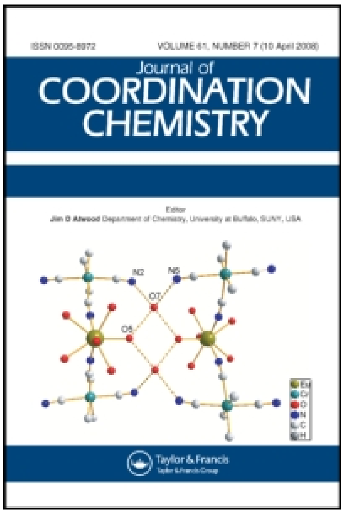

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A POTENTIOMETRIC STUDY OF METAL CHELATES WITH PENTAETHYLENEHEXAAMINEOCTAACETIC ACID

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A POTENTIOMETRIC STUDY OF METAL CHELATES WITH PENTAETHYLENEHEXAAMINEOCTAACETIC ACID

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The protonation constants of pentaethylenehexaamineoctaacetic acid, PHOA, were determined by potentiometric titration in aqueous solution at an ionic strength of 0.10 M KNO_3 and at 25°C. The formation constants of various metal–PHOA complexes were also obtained by titrating mixtures of metal to ligand in molar ratios of 1 : 1 and 2 : 1. Calculations were performed with the computer program BEST. Individual formation constants are reported for Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II) with PHOA as well as their related protonated species. The stabilities of the 1 : 1 and 2 : 1 complexes are similar in many respects to complexes formed with tetraethylenepentaamineheptaacetic acid (TPHA). The similarities in the stabilities of both the 1 : 1 and 2 : 1 complexes with PHOA and those with TPHA are explained in terms of ligand denticity and steric effects. Mercury(II)–PHOA complexes exhibited the highest formation constants, followed by copper(II)–PHOA complexes which had higher $\log K_{ML}$'s than those for Co(II), Ni(II), Zn(II), Cd(II) and Pb(II).

Keywords: Pentaethylenehexaamineoctaacetic acid; tetraethylenepentaamineheptaacetic acid; metal complex stabilities; potentiometry; protonation constants

INTRODUCTION

The octaanion of pentaethylenehexaamineoctaacetic acid (PHOA) can be represented as a tetradecadentate ligand with six nitrogen and eight

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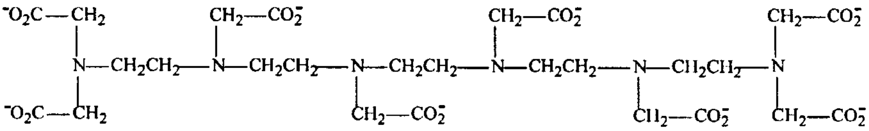

PHOA (octaanion of pentaethylenehexaamineoctaacetic acid)

carboxylate binding sites. Letkeman and Martell were the first to publish a complete set of protonation constants for this new ligand[1] in 1979. That work also included an NMR study of the ligand to determine its particular protonation scheme. Since then nothing has been reported regarding the protonation of PHOA, nor its complexation with metal ions. The reason for the absence of any PHOA studies can be attributed to its complex preparation and the extreme difficulty of purification and of precipitating the ligand from aqueous solution.

This work is an extension of earlier papers dealing with TPHA (tetraethylenepentaamineheptaacetic acid).[1-4]

EXPERIMENTAL

Reagents

Standard base was prepared from "Dilute It" (J.T. Baker) KOH concentrate by dilution under CO_2-free conditions, and the 0.10 M solution was standardized against reagent grade potassium acid phthalate (KHP). The KOH solution was stored in a glass bottle protected against the atmosphere with a tube of dry soda lime. Commercial samples of EDTA and DTPA (diethylenetriaminepentaacetic acid) (J.T. Baker) were used after precipitation from water. The metal solutions were prepared from their respective nitrate salts (reagent grade) purchased from Fisher Scientific and J.T. Baker. These solutions were standardized by EDTA titration according to the procedures of Schwarzenbach and Flaschka.[5] The amount of dissolved CO_2 in the potassium hydroxide titrant was periodically checked by a Gran-Plot analysis.[6] When the amount of CO_2 exceeded 0.7%, a fresh solution of KOH was prepared. All solutions were adjusted to an ionic strength of 0.10 M with KNO_3.

PHOA Synthesis

A sample of PHOA was obtained from Dr. Ichiro Murase (Dojindo Laboratories, Kumamoto, Japan), and was prepared from pentaethylenehexaamine hexahydrochloride that was obtained by fractional distillation of a technical grade polyamine mixture (Seitetsu Kagaku Co. Ltd., Japan) under vacuum using a distillation column (1 m in length, 4 cm in diameter) packed with small glass tubing. A fraction of boiling point 218–223°C/9–10 mmHg was collected and converted to a hydrochloride and purified by repeated recrystallization from dilute ethanol. A 25 mL solution of pentaethylenehexaamine hexahydrochloride (22.6 g, 0.05 mol) was neutralized with a 30% aqueous sodium hydroxide solution and to this was added 42.8 g of chloroacetic acid (0.45 mol) which had been dissolved in 50 mL of water and neutralized with 30% aqueous sodium hydroxide, with care to keep the temperature below 10°C. The reaction mixture was gradually heated to 70°C at constant p[H] (10.0) by dropwise addition of 30% aqueous sodium hydroxide. The addition took approximately 30 min, while the mixture was gradually heated to 90°C, and then kept at a constant temperature of 95°C for 1 h. After it was cooled to room temperature, the mixture was made strongly acidic by addition of concentrated hydrochloric acid. The resulting product was concentrated to a small volume on a rotary evaporator; the sodium chloride produced was filtered off and the resulting filtrate was again concentrated to yield a syrup. Methanol was added to the syrup and the sodium chloride produced was filtered off. Subsequent additions of methanol followed by evaporation of the filtrate continued until no more sodium chloride was produced from the syrup. To the syrupy residue was added concentrated hydrochloric acid and the solution was allowed to stand at room temperature for approximately one month. The first crystallization proceeded very slowly and the crystals produced were washed with methanol and then recrystallized from a minimum amount of hot water containing a few drops of hydrochloric acid. The crystallization from hot water took approximately one week. The crystals were again washed with methanol and dried over P_4O_{10} under vacuum at room temperature. The compound was analyzed as $C_{26}H_{44}N_6O_{16} \cdot 5HCl \cdot H_2O$ and had a purity of 96% from potentiometric titration data. Analysis Found: C, 34.29; H, 5.47; N, 9.08. Calculated values for the above compound are: C, 34.81; H, 5.74; N, 9.37.

Potentiometric Measurements

Samples of 0.09–0.11 mmol of solid ligand (molecular weight determined by titration) were diluted with 40.0 or 50.0 mL of distilled water in a sealed, thermostatted (25 ± 0.05°C) potentiometric titration vessel equipped with a Sargent blue type glass electrode and calomel reference electrode, N_2 inlet and bubbler outlet, and a graduated (Metrohm) 10 mL microburet. The test solution, adjusted to 0.10 M in KNO_3, was titrated with 0.10 M standard CO_2-free KOH while $-\log[H^+]$ was measured with a Fisher Accumet Model 50 p[H] meter calibrated with strong acid and strong base so as to read directly in hydrogen ion concentration ($pK_w = -\log[H^+][OH^-]$ was 13.80). The maximum variation between calculated and observed values of p[H] in this calibration was ±0.01 p[H] unit throughout the p[H] range 2.0–10.5. The p[H] readings were recorded when the drift was less than 0.001 units per minute. Equilibrium was established within 2–6 min for a given p[H] reading. Individual titrations usually consisted of some 55–75 p[H] readings over a period of 3–6 h. These readings started at p[H] 2 and ended at p[H] 11. Due to a very limited supply of PHOA, experiments were run in duplicate only. Typical concentrations of experimental solutions were 0.0020 M ligand with the molar concentration of metal ions equivalent to, or twice that of, PHOA for the study of metal complexation. In this paper the term p[H] is used synonymously with $-\log[H^+]$.

Computations

Protonation constants of PHOA were calculated from our titration data by the use of a FORTRAN program PKAS.[7] The formation constants of metal–PHOA complexes and their protonated analogues were calculated with the FORTRAN program BEST.[7] The program refines formation constants by iterative nonlinear least-squares fit of potentiometric equilibrium curves through a set of simultaneous mass balance equations for all the components expressed in terms of known and unknown equilibrium constants. For example, the p[H] profile of a metal–PHOA system is analyzed with the protonation constants of ligand (determined previously by separate experiments) and a series of metal–PHOA chelate formation, protonation, and deprotonation constants as unknowns (but with reasonable initial estimated values). Stability constants of 1 : 1 and 2 : 1 metal to ligand complexes were evaluated from the p[H] profiles for the systems containing 1 : 1 and 2 : 1 molar stoichiometry of metal ion to ligand, respectively. The errors reported (σ_{fit}) are based on the differences between the calculated and experimental hydrogen ion concentrations over the entire equilibrium curve for each system. The species considered present in the experimental solutions were those that one would expect to form according to previous experimental information obtained from similar complexation for TTHA (triethylenetetraaminehexaacetic acid) and TPHA. Species distribution curves were calculated and plotted with the FORTRAN program SPE.[7] An *a* value is the ratio of moles of base added to moles of ligand.

Since calculations revealed relative errors from 0.032 to 0.006 σ p[H] units, the stability constants are reported to ±(0.2–0.6) $\log K_{ML}$ units. Sample purity and the difficulty of fitting a ligand with eight acetate groups are likely causes for the relatively large range of uncertainty.

RESULTS AND DISCUSSION

Table I compares the literature values for the protonation constants of PHOA and Figure 1 illustrates the species distribution curves of PHOA *vs* p[H]. The ionization constants are defined by equation (1) below.

$$H_{9-x}L^{1-x} \rightleftharpoons H^+ + H_{8-x}L^{-x} \qquad K_x = \frac{[H^+][H_{8-x}L^{-x}]}{[H_{9-x}L^{1-x}]} \tag{1}$$

TABLE I Protonation constants of PHOA

pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	pK_7	pK_8	
2.09	2.48	3.42	4.36	6.11	8.79	9.84	10.80	This work[a]
2.02	2.52	3.57	4.48	6.20	8.85	9.96	10.85	Letkeman Ref. 1

[a] The uncertainties for individual pKa's are ±0.08 for an average of four experiments.

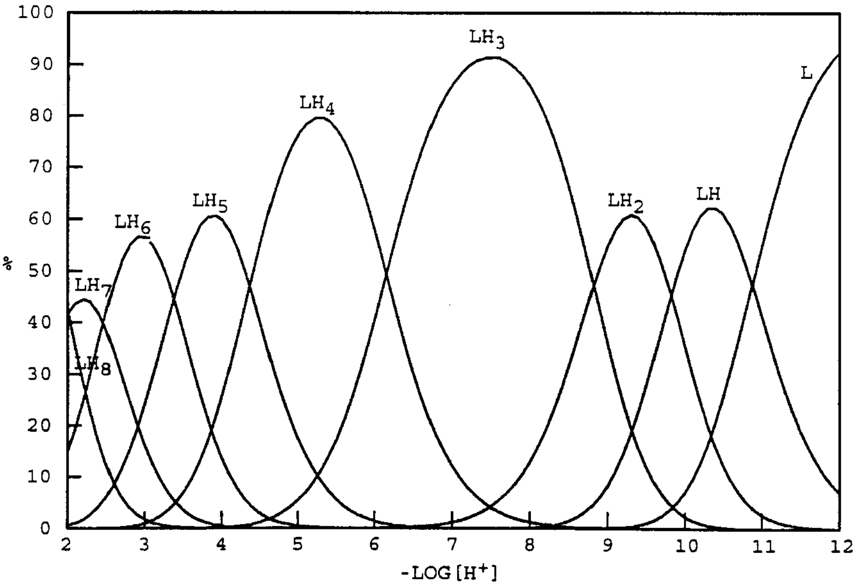

FIGURE 1 Species distribution diagram for PHOA as a function of p[H].

where x designates the number of protons, *i.e.* eight protons for PHOA. From Table I, one can predict that when titrating PHOA with standard base, there should be an inflection point on the graphical plot of ligand *vs.* p[H] between pK_5 and pK_6. This would correspond to 5 mol of base added. This break in the p[H] curve can be used as a measure of the purity of the ligand and was also observed in NMR protonation studies.[1,2]

Figure 2 illustrates a typical set of titration curves for ligand, 1 : 1 and 2 : 1 metal–PHOA complexes. The 1 : 1 metal–PHOA curves have a gradual inflection from 4*a* to 7*a*, (*a* = moles base/mole ligand) indicating a series of protonated complexes as seen in Figure 3 (for zinc(II) 1 : 1 system). The most prominent complex is the mono-protonated, MHL, from p[H] 7 to 11. The 2 : 1 metal–PHOA titration curves have inflection points at 7*a*, indicating very stable complex formation for the mono-protonated M_2HL species. This is also evident from the species distribution curves in Figure 4. Both the 1 : 1 and 2 : 1 complexes have numerous protonated species as would be expected from a ligand having eight carboxylic acid groups in a long molecule containing six amino groups. Formation constants quoted in this paper for ligands other than TPHA and PHOA (Tables II and III) were taken from the NIST database.[8] The stability constants of both 1 : 1 and 2 : 1 complexes are defined by equations (2)–(5) where n represents the charge

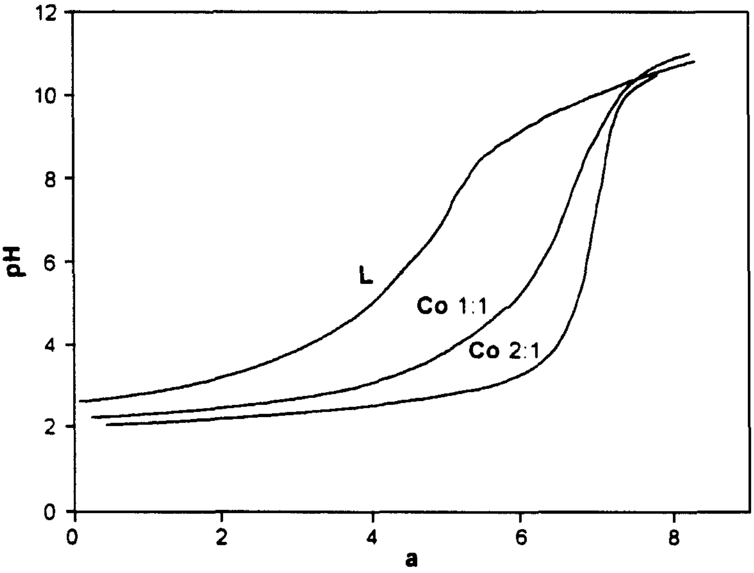

FIGURE 2 Titration curves for free PHOA (0.0021 M) and in the presence of 0.002 M and 0.004 M of Co^{2+} at 25°C, $\mu = 0.10$ (KNO_3).

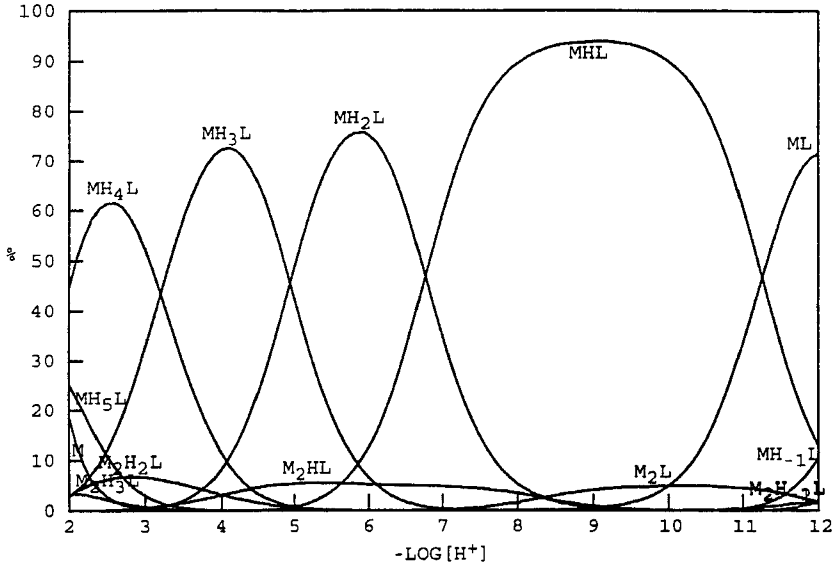

FIGURE 3 Species distribution diagram for 1 : 1 Zn(II)–PHOA system as a function of p[H].

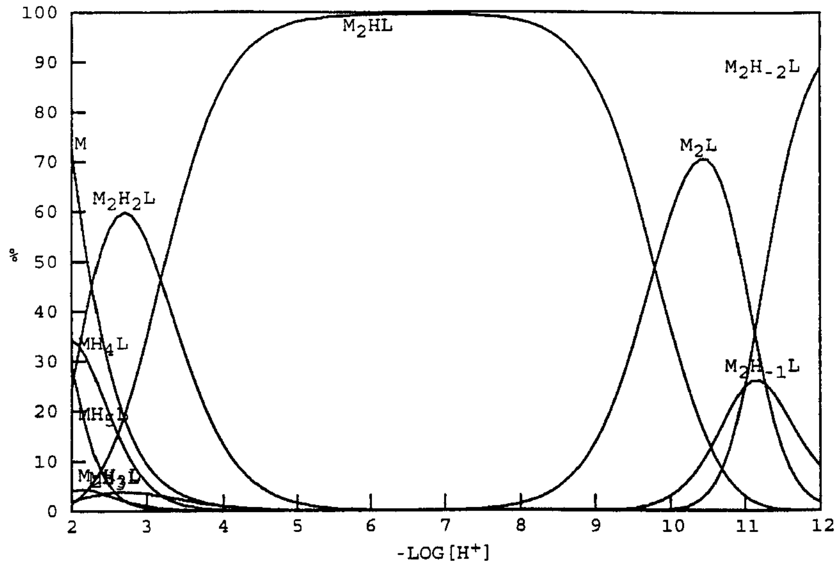

FIGURE 4 Species distribution diagram for the 2 : 1 Zn(II)–PHOA system as a function of p[H].

TABLE II Stability constants [log K_{ML}] of 1 : 1 metal–ligand complexes

Ligand	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}
EDTA	16.3	18.6	18.8	16.5	16.4	18.0	21.5
DTPA	19.3	20.2	21.4	18.3	19.0	18.7	26.4
TTHA	18.4	19.4	21.0	18.0	18.6	18.5	26.9
TPHA[a]	17.9	18.5	20.3	18.0	18.6	18.1	27.0
PHOA[b]	18.0	18.1	20.5	17.8	18.2	17.9	27.0

[a]Calculated constants from previous work.[9] [b]Calculated constants from this work with uncertainties of ±0.2 log units.

TABLE III Stability constants [log K_{M_2L}] of 2 : 1 metal–ligand complexes

Ligand	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}
DTPA	3.7	5.5	6.8	4.5	3.3	5.0	—
TTHA	9.7	13.0	13.4	11.9	11.3[b]	10.8	12.3
TPHA[a]	14.6	14.3	13.0	13.8	14.2	13.4	20.6
PHOA[b]	14.2	13.0	13.5	13.0	12.9	13.1	20.6

[a]Calculated constants from previous work.[9] [b]Calculated constants from this work with uncertainties of ±0.3 log units.

TABLE IV Stability constants [log K_{ML}] of metal–PHOA complexes

Species	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}	*Errors*
ML[a]	18.0	18.1	20.5	17.8	18.2	17.9	27.0	±0.2
MHL[a]	11.9	12.6	13.5	11.8	12.5	12.8	12.8	±0.3
MH_2L	6.8	7.1	6.3	6.2	6.9	6.8	7.0	±0.4
MH_3L	4.5	5.0	3.6	4.7	4.2	4.6	4.8	±0.5
MH_4L	3.0	3.2	2.5	3.1	2.4	2.9	2.2	±0.6
M_2L[a]	14.2	13.0	13.5	13.0	12.9	13.1	20.6	±0.3
M_2HL[a]	10.5	10.9	9.5	9.6	9.7	9.0	10.3	±0.4
M_2H_2L	3.5	4.0	3.5	3.3	3.2	3.8	4.1	±0.5
M_2H_3L	2.0	1.8	1.8	2.0	2.2	2.1	2.0	±0.6

[a]Defined by equations (2)–(5). Other constants are extensions of equations (4) and (5). *Note:* The error range is the uncertainty for two experiments for each mole ratio of metal to ligand, *i.e.*, 1 : 1 and 2 : 1 complexes for each metal.

on the deprotonated ligand (Table IV)

$$M^{2+} + L^{n-} \rightarrow ML^{2-n} \quad K_{ML} = \frac{[ML^{2-n}]}{[M^{2+}][L^{n-}]} \tag{2}$$

$$ML^{2-n} + M^{2+} \rightarrow M_2L^{4-n} \quad K_{M_2L} = \frac{[M_2L^{4-n}]}{[ML^{2-n}][M^{2+}]} \tag{3}$$

$$ML^{2-n} + H^{+} \rightarrow MHL^{3-n} \quad K_{MHL} = \frac{[MHL^{3-n}]}{[ML^{2-n}][H^{+}]} \tag{4}$$

$$M_2L^{4-n} + H^{+} \rightarrow M_2HL^{5-n} \quad K_{M_2HL} = \frac{[M_2HL^{5-n}]}{[M_2L^{4-n}][H^{+}]} \tag{5}$$

Mononuclear Complexes

Table II compares the formation constants for 1 : 1 metal–PHOA complexes with those of EDTA, DTPA, TTHA and TPHA taken from the NIST database[8] and previous work.[9] The octadentate DTPA ligand is clearly the strongest complexing agent for divalent metal ions. The only exception is that of mercury where the stability of the complexes are similar for the higher analogues of DTPA. The larger TTHA and TPHA ligands, though having many more coordination sites compared to DTPA, are unable to match the chelating ability of DTPA, presumably because of steric hindrance effects in the larger ligands. The same holds true for metal–PHOA complexes, with stability constants slightly less (approximately ≤ 0.3 log units) than those exhibited by metal–TPHA complexes, with the possible exception of Cu(II) which tends to form a slightly more stable complex with PHOA than it does with TPHA. However, this observation may not be significant in light of an uncertainty range of ± 0.2 $\log K_{\mathrm{ML}}$. Mercury(II), preferring linear, and at most tetrahedral coordination, forms complexes of equal strength with DTPA, TTHA, TPHA and PHOA.

Figure 3 illustrates a typical 1 : 1 metal–PHOA system. The metal–PHOA complex is slowly deprotonated as the p[H] increases. Hence the titration curve (Figure 2) gradually approaches an inflection at 7*a* moles of base. Here (see Figure 3) the mono-protonated complex, MHL is the predominant species from p[H] 7 to 11. The unprotonated complex, ML, forms above p[H] 9.0 along with various hydroxy chelates of both the 1 : 1 and 2 : 1 types. It becomes difficult to fit the experimental p[H] curve to the theoretical curve in the upper basic region due to limitations of the glass electrode.

Binuclear Complexes

Table III compares the formation of 2 : 1 metal complexes with DTPA, TTHA, TPHA and PHOA. In previous work, Letkeman *et al.*, studied 2 : 1 metal complexes with TPHA and found that TPHA forms stronger 2 : 1 metal complexes than does DTPA or TTHA.[9] This was the case except for Cu(II) which has the highest stability for TTHA complexes. The above results were rationalized on grounds that complete complexation of two metal ions each preferring octahedral coordination should be accomplished best by a ligand with twelve coordination sites, *i.e.* TPHA. In the case of Cu(II), which prefers four coordination sites, the decadentate TTHA ligand can accommodate all the bonding requirements of copper and hence the TTHA complex has the highest $\log K_{\mathrm{M_2L}}$.

The next higher analogue, PHOA, with 14 coordination sites also forms stronger 2 : 1 metal complexes than either TTHA or DTPA, but the PHOA complexes are slightly weaker than those formed with TPHA. Apparently the extra amino-acetate groups of PHOA interfere with the complexation sterically. Because divalent copper prefers square-planar coordination, an attempt was made to titrate a 3 : 1 copper–PHOA mixture, however, precipitation set in after p[H] 6 indicating that the Cu_3PHOA complex was relatively weak. Incorporating Cu_3PHOA into the computer model [below p[H] 6.0] did indicate an approximate value of $\log K_{M_3L} = 3.0$.

Figure 4 shows the species distribution curves for a Zn_2PHOA system which is also typical for the other 2 : 1 metal–PHOA mixtures. The M_2HL complex is predominant from p[H] 4 to 9 with a sharp inflection at 7*a* moles of base as seen from Figure 3. At p[H] 8.0 the unprotonated M_2L complex begins to form and reaches a maximum between p[H] values of 10 and 11. At higher p[H] the hydroxy complexes prevail. Actually the 2 : 1 mixtures yield lower σ (p[H]) errors as compared to the 1 : 1 complexes; *i.e.*, there is a better computer fit between the experimental p[H] curve and the calculated p[H] curve for the 2 : 1 metal–PHOA systems.

SUMMARY

The mononuclear complexes of PHOA are less stable than those for TPHA or TTHA as can be seen in Figure 5. It is clear that DTPA is the superior complexing agent for 1 : 1 metal–ligand complexes in the EDTA–PHOA series of ligands. This can easily be rationalized, since the octahedral coordination of metal ions is completely met by the DTPA ligand, having two extra bonding sites. These extra sites put DTPA at a decided advantage over EDTA, and yet to add 4, 6 or even 8 extra coordination sites does not improve the stability at all. This conclusion can be reached from Table II. It does appear that DTPA has just the right geometry for octahedral coordination of divalent metals. The mercury complexes also show very little variation in stability from DTPA to PHOA as seen from Table II. Two possible configurations of 1 : 1 metal–PHOA complexes are given in Figures 7 and 8. These model structures are based in part on earlier NMR studies of TPHA[2] which indicated that the central nitrogen atom is coordinated to the metal at all times until the p[H] drops below 3.0. Symmetrically and statistically Figure 8 would be the preferred structure.

For the binuclear metal–PHOA complexes there is no advantage in lengthening the chain beyond TPHA, as can be seen from Table III and

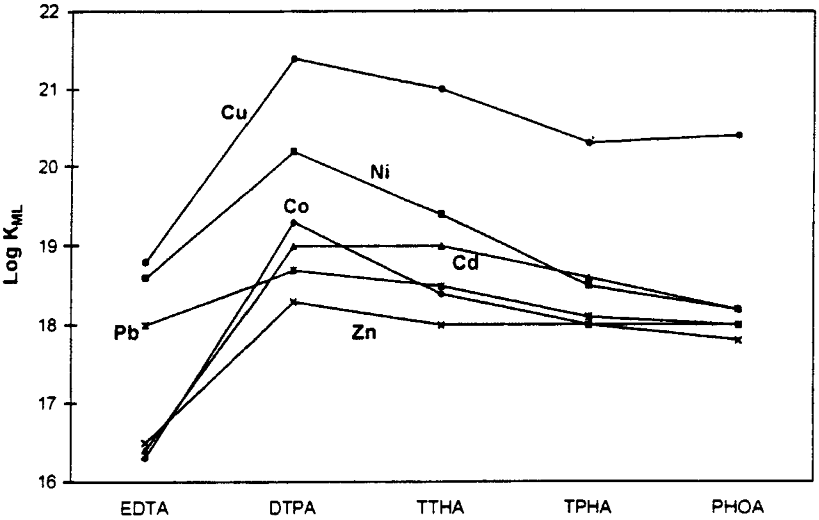

FIGURE 5 Comparison of log K_{ML} for Cu(II), Ni(II), Co(II), Cd(II), Zn(II) and Pb(II) for "homologous" analogs from EDTA to PHOA.

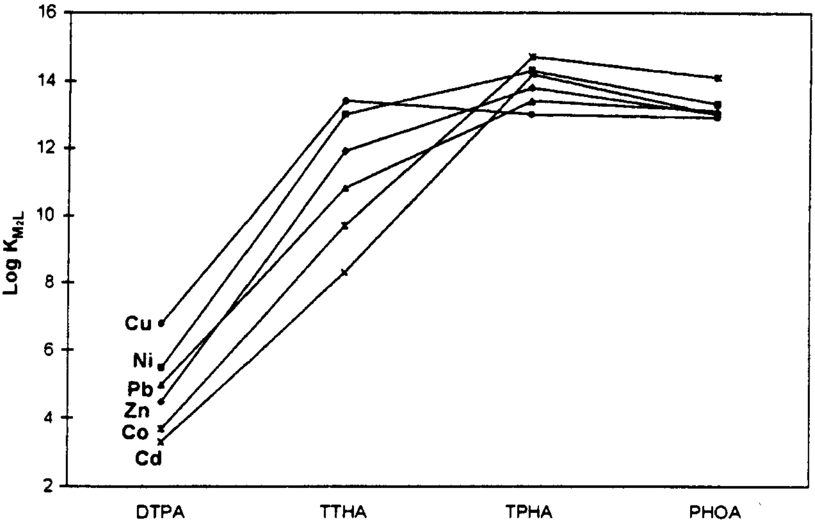

FIGURE 6 Comparison of log K_{M_2L} for Cu(II), Ni(II), Co(II), Cd(II), Zn(II) and Pb(II) as a function of "homologous" EDTA analogs.

Figure 6. Cu_2PHOA tops out at TTHA. Thus TPHA is preferred for the binuclear complexes just as DTPA exhibits the strongest bonding for mononuclear metal complexes. Possible configurations for the 2 : 1 metal–PHOA complexes are given in Figures 9 and 10, on the assumption that

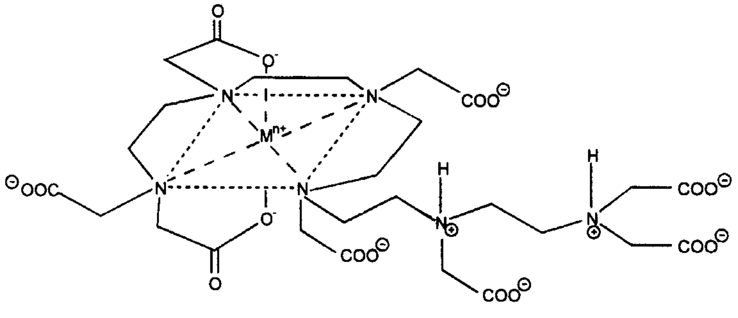

FIGURE 7 Schematic diagram for discussing the probable coordinate bonding sites in 1 : 1 complexes containing $2H^+$.

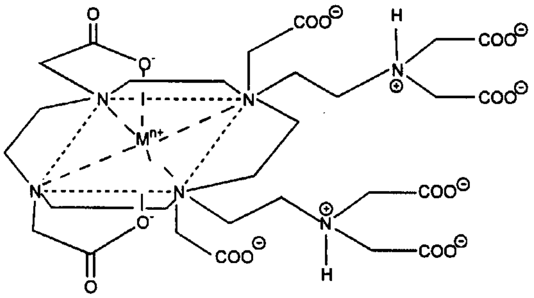

FIGURE 8 Alternate possible coordination for MH_2L.

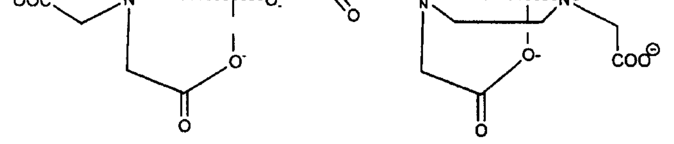

FIGURE 9 Coordination scheme for M_2L showing possible excess coordination capacity.

nitrogen bonding sites are preferred by the metal ion until the p[H] is well below 4.0. It is reasonable to assume that the end nitrogens would unwrap first as the p[H] is lowered and protonation of the complex takes place.

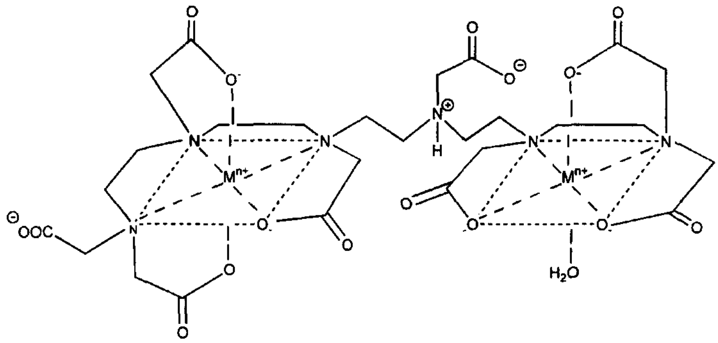

FIGURE 10 One of several possible M_2HL coordination diagrams.

These results indicate that for linear polyamine polycarboxylic acids, lengthening the polyamine chain (and the denticity) of the ligand offers no increase for the comparison of PHOA with TPHA. In fact, except for Cu(II), there is a slight decrease. Therefore the usefulness of PHOA as a complexing agent is limited. Moreover, the extreme difficulty of its preparation and subsequent precipitation from aqueous solution make it much too expensive for practical purposes in the laboratory or in industry.

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