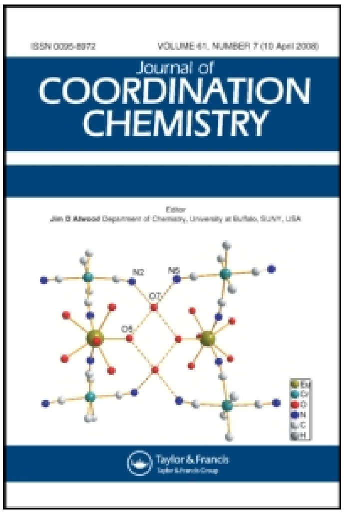

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A POTENTIOMETRIC STUDY OF METAL CHELATES WITH TETRAETHYLENEPENTAAMINEHEPTA-ACETIC ACID

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A POTENTIOMETRIC STUDY OF METAL CHELATES WITH TETRAETHYLENEPENTAAMINEHEPTA-ACETIC ACID

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The protonation constants of tetraethylenepentaamineheptaacetic acid, TPHA, 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–TPHA 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 stability constants are reported for Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Pb(II) with TPHA as well as their related protonated species. The stabilities of the 1 : 1 complexes parallel to those of similar complexes with DTPA and TTHA. However the 2 : 1 complexes have significantly larger $\log K_{ML}$'s than their TTHA counterparts. The extra stability of the 2 : 1 metal–TPHA complexes is explained in terms of ligand denticity and steric effects. Mercury(II)–TPHA complexes exhibited the highest formation constants and the copper–TPHA complexes had slightly higher $\log K_{ML}$'s than those for Co(II), Ni(II), Zn(II), Cd(II) and Pb(II).

Keywords: Tetraethylenepentaamineheptaacetic acid; potentiometry; protonation constants; stability constants; divalent metal complexes

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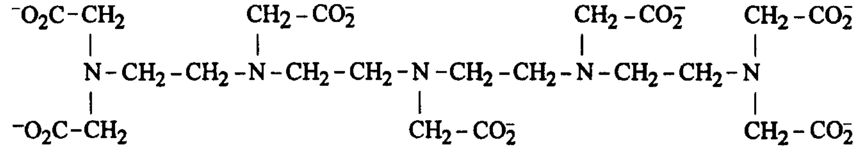
* Corresponding author. Fax: 409 845 4719.

INTRODUCTION

The heptaanion of TPHA can be represented as a dodecadentate ligand with five



$$\begin{array}{ccccccccc} {}^{-}O_2C-CH_2 & & CH_2-CO_2^- & & & & CH_2-CO_2^- & & CH_2-CO_2^- \\ | & & | & & & & | & & | \\ N & -CH_2-CH_2- & N & -CH_2-CH_2- & N & -CH_2-CH_2- & N & -CH_2-CH_2- & N \\ | & & & & | & & & & | \\ {}^{-}O_2C-CH_2 & & & & CH_2-CO_2^- & & & & CH_2-CO_2^- \end{array}$$

TPHA (Tetraethylenepentaamineheptaacetic acid)

amino and seven carboxylate binding sites. Dyatlova and coworkers published an incomplete set of protonation constants for this new ligand[1] in 1962. Their study omitted the first two ionization constants which were later assumed to be $pK_1 = 2.0$ and $pK_2 = 2.5$ by Masuda.[2] One of the first uses made of TPHA was to extract radionuclides from experimental rats.[3,4] Pribil and Vesely studied the possible analytical applications of TPHA for complexometric titrations.[5] A number of papers followed in which the authors accepted the Dyatlova pK_a's as correct values. These early studies included TPHA complexes with alkaline earth divalent metals as well as some transition metals.[2,6–8] Further investigations included rare-earth elements.[9,10] In general, the stability of 1 : 1 metal complexes were highest for DTPA with a small decline for both TTHA and TPHA, respectively.[6] The latest publication of TPHA involved a comparison of various Ga(III) complexes with ten ligands ranging from acetates to phenolates.[11]

Letkeman and Sawyer carried out an NMR study of TPHA[12] and saw evidence that the last deprotonation step was well above pH = 10, contrary to the Dyatlova results. This led Letkeman and Martell[13] to revisit the protonation study of a series of polyaminopolycarboxylic acids in aqueous media with identical ionic strength and temperature *via* potentiometric titration and NMR methods. This new set of pK_a's for TPHA satisfied both the NMR results and potentiometric titration data. As a result, most of the metal–TPHA formation constants reported before 1979, were flawed because of the use of incorrect pK_a's in their algebraic solutions.

This study is a natural extension of our earlier work on TPHA.[11–13] It also serves as a comparative study of the stabilities of seven divalent metal–aminocarboxylic acid complexes in aqueous media with the higher analogues of EDTA, including the present addition of selected divalent metal–TPHA complexes.

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. 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 (J.T. Baker) were used after crystallization from water. TPHA samples were obtained from both Geigy Chemical Corp (Basel, Switzerland) and from Dr. Ichiro Murase (Dojindo Laboratories, Kumamoto, Japan). The Geigy sample (96% pure) was obtained as $C_{22}H_{37}N_5O_{14}$ and used without further purification. The Murase sample was synthesized by alkylation of a purified sample of tetraethylenepentaamine with chloroacetic acid[14] and analyzed as $C_{22}H_{37}N_5O_{14}\cdot 4HCl\cdot 2H_2O$ with a purity of 96.5% from potentiometric titration data. The metal solutions were prepared from their respective nitrate salts (reagent grade) purchased from Fisher Scientific and J.T. Baker. The amount of dissolved CO_2 in the potassium hydroxide titrant was periodically checked by a Gran-Plot analysis.[15] Normally the amount of CO_2 was less than 0.7%, but when it exceeded that value, a fresh KOH solution was prepared. All solutions were adjusted to an ionic strength of 0.100 M with KNO_3.

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, thermostated ($25 \pm 0.05°C$) potentiometric titration vessel equipped with a Sargent blue type glass–calomel combination electrode, N_2 inlet and outlet, and a graduated (Metrohm) 10 mL microburet. The test solution, adjusted to 0.10 M in KNO_3, was titrated with 0.100 M standard CO_2-free KOH while $-\log [H^+]$ was measured with a Fisher Accumet Model 50 pH meter calibrated with strong acid and strong base so as to read directly in hydrogen ion concentration. A Gran plot of the calibration data in the basic region was used to determine an experimental value for the ion product of water, *i.e.* $pK_w = -\log[H^+][OH^-]$ was 13.79. The maximum variation between calculated and observed values of pH in this calibration was ±0.01 pH unit throughout the pH range of 2.0–10.5. Typical concentrations of experimental solutions were 0.0020 M in ligand with the molar concentration of metal ions equivalent to, or twice that of, TPHA for the study of metal complexation. With a very limited supply of TPHA available, experiments were run in duplicate or triplicate only. The pH readings were recorded when the drift was less than 0.001 units per min. In most instances equilibrium was established within 2–5 min. With this procedure 55–85 titration points (per experiment) were recorded over periods of 2–5 h. The individual titrations were performed over a pH range from 2.0 to 11.0. Periodically, as a double check on our potentiometric set-up, a sample of pure DTPA was titrated and the calculated pK_a's compared very closely to the literature values. In this paper the term pH is used synonymously with $-\log[H^+]$.

Computations

Protonation constants of TPHA were calculated from our potentiometric data by the use of a FORTRAN program pK_a's.[16] The formation constants of metal–TPHA complexes and their protonated analogs were calculated with the FORTRAN program BEST.[16] Due to the limited supply of TPHA, all experiments were done in triplicate only except for the determination of the pK_a's. The BEST program refines stability constants by iterative nonlinear least-squares fits 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 pH profile of a metal TPHA system is analyzed with the protonation constants of ligand (determined previously by separate experiments) and a series of metal–TPHA 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 pH profiles for the systems containing 1 : 1 and 2 : 1 molar stoichiometry of metal ion to ligand, respectively. The errors reported $(\sigma\ \mathrm{pH})_{\mathrm{fit}}$ 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 established principles of coordination chemistry and previous experimental information obtained from similar complexation for DTPA and TTHA. Species distribution curves were calculated and plotted with the Fortran program SPE.[16] An a value is the ratio of moles of base added to moles of ligand.

RESULTS AND DISCUSSION

Table I summarizes the literature values for the ionization constants of TPHA and Figure 1 illustrates the species distribution of TPHA *vs.* pH. The ionization constants are defined by Equation (1) below:

$$H_{8-x}L_{1-x} \rightarrow H^+ + H_{7-x}L^{-x} \quad K_1 = \frac{[H^+][H^{7-x}L^{-x}]}{[H^{8-x}L^{1-x}]} \qquad (1)$$

where x designates the dissociation step for the H_7L type ligand TPHA.

TABLE I Protonation constants of TPHA

pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	pK_7	*Reference*
—	—	2.73	3.82	5.56	8.88	9.95	[1]
1.84	2.30	2.92	3.90	5.33	8.23	9.99	[7]
2.00	2.50	2.73	3.82	5.56	8.88	9.95	[2]
2.00	2.69	3.78	4.75	8.13	9.87	10.76	[13]
2.14	2.65	3.77	4.62	8.25	9.68	10.37	[11]
2.08	2.63	3.72	4.63	8.17	9.73	10.48	this work[a]

[a] The uncertainty for individual pK_a's is ±0.08 for an average of five experiments.

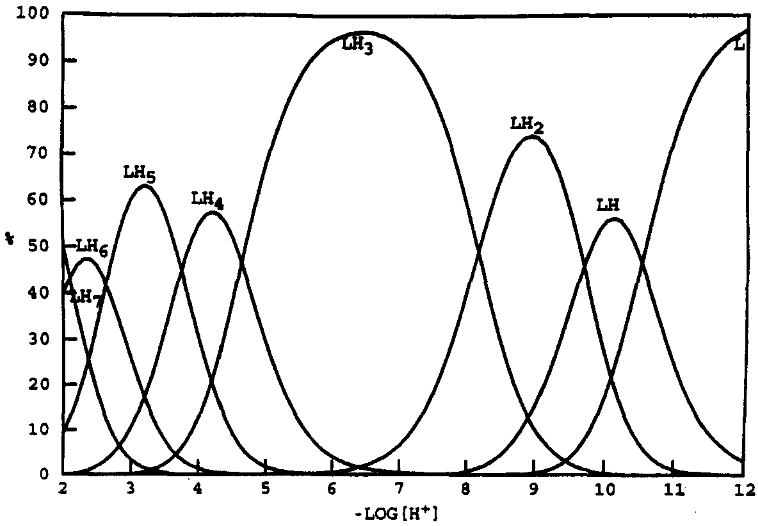


FIGURE 1 Species distribution curves for TPHA *vs.* pH.

It becomes obvious, that when titrating TPHA with standard base, there should be an inflection point on the graphical plot of ligand *vs.* pH between pK_4 and pK_5. This would correspond to $4a$ moles of base added. This break in the pH curve can be used as a measure of the purity of the ligand. It is interesting to note that the NMR studies also show a definite break in the protonation scheme for four moles of added base per mole of ligand.[12]

Figure 2 illustrates a typical set of titration curves for ligand, 1 : 1 and 2 : 1 metal–TPHA complexes. The 1 : 1 metal–TPHA curve has a sharp inflection point at $6a$, indicating the formation of a very strong MHL complex. The 2 : 1 metal–TPHA complexes have inflection points at 7a, indicating stable complex formation of the nonprotonated species, M_2L. Both the 1 : 1 and 2 : 1 complexes have numerous protonated species as would be expected from a ligand having seven carboxylic acid groups in the molecule. Stability constants other than those of TPHA quoted in this paper (Tables II and III) were taken from the NIST data-base.[17] The chelate stability constants of both 1 : 1 and 2 : 1 complexes are defined by Equations (2)–(5) where n represents the charge on the deprotonated ligand.

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

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

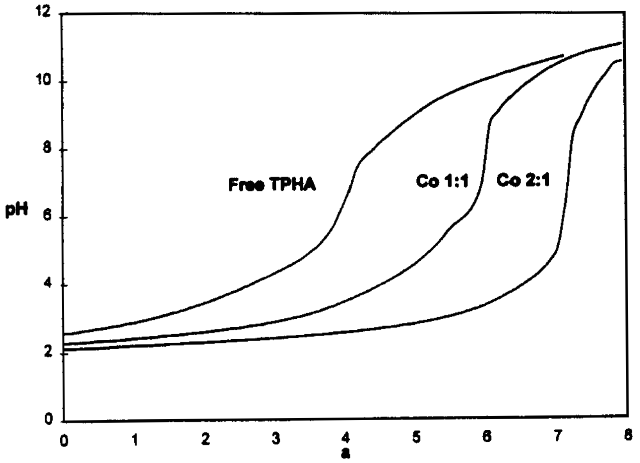


FIGURE 2 Titration curves for free TPHA and metal–TPHA mixtures.

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

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

Mononuclear Complexes

Figure 3 illustrates the distribution of various species, as a function of pH, for a 1 : 1 Cd(II)–TPHA system. This figure is typical of all the divalent metals studied, except for the contribution of the 2 : 1 complex, which does vary with the magnitude of the log $K_{\mathrm{M_2L}}$. At low pH the protonated species are prevalent with the mono-protonated MHL complex predominant from pH = 6 to pH = 9. Beyond pH = 9 the non-protonated 1 : 1 complex appears along with some complexes containing hydroxyl ions. No attempt was made to determine the stability of the hydroxy species.

Table II and Figure 4 compare the formation constants for 1 : 1 metal–TPHA complexes with those of EDTA, DTPA and TTHA. The octadentate DTPA ligand is clearly the strongest complexing agent for divalent metal ions. The only exception is for mercury where the stability of the complexes

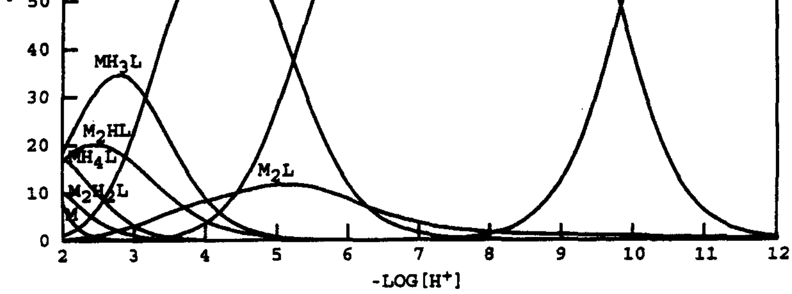


FIGURE 3 Species distribution curves for [1 : 1] Cd(II)–TPHA *vs*. pH.

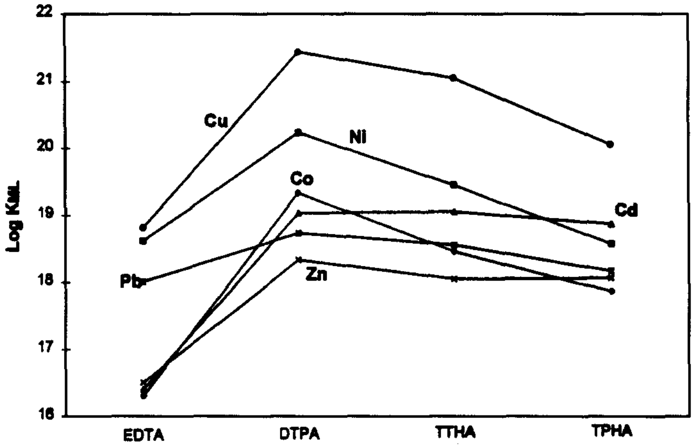


FIGURE 4 Dependence of the stability of 1 : 1 complexes on the denticity of the ligand.

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

[a] Calculated constants from this work with an uncertainty of ± 0.2 log units.

are similar for the higher analogs of DTPA. One can rationalize the slight decline in stability of complexes with TTHA and TPHA on the grounds of steric hindrance for larger ligands since only six coordinating sites are needed for these divalent metal ions. Mercury on the other hand has a coordination number of only two or four at the most. This appears to be met equally well by DTPA, TTHA and TPHA. This exception could be stretched to include Zn(II), Cd(II) and Pb(II) since the log K_{ML}'s vary by only 0.5 log units or less in each case. Such an argument could be based on the filled 3*d* orbitals for Zn(II), Cd(II), Hg(II) and Pb(II). However Co(II), Ni(II) and Cu(II) show a definite decline in stability from DTPA to TPHA. The relative error for the above calculations of formation constants ranged from 0.018–0.004 σ (pH) units, with most experiments running well below 0.01 σ (pH). Hence the stability constants determined in this work are reported to within ± 0.2–0.5 log K_{ML} (Tables II–IV).

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[a]	10.8	12.3
TPHA[a]	14.6	14.3	13.0	13.8	14.2	13.4	20.6

[a] Calculated constants from this work with an uncertainty of ± 0.3 log units.

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

Species	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}	*Error*
ML	17.9	18.5	20.3	18.0	18.6	18.1	27.0	± 0.2
MHL	9.6	9.7	9.3	9.7	9.6	9.4	12.0	± 0.2
MH_2L	5.3	5.5	5.0	5.7	5.1	5.3	5.0	± 0.3
MH_3L	4.1	3.9	3.0	3.8	3.0	3.5	3.3	± 0.4
MH_4L	2.6	1.9	2.3	2.0	1.9	2.7	2.3	± 0.5
M_2L	14.6	14.3	13.0	13.8	14.2	13.4	20.6	± 0.3
M_2HL	4.1	4.0	3.9	4.2	3.7	4.0	4.1	± 0.4
M_2H_2L	2.2	1.9	2.5	2.0	1.8	2.3	2.0	± 0.5

Note: The error range is the uncertainty of two/three experiments for each mole ratio of metal to ligand, *i.e.* 1 : 1 and 2 : 1 mixtures of metal to ligand.

Binuclear Complexes

Figure 5 illustrates the species distribution for a 2 : 1 Co(II)–TPHA mixture, which again is typical for all of the other metals in this study. At low pH the protonated species prevail, but the 2 : 1 complex dominates from pH = 5 to pH = 10. In the 2 : 1 mixtures, the hydroxy-complexes are more pronounced at high pH than for the 1 : 1 mixtures. Hence one must include hydroxy-complexes in the computer model in order to fit the experimental data.

Table III lists the formation constants for 2 : 1 metal complexes with DTPA, TTHA and TPHA. In Figure 6 these stability constants are plotted against the denticity of the various ligands. Very clearly the ligand with the most sites for coordination is the strongest complexing ligand, *i.e.*, TPHA. Most divalent metals would need at least twelve coordination sites for complete saturation of a 2 : 1 complex. Theoretically this should be met by the dodecadentate ligand, TPHA. Experimental data confirm this application of coordination theory. It should be interesting to see how the next higher analog, *i.e.*, pentaethylenehexaamineoctaacetic acid, PHOA, compares in coordinating ability to TPHA.

It appears that there is no advantage for copper to bind to TPHA as compared to TTHA. This is probably explained by the fact that Cu(II) usually only binds strongly to four sites because of the Jahn–Teller effect. This being the case, TTHA has sufficient coordinating sites with ten available

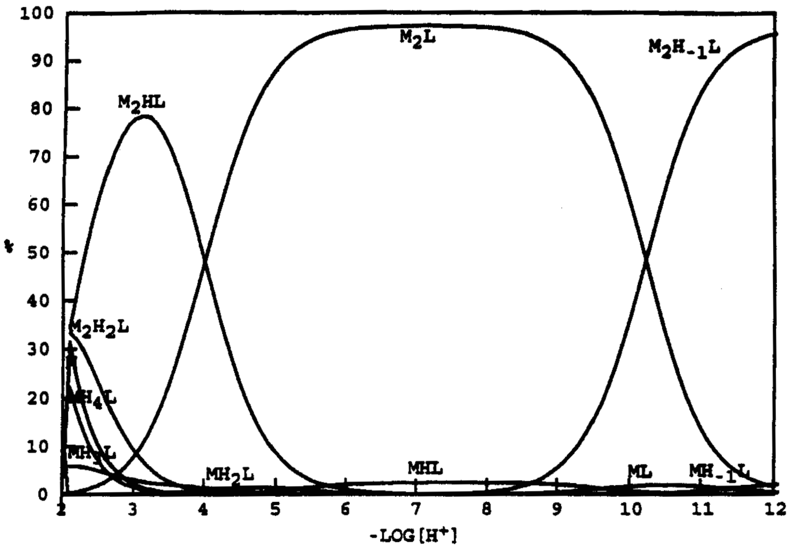


FIGURE 5 Species distribution curves for [2 : 1] Cd(II)–TPHA *vs*. pH.

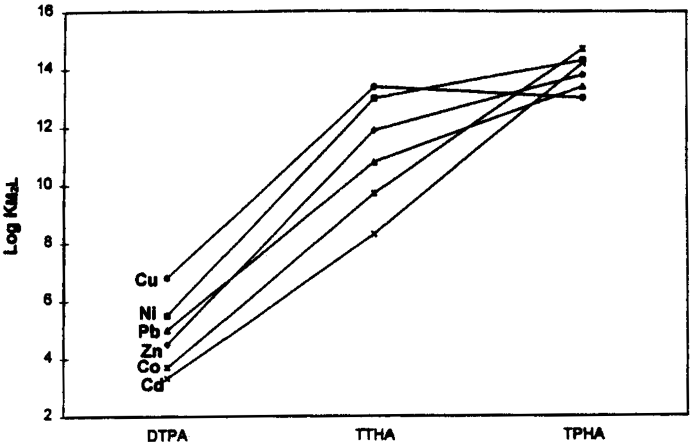


FIGURE 6 Dependence of the stability of 2 : 1 complexes on the denticity of the ligand.

spots. It is interesting to note that Hg(II) does not form a 2 : 1 complex with DTPA and yet does with the ligands TTHA and TPHA. The log K_{ML}'s for Hg(II) complexes are a number of orders of magnitude larger than for the other transition metals when bound to aminocarboxylic acid type ligands.

SUMMARY

Lengthening the chain in the series, DTPA–TPHA does not improve the metal–ligand bonding for the selected 1 : 1 metal-complexes in question. A small decrease in the stability constants can be seen in Figure 4 and Table II. This may be due to the lower negative charge on the nitrogen sites in the ligand. Conversely, it can be argued that the solution conformations of the ligand are not sterically favorable since such a long-chained ligand would become coiled making it difficult to accommodate the coordination requirements of divalent metals. Two possible conformations for the 1 : 1 complexes are illustrated in Figures 7 and 8.

For the binuclear metal complexes of TPHA, a marked improvement in stability can be seen from Table III and Figure 6. This was expected because a dodecadentate ligand can supply the necessary coordination sites for two metals at the same time. Hence there are larger $\log K_{M_2L}$ values for each metal as compared to TTHA. The largest difference is observed for the Hg_2TPHA complex with much smaller differences in the formation constants for the other metals. Figures 9 and 10 show possible structures for both protonated and unprotonated 2 : 1 metal–TPHA complexes.

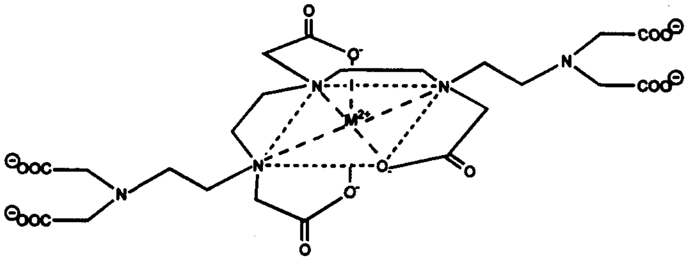


FIGURE 7 Possible configuration of a 1 : 1 metal–TPHA complex.

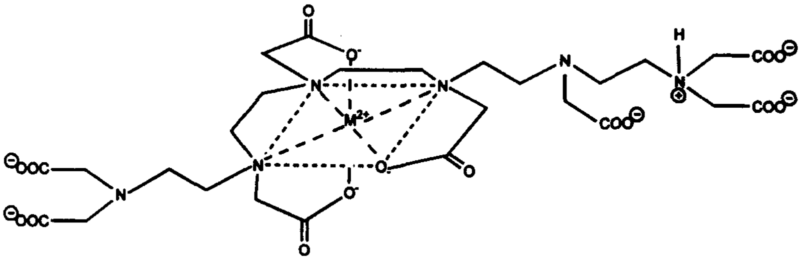


FIGURE 8 Possible configuration of a monoprotonated 1 : 1 metal–TPHA complex.

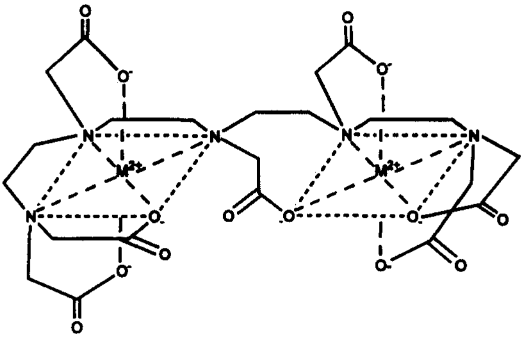


FIGURE 9 Possible configuration of a 2 : 1 metal–TPHA complex.

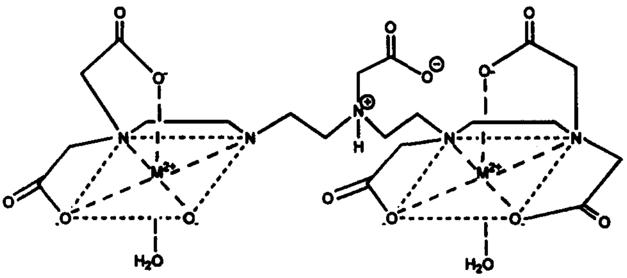


FIGURE 10 Possible configuration of a monoprotonated 2 : 1 metal–TPHA complex.

Close inspection of Figure 6 indicates that the transition metals with incomplete 3*d* orbitals, *i.e.* Co(II), Ni(II) and Cu(II), exhibit slightly lower formation constants for TPHA complexes as compared to TTHA, which in turn are also lower than those for DTPA. Thus one could speculate that the completely filled *d* shell metal ions (Zn(II), Cd(II), Hg(II) and Pb(II)) are somehow better able to fit into the coordination spheres of TPHA than Co(II), Ni(II) or Cu(II) ions.

Thus the only obvious advantage of using TPHA would be that it could chelate two moles of metal to every one mole of ligand more efficiently than either TTHA or DTPA. However, considering the cost of preparing a sample of TPHA, one is better off to use two moles of EDTA or DTPA in order to accomplish the same task. Therefore the analytical applications of TPHA are limited.

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References

[1] N.M. Dyatlova, Yu.E. Belugin and V.Ya. Temkima, *Chem. Abstr.* **62**, 2288c (1965); N.M. Dyatlova, Y.F. Belugin and V.Ya. Temkina, *Tr. Soveshch. Fiz. Metodam Issled. Org. Soedin. Khim. Protesessov* **55** (1962).
[2] Y. Masuda, Y. Hirai and E. Sekido, *Bulletin of the Chemical Society of Japan* **44**, 2381 (1971).
[3] A. Catsch and D. Schindewolf-Jordan, *Experentia* **17**, 205 (1961).
[4] A. Catsch and D. Schindewolf-Jordan, *Nature* **191**, 715 (1961).
[5] R. Pribil and V. Vesély, *Talanta* **12**(2), 191 (1965).
[6] N.M. Dyatlova and R.P. Lastovskii, *Russ. Chem. Rev.* **34**, 481 (1965).
[7] A. Bohigian, Jr. and A.E. Martell, *Inorg. Chem.* **4**, 1264 (1965).
[8] A. Bohigian, Jr. and A.E. Martell, *J. Amer. Chem. Soc.* **89**, 832 (1966).
[9] D. Site and R.D. Baybarz, *J. Inorg. Nucl. Chem.* **31**, 2201 (1969).
[10] S. Misumi, S. Kida and M. Aihara, *Coord. Chem. Rev.* **3**, 189 (1968).
[11] R.J. Motekaitis and A.E. Martell, *Inorg. Chem.* **19**, 1646–1651 (1980).
[12] P. Letkeman and D.T. Sawyer, *Can. J. Chem.* **49**, 2096 (1971).
[13] P. Letkeman and A.E. Martell, *Inorg. Chem.* **18**(5), 1284 (1979).
[14] I. Murase, T.A. Bohigian and A.E. Martell, *Preparations of Complexes and Reaction Properties of Ligands*, eds., S. Nakahara and M. Shibata, Nankodo: Kyoto, p. 126 (1970).
[15] F.J.C. Rossotti and H. Rossotti, *J. Chem. Ed.* **42**, 375 (1965).
[16] A.F. Martell and R.J. Motekaitis, *Determination and Use of Stability Constants*, 2nd edn., VCH Publishers: New York (1992).
[17] R.M. Smith, R.J. Motekaitis and A.E. Martell, eds., *NIST Critical Stability Constants of Metal-Complexes Database*, Gaithersburg: Maryland (1993).