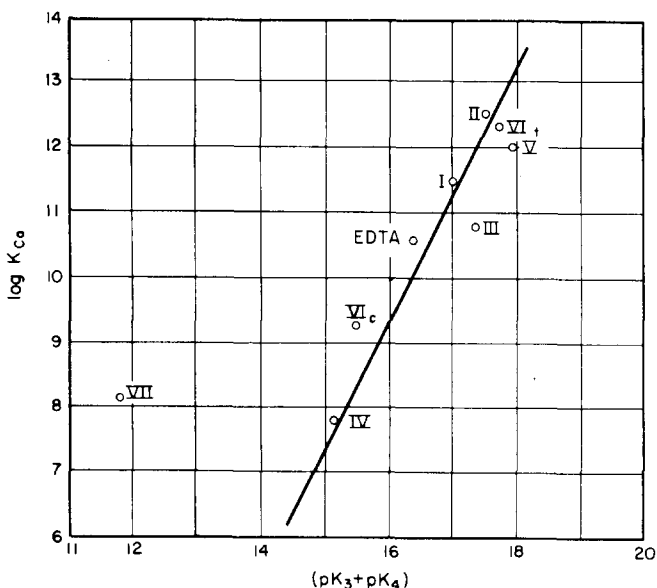


FIG. 8.—Plot of  $\log K_{Ca}$  vs  $(pK_3 + pK_4)$  for a number of compounds.

I C-Me-EDTA; II 2,3-diaminobutane-NNN'N'-tetraacetic acid; III EDDADP; IV 1,2-cyclobutanediamine-NNN'N'-tetraacetic acid; V trans-1,2-cyclopentanediamine-NNN'N'-tetraacetic acid; VIc cis-1,2-cyclohexanediamine-NNN'N'-tetraacetic acid; VIi trans-1,2-cyclohexanediamine-NNN'N'-tetraacetic acid; VII *o*-PDTA

(II) A. J. HUGGARD and S. P. WILFORD. Unpublished work. (IV) and (V) V. G. YASHUNSKII, *J. Gen. Chem. (USSR)* **28**, 1026 (1958). (VIc) H. KROLL and M. GORDON, *Abstr. Amer. Chem. Soc. Meeting*, New York (September, 1960). (VIi) V. G. YASHUNSKII and M. N. SHCHUKINA, *J. Gen. Chem. (USSR)* **28**, 230 (1958).

The values of the acid dissociation constants for CTHA are as expected for a hexacetic acid based on a triamine—i.e. three strongly acidic protons and three betaine protons. The considerable stability of the chelate  $M_2L$ , compared with the stability of the chelate  $ML$  (i.e. for CTHA,  $\log K_{CaL} - \log K_{Ca_2L} = 1.9$  whereas for TTHA,  $\log K_{CaL} - \log K_{Ca_2L} = 6.0$ ), and the relatively low value of the chelate stability constants for the chelate  $ML$ , suggest that the three iminodiacetic acid groupings are not all operative in forming the latter. This implies that the CTHA molecule exists in solution as the triequatorial form, the energy released when a chelate is formed being insufficient to cause a change to the triaxial form which might be expected to give a more stable chelate (since CTHA exists in solution in a tri-betaine form, a considerable energy difference between the tri-axial and tri-equatorial forms will exist owing to the mutual repulsion of the positively charged nitrogen centres).

The acid dissociation constants for TTHA agree reasonably well with those obtained by FROST,<sup>(25)</sup> allowing for the difference in temperature. Examination of the titration curves for TTHA with equimolar metal present (Fig. 3) indicates that the magnesium curve intersects both the strontium and the barium curves. These intersections are due to the greater acidities (as shown by  $K_{MHL}^H$ ) of the protonated strontium and barium chelates compared to the corresponding magnesium chelate. It can be shown, using Equation (13) that, depending on the relative magnitudes of  $K_{MHL}^H$  and  $K_{MHL}$ , this may lead to a reversal of affinity orders. Thus with the magnesium and strontium chelates it is found that  $K_{SrL} > K_{MgL}$  although  $K_{MgHL} > K_{SrHL}$ , but no such reversal occurs for magnesium and barium. It is evident that some effect must operate on the release of the last proton which is relatively less favourable for the magnesium chelate than for the chelates of strontium and of barium—possibly a steric effect connected with the small size of the magnesium ion (radius 0.66 Å), as compared to the strontium ion (radius 1.18 Å) and the barium ion (radius 1.34 Å), and the ensuing mutual repulsion of donor groups. DURHAM and RYSKIEWICH<sup>(26)</sup> found analogous results with diethylenetriamine-penta-acetic acid (DTPA). A similar effect is found for the calcium curve, which intersects both the strontium and the barium curves, but as in the magnesium/barium case this does not lead to any reversal of affinity orders.

In conclusion it may be said that the results of this study agree well with the known chelate stability orders for the alkaline earth metals. That is, for calcium, strontium and barium the order is invariably  $K_{Ca} > K_{Sr} > K_{Ba}$ , but as has been noted previously, the position of magnesium is not fixed.

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<sup>(25)</sup> A. E. FROST, *Nature, Lond.* **178**, 322 (1956).

<sup>(26)</sup> E. J. DURHAM and D. P. RYSKIEWICH, *J. Amer. Chem. Soc.* **80**, 4812 (1958).