

(en<sub>3</sub>)<sub>3</sub><sup>2+</sup>, 73117-32-5; Ru(NH<sub>3</sub>)<sub>5</sub>NCS<sup>2+</sup>, 44819-58-1; Ru(NH<sub>3</sub>)<sub>5</sub>NCS<sup>+</sup>, 73117-33-6; Ru(ND<sub>3</sub>)<sub>5</sub>NCS<sup>2+</sup>, 73117-34-7; Ru(ND<sub>3</sub>)<sub>5</sub>NCS<sup>+</sup>, 73117-35-8; Co(en<sub>H</sub>)<sub>3</sub><sup>3+</sup>, 14878-41-2; Co(en<sub>H</sub>)<sub>3</sub><sup>2+</sup>, 23523-25-3; Co(en<sub>D</sub>)<sub>3</sub><sup>3+</sup>, 23420-60-2; Co(en<sub>D</sub>)<sub>3</sub><sup>2+</sup>, 73117-16-5; Co(sepulchrate)<sup>3+</sup>, 72496-77-6; Co(sepulchrate)<sup>2+</sup>, 63218-22-4; Ru(NH<sub>3</sub>)<sub>5</sub>OH<sup>2+</sup>, 38331-41-8; Ru(NH<sub>3</sub>)<sub>5</sub>OH<sup>+</sup>, 73117-17-6; Ru(ND<sub>3</sub>)<sub>5</sub>OD<sup>2+</sup>, 73117-18-7; Ru(ND<sub>3</sub>)<sub>5</sub>OD<sup>+</sup>, 73117-19-8; *c*-Ru(NH<sub>3</sub>)<sub>4</sub>(OH)<sub>2</sub><sup>3+</sup>, 38139-18-3; *c*-Ru(NH<sub>3</sub>)<sub>4</sub>(OH)<sub>2</sub><sup>2+</sup>, 29946-00-7;

*c*-Ru(NH<sub>3</sub>)<sub>4</sub>(OD)<sub>2</sub><sup>3+</sup>, 73117-20-1; *c*-Ru(NH<sub>3</sub>)<sub>4</sub>(OD)<sub>2</sub><sup>2+</sup>, 73117-21-2; Cr(OH)<sub>2</sub><sup>3+</sup>, 14873-01-9; Cr(OH)<sub>2</sub><sup>2+</sup>, 20574-26-9; Cr(OD)<sub>2</sub><sup>3+</sup>, 44437-80-1; Cr(OD)<sub>2</sub><sup>2+</sup>, 73117-22-3; Fe(OH)<sub>6</sub><sup>3+</sup>, 15377-81-8; Fe(OH)<sub>6</sub><sup>2+</sup>, 15365-81-8; Fe(OD)<sub>6</sub><sup>3+</sup>, 73117-23-4; Fe(OD)<sub>6</sub><sup>2+</sup>, 69701-34-4; V(OH)<sub>6</sub><sup>3+</sup>, 21374-21-0; V(OH)<sub>6</sub><sup>2+</sup>, 15696-18-1; V(OD)<sub>6</sub><sup>3+</sup>, 73117-24-5; V(OD)<sub>6</sub><sup>2+</sup>, 73117-25-6; Eu<sup>3+</sup>, 22541-18-0; Eu<sup>2+</sup>, 16910-54-6; U<sup>4+</sup>, 16089-60-4; U<sup>3+</sup>, 22578-81-0; Tl<sup>3+</sup>, 14627-67-9; Tl<sup>+</sup>, 22537-56-0; UO<sub>2</sub><sup>2+</sup>, 16637-16-4; UO<sub>2</sub><sup>+</sup>, 21294-41-7.

Contribution from the Department of Chemistry,  
Texas A&M University, College Station, Texas 77843

## Gallium Complexes of Multidentate Ligands in Aqueous Solution

RAMUNAS J. MOTEKAITIS and ARTHUR E. MARTELL\*

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Gallium(III) was equilibrated in dilute aqueous solution at 25 °C,  $\mu = 0.100$  M, with ten multidentate ligands containing combinations of phosphonate, acetate, phenolate, and tertiary amino donor groups, and hydrogen ion concentrations were determined potentiometrically as a function of added standard alkali. Stability constants, chelate protonation constants, hydrolysis constants, and formation constants were calculated for all systems, thus providing a quantitative description of the concentrations of gallium-ligand species present as a function of hydrogen ion concentration. Correlations of stability constants with basicities of the ligands and of chelate hydrolysis constants with stability constants are provided for the present work and for previously published values of related ligands. Probable coordinate bonding sites and the stereochemistry of metal-ligand interactions are inferred from the thermodynamic data.

### Introduction

Harris and Martell<sup>1</sup> described the interactions of gallium(III) with 16 multidentate ligands and reported the equilibrium constants involving the presence of protonated chelates, oligated chelates, and some polynuclear species. Letkeman et al.<sup>2</sup> extended the study to the interaction of gallium(III) with several phenolic and 1,2-dihydroxy aromatic ligands. Apart from these two definitive studies no other comprehensive work on gallium(III) and its interaction with multidentate ligands has become available.

It was found by Harris and Martell<sup>1</sup> that the equilibrium constants for the reactions of Ga(III) with certain strongly binding ligands could not be measured potentiometrically, since even at the lowest measurable pH, Ga(III) ion is 100% complexed. These cases were solved by a novel experimental approach—the measurement of metal or ligand displacement reactions. Metal-metal competitive equilibria were determined spectrophotometrically, and ligand-ligand competition reactions were followed potentiometrically. In the present paper, a completely new competitive equilibrium technique is employed—the displacement of strongly bound ligands from the coordination sphere of the Ga(III) ion by hydroxide ions. The very strong tendency of the Ga(III) ion to undergo hydrolysis to Ga(OH)<sub>4</sub><sup>-</sup> turns out to be an asset which makes possible potentiometric measurements of stability constants that could not be determined any other way. As the pH is increased, virtually every multidentate ligand dissociates from gallium and is replaced by four hydroxide ions. Therefore this new method has wide application to many chelates of Ga(III) and is now offered as a powerful technique for measurement of chelate equilibria of amphoteric metal ions. One of the ligands that has been determined by this new method in the present study is triethylenetetraminehexaacetic acid (TTHA), a decadentate ligand for which no satisfactory competing chelating was found by Harris and Martell.<sup>1</sup>

The multidentate ligands which form the basis of this study and their abbreviations in parentheses are *N*-(2-hydroxy-5-sulfobenzyl)ethylenediamine-*N,N'*-bis(methylenephosphonic)

acid (MSHBEDPO), triethylenetetraminehexaacetic acid (TTHA), tetraethylenepentamineheptaacetic acid (TPHA), ethylenediamine-*N,N'*-diacetic-*N,N'*-bis(methylenephosphonic) acid (EDDADPO), glycine-*N,N'*-bis(methylenephosphonic) acid (GDPO), ethylenediamine-*N,N'*-bis(methylenephosphonic) acid (EDDPO), 1-hydroxyethane-1,1-diphosphonic acid (HEDPO), (2-hydroxybenzyl)iminobis(methylenephosphonic) acid (HBIDPO), ethylenediamine-*N,N'*-*N,N'*-tetrakis(methylenephosphonic) acid (EDTPO), and *N*-(phosphonomethyl)iminodiacetic acid (PMIDA). For each of the above ligands, the stability constant of the gallium(III) chelates and all other significant related equilibrium constants are now reported.

### Experimental Section

**Reagents.** EDDPO was synthesized from ethylenediamine, formaldehyde, and phosphorus acid in aqueous hydrochloric acid medium as outlined by Moedritzer and Irani.<sup>3</sup> The ligands GDPO and PMIDA were prepared by a similar method from glycine and iminodiacetic acid, respectively. The chelating agent HBIDPO was prepared by the alkylation of iminobis(methylenephosphonic) acid (IDPO) with *o*-acetoxybenzyl bromide with the method described by Harris et al.,<sup>4</sup> while IDPO was prepared by the procedure of Moedritzer.<sup>5</sup> The ligand MSHBEDPO was prepared by the reaction of *p*-hydroxyphenylsulfonic acid and formaldehyde with EDDPO as outlined by Kroll et al.<sup>6</sup> Only monosubstitution products could be isolated in pure form. TPHA was synthesized by alkylation of a purified sample of tetraethylenepentamine with chloroacetic acid.<sup>7</sup> The decadentate polyaminopolycarboxylic acid TTHA was obtained commercially from Dojindo Pharmaceutical Laboratories, Japan. The chelating agent HEDPO was kindly supplied by the Monsanto Chemical Co. The ligand EDTPO was synthesized by the method described by Motekaitis et al.,<sup>8</sup> while EDDADPO was prepared by alkaline bromoacetic acid alkylation of EDDPO.

**Procedure.** The potentiometric equilibrium measurements were performed by using the procedure outlined previously.<sup>1</sup> All constants

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Table I. Protonation Constants of the Ligands<sup>a, b</sup>

| ligand   | log $K_1$ | log $K_2$ | log $K_3$ | log $K_4$ | log $K_5$ | log $K_6$ | log $K_7$ | log $K_8$ | ref                    |
|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|------------------------|
| TTHA     | 10.63     | 9.58      | 6.17      | 4.07      | 2.78      | 2.20      | ~1.6      |           | 1                      |
| TPHA     | 10.37     | 9.68      | 8.25      | 4.62      | 3.77      | 2.65      | 2.14      | ~1.65     | this work <sup>a</sup> |
| EDDADPO  | 10.43     | 7.81      | 6.38      | 3.90      | 2.49      | 1.66      |           |           | this work              |
| GDPO     | 10.80     | 6.37      | 5.01      | 2.00      | 1.73      |           |           |           | this work              |
| EDDPO    | 10.60     | 7.72      | 5.74      | 4.58      |           |           |           |           | 8                      |
| HEDPO    | 11.10     | 7.01      | 2.80      |           |           |           |           |           | 12                     |
| HBIDPO   | 11.08     | 9.44      | 6.24      | 4.89      | ~0.9      |           |           |           | this work              |
| EDTPO    | 13.14     | 10.01     | 8.13      | 6.57      | 5.26      | 3.15      | ~1.37     |           | 8                      |
| PMIDA    | 10.29     | 5.57      | 2.44      | ~1.23     |           |           |           |           | this work              |
| MSHBEDPO | 11.93     | 9.17      | 8.04      | 6.12      | 2.98      |           |           |           | this work              |

<sup>a</sup> Standard deviations for this work are 0.01 (TPHA), 0.05 (EDDADPO), and 0.02 (GDPO, HBIDPO, PMIDA, and MSHBEDPO). <sup>b</sup>  $\mu = 0.100$  M ( $\text{KNO}_3$ ),  $t = 25.00 \pm 0.05$  °C.

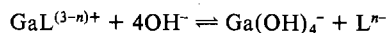
reported in this work are calculated from experiments done at  $25.00 \pm 0.01$  °C with an initial supporting electrolyte consisting of 0.100 M  $\text{KNO}_3$ . Also the term "pH", in this paper, refers to  $-\log [\text{H}^+]$ . The four successive proton dissociation constants for gallium(III) ion used in the calculations are  $10^{-2.91}$ ,  $10^{-3.70}$ ,  $10^{-4.40}$ , and  $10^{-5.77}$ .<sup>9</sup> Stock gallium solutions were prepared by dissolving an accurately weighted quantity of 99.99% pure gallium metal in concentrated HCl. The exact amount of excess (about fourfold) hydrochloric acid in the  $\text{Ga}^{\text{III}}$  solution was determined by a Gran's plot<sup>10</sup> of  $(V_0 + V_{\text{KOH}}) \times 10^{-\text{pH}}$  vs.  $V_{\text{KOH}}$ , where  $V_0$  = the initial volume of gallium(III) solution, and  $V_{\text{KOH}}$  is the volume of added standard KOH. The intercept on the abscissa obtained by extrapolating the straight-line portion of the plot is a direct measure of the excess acid present. The excess acid was also checked by the procedure of Harris and Martell.<sup>1</sup>

**Calculations.** The computations were performed with a CDC-1604A computer. At every potentiometric equilibrium point simultaneous mass balance equations (eq 1) for all components present

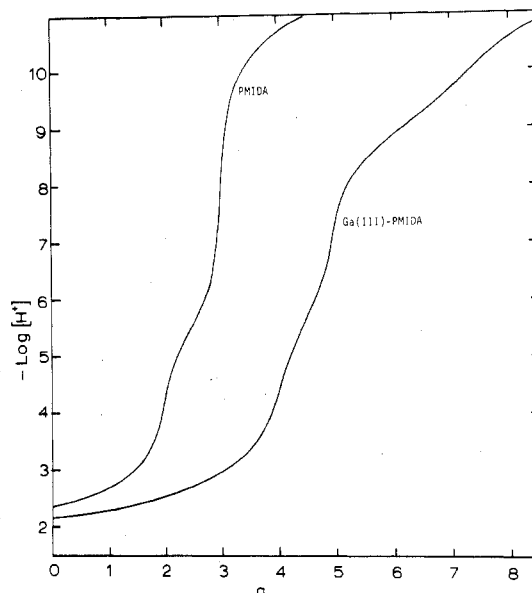
$$T_i = \sum_j e_{ij} \beta_j \prod_k [C_k]^{e_{kj}} \quad (1)$$

were set up in terms of known and unknown overall formation constants. In eq 1  $T_i$  is the analytical concentration of the  $i$ th component (e.g., gallium, ligand, hydrogen ions),  $\beta_j$  is the overall formation constant of the  $j$ th species which is represented by the stoichiometry given by the exponent  $e_{ij}$ . Thus the product of  $\beta_j$  and  $\prod_k [C_k]^{e_{kj}}$  represents the concentration of a given species  $j$ . This set of simultaneous equations was solved for  $[C_k]$ , the concentration of each component in its most deprotonated form. The value of  $[C_k]$  is special when it represents the calculated concentration of hydrogen ion, which then may be readily compared with the measured hydrogen ion concentration. Subsequently, the unknown equilibrium constants were adjusted either manually or statistically until there was no further improvement in the calculated and observed  $[\text{H}^+]$  values taken from the potentiometric equilibrium curve. This method differs from previously employed standard approaches<sup>11</sup> in that the solution is obtained in terms of  $[\text{H}^+]$  rather than the amount of added acid or base (or other reagent). The approach used here represents an improvement over previous methods because it addresses itself to the values of pH as a function of added base rather than the less meaningful reverse process: i.e., how much base needs to be added to obtain the observed pH value. Another advantage results from the fact that "smoothing" of the data is not necessary, and since all mathematical manipulations and differentiations are limited to exact expressions (eq 1), the solutions are also exact.

The potentiometric studies of the gallium(III) complexes involved in the present study provide two characteristically different types of experimental data. At low pH, gallium(III) is either 100% complexed or partially complexed. In the former case, the constant  $K_{\text{ML}}$  was calculated at higher pH values by relying on the following competition or displacement reaction:



This reaction was observed as the dominant one taking place with increasing pH for most gallium(III) chelates in the present study.



**Figure 1.** Potentiometric equilibrium curves of PMIDA, *N*-(phosphonomethyl)iminodiacetic acid, in the absence and in the presence of  $\text{Ga}^{\text{III}}$  ion: upper curve, PMIDA alone, at an initial concentration of  $3.50 \times 10^{-3}$  M; lower curve,  $[\text{PMIDA}]_{\text{tot}} = 2.40 \times 10^{-3}$  M,  $[\text{Ga}^{3+}]_{\text{tot}} = 2.38 \times 10^{-3}$  M. Temperature = 25 °C;  $\mu = 0.1$  M ( $\text{KNO}_3$ );  $a$  = moles of standard alkali added per mole of ligand present.

In the latter case, where  $\text{Ga}(\text{III})$  complexation was not complete, the low pH values were used in the determination of  $K_{\text{ML}}$ . Potentiometric data obtained as a function of added base in the high-pH region can be considered as constituting a "retroformation" or metal chelate displacement curve.

## Results

The ligands studied, together with their protonation constants, are listed in Table I. For some of these ligands, the protonation constants were not measured previously, and were therefore determined by standard potentiometric methods, as indicated in the Table I. The remaining values for well-known ligands were taken from the critical compilation by Smith and Martell.<sup>12</sup> In either case, the protonation constants are defined by eq 2. The charge on the most deprotonated form of the ligand varied from  $-4$  to  $-7$ .

$$k_n^{\text{H}} = [\text{H}_n\text{L}]/[\text{H}_{n-1}\text{L}][\text{H}^+] \quad (2)$$

**Chelate Formation Curves.** A representative potentiometric equilibrium curve for formation of a 1:1 gallium(III) chelate and its conversion to  $\text{Ga}(\text{OH})_4^-$  and ligand is presented in Figure 1. The early part is calculated for complete coordi-

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(10) Rosotti, F. J. C.; Rossotti, H. J. *Chem. Educ.* **1965**, *42*, 1375.

(11) Gaizer, F. *Coord. Chem. Rev.* **1979**, *27*, 195.

(12) Smith, R. M.; Martell, A. E. "Critical Stability Constants"; Plenum: New York, 1977; Vol. 3.

(13) Smith, R. M.; Martell, A. E. "Critical Stability Constants"; Plenum: New York, 1977; Vol. 1.

**Table II.** Logarithmic Values of Chelate Protonation Constants of Gallium(III) Chelates Measured at 25 °C and  $\mu = 0.100$  M (KNO<sub>3</sub>)

| ligand   | $\log K_{\text{MH}_1\text{L}}^{\text{H}}$ | $\log K_{\text{MH}_2\text{L}}^{\text{H}}$ | $\log K_{\text{MH}_3\text{L}}^{\text{H}}$ | $\log K_{\text{MH}_4\text{L}}^{\text{H}}$ |
|----------|---|---|---|---|
| TTHA     | 5.30 (3)                                  | 3.96 (2)                                  | 2.56 (1)                                  |   |
| TPHA     | 7.87 (5)                                  | 4.90 (5)                                  | 3.70 (3)                                  | 2.50 (1)                                  |
| EDDADPO  | 5.10 (2)                                  | 2.24 (1)                                  |   |   |
| GDPO     | 4.09 (3)                                  | 2.51 (1)                                  |   |   |
| EDDPO    | 5.0 (1)                                   | ~1.5 (1)                                  |   |   |
| HEDPO    | 3.04 (1)                                  |   |   |   |
| HBIDPO   | 5.60 (1)                                  | 3.30 (1)                                  |   |   |
| EDTPO    | 6.65 (2)                                  | 5.10 (2)                                  | 3.29 (1)                                  | 2.46 (1)                                  |
| PMIDA    | 3.10 (2)                                  |   |   |   |
| MSHBEDPO | 8.98 (3)                                  | 4.01 (1)                                  | 2.82 (1)                                  |   |

**Table III.** Logarithmic Values of Chelate Hydrolysis Constants (Eq 4) for Gallium Chelates at 25 °C and  $\mu = 0.100$  M (KNO<sub>3</sub>)

| ligand  | $\log K_{\text{M(OH)L}}^{\text{H}}$ | ligand   | $\log K_{\text{M(OH)L}}^{\text{H}}$ |
|---------|-------------------------------------|----------|-------------------------------------|
| TTHA    | 9.64 (1)                            | HEDPO    | 5.00 (6)                            |
| TPHA    | 9.77 (3)                            | HBIDPO   | 6.95 (9)                            |
| EDDADPO | 8.42 (1)                            | EDTPO    | 10.06 (2)                           |
| GDPO    | 6.6 (1)                             | PMIDA    | 5.95 (3)                            |
| EDDPO   | 7.2 (1)                             | MSHBEDPO | 10.36 (2)                           |

nation of gallium to PMIDA (H<sub>4</sub>L), while, quite obviously, between  $a = 3$  and 4 there is evidence for the presence of the protonated form of the metal chelate MHL. Between  $a = 4$  and 5, a MLOH species is evident, while beyond  $a = 5$ , the "retroformation" reaction involving conversion to Ga(OH)<sub>4</sub><sup>-</sup> and free ligand takes place.

**Protonated Chelates.** Inspection of the lower buffer regions of the formation curves indicated nearly complete coordination of gallium ion as well as the presence of significant concentrations of protonated chelates. The values of the protonation constants of the gallium(III) chelates detected in this study are listed in Table II and are defined by eq 3. While all

$$K_{\text{MH}_n\text{L}}^{\text{H}} = [\text{MH}_n\text{L}] / [\text{H}^+][\text{MH}_{n-1}\text{L}] \quad (3)$$

ligands studied were found to produce at least one protonated chelate, several show the presence of up to four such species, depending on the pH range under consideration.

**Hydroxo Metal Chelates.** Interpretations of the buffer regions beyond  $a = n$ , where  $n$  is the number of acidic hydrogens originally present in the neutral ligand, were always found to be consistent with the observation of initial formation of a hydroxo metal chelate species, followed by conversion of the metal ion to the hydroxo complex Ga(OH)<sub>4</sub><sup>-</sup> in a higher pH buffer region. The gallium chelate hydrolysis constants are defined by eq 4. The values of the hydrolysis constants that were obtained are listed in Table III.

$$K_{\text{MOHL}}^{\text{H}} = [\text{ML}] / [\text{MOHL}][\text{H}^+] \quad (4)$$

The possibility that some of the hydroxo chelates dimerize or further polymerize was considered. A study of the concentration dependence of hydrolysis was not initiated in view of the fact that the ionic charge of the ligands varied from -4 to -7. This means that the charges on the corresponding monohydroxo chelates of GaOHL vary from -2 through -5, and polynuclear complex formation was thus considered precluded on electrostatic grounds.

**Formation Constants  $K_{\text{ML}}$ .** Table IV contains quantitative data on gallium(III)-deprotonated ligand interaction in terms of the normal formation constants  $K_{\text{ML}}$ , defined by eq 5. The

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

constants vary from about 18 to 32 logarithm units, indicating a high degree of correlation with charge type, multidenticity, and variation in structure of the ligands.

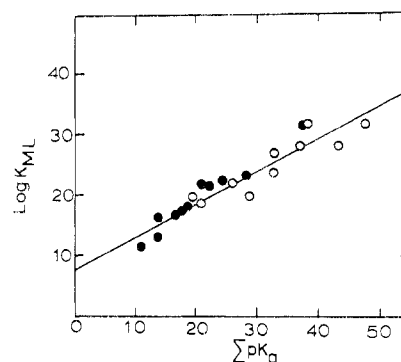
**Table IV.** Formation Constants of Gallium Chelates in Aqueous Solution at 25 °C and  $\mu = 0.100$  M (KNO<sub>3</sub>)

| ligand  | $\log K_{\text{ML}}$ | ligand   | $\log K_{\text{ML}}$ |
|---------|----------------------|----------|----------------------|
| TTHA    | 28.21 (1)            | HEDPO    | 18.52 (1)            |
| TPHA    | 28.16 (1)            | HBIDPO   | 23.78 (3)            |
| EDDADPO | 26.82 (2)            | EDTPO    | 31.83 (2)            |
| GDPO    | 21.93 (4)            | PMIDA    | 19.50 (1)            |
| EDDPO   | 19.84 (1)            | MSHBEDPO | 31.55 (1)            |

**Table V.** Statistical Parameters for Correlation of  $\log K_{\text{ML}}$  vs.  $\Sigma \text{p}K_a$ 

| ref       | slope <sup>a</sup> | intercept <sup>a</sup> | $\sigma_Y^b$ | var <sup>c</sup><br>( $\Sigma \text{p}K_a$ 's) | var <sup>c</sup><br>( $\log K_{\text{ML}}$ ) | $r^d$ |
|-----------|--------------------|------------------------|--------------|--|--|-------|
| this work | 0.50 (0.07)        | 8.8 (3.3)              | 1.9          | 75.6   | 22.3   | 0.92  |
| 1         | 0.72 (0.05)        | 4.6 (1.7)              | 1.2          | 52.4   | 28.7   | 0.98  |
| combined  | 0.55 (0.04)        | 7.7 (2.3)              | 1.9          | 100.2  | 33.6   | 0.95  |

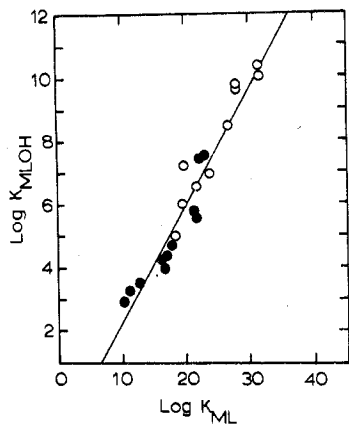
<sup>a</sup> From Figure 2. <sup>b</sup>  $\sigma_Y$  = standard deviation in calculated  $Y$  values. <sup>c</sup> Variance. <sup>d</sup> Product moment correlation coefficient.

**Figure 2.** Correlation of  $\log K_{\text{ML}}$  of gallium(III) chelates with  $\Sigma \log K_n^{\text{H}}$  of ligands ( $r = 0.95$ ): O represents this work; ● represents values from Harris and Martell.<sup>1</sup>

The various equilibrium constants reported here cannot be compared with other published values since none of these systems, with the exception of the TTHA chelate, have been reported previously. Harris and Martell<sup>1</sup> studied the TTHA-Ga(III) system but did not report a value for  $\log K_{\text{ML}}$ . A correlation of the stability data that may be made is the variation of  $\log K_{\text{ML}}$  vs. the overall basicity of the ligands, as measured by the summation of their  $\text{p}K_a$ 's. Also of interest is the correlation of  $\log K_{\text{MOHL}}^{\text{H}}$  vs.  $\log K_{\text{ML}}$  for the various ligands studied.

## Discussion

**Formation Constant Correlations.** It has been found previously<sup>1</sup> that for trivalent ions in general, and for gallium in particular, there is a very high correlation between the  $\log K_{\text{ML}}$  and  $\Sigma_{i=1}^n \log K_i^{\text{H}}$ , where  $\Sigma_{i=1}^n \log K_i^{\text{H}}$  is a measure of the overall  $\sigma$  basicity of the ligand in question. All of the available reliable data for  $\log K_{\text{ML}}$  vs.  $\Sigma_{i=1}^n \log K_i^{\text{H}}$  were combined, and the least-squares line was calculated. Figure 2 shows the resulting diagram comparing the experimental points with the least-squares line, while Table V contains the pertinent statistical parameters for the correlation. Harris and Martell<sup>1</sup> obtained a somewhat higher slope, probably because the range of the  $\text{p}K$  sum that they employed was more limited than that employed in the present study. Specifically, the ligand basicity sum of Harris and Martell<sup>1</sup> varied from only 10 logarithm units for HIDA to 28 logarithm units for DTPA (excepting 38 logarithm units for EHPG). It is clear from Figure 2 that the combined correlation represents a significant improvement in that the range of basicities studied is 10 to 48 logarithm units and provides a more accurate perspective of the variation of formation constants of Ga(III) chelates with the basicities



**Figure 3.** Regression analysis of the logarithm of the chelate hydrolysis constant vs.  $\log K_{ML}$  ( $r = 0.97$ ): O represents this work; ● represents values from Harris and Martell.<sup>1</sup>

of the ligands. It is significant that the slope of 0.55 for the combined data is very close to 0.50, the slope found when the data used in the correlation are restricted to the present work, as indicated in Table V.

There is also an interesting inverse correlation between the logarithm of the chelate hydrolysis constants,  $\log K_{MOHL}^H$ , and the logarithms of the formation constants,  $K_{ML}$ . This is shown in Figure 3, which illustrates the variation of  $\log K_{MOHL}^H$  vs.  $K_{ML}$  for all of the reliable data available from the literature as well as from the present work. The correlation coefficient  $r$  was found to be 0.97. Additional statistical parameters are listed in Table VI. The data used in the construction of Figure 3 represent a much wider spread of equilibrium constants,  $\log K_{MOHL}^H$  and  $\log K_{ML}$ , than has been previously available. The fact that nearly perfect correlation exists between  $\log K_{MOHL}^H$  and  $\log K_{ML}$  for ligands with such a wide variety of donor groups and charges is quite remarkable. The magnitude of  $\log K_{ML}$  does not represent a property of the chelate ML but of the tendency for its formation, so that the correlation could be constructed as a relationship between  $\log K_{MOHL}$  vs. ligand basicity; i.e., if  $\log K_{MOHL}^H$  correlates with  $\log K_{ML}$  and  $\log K_{ML}$  correlates with the  $\sum pK_a$ 's, then  $\log K_{MOHL}^H$  is a measure of the ability of gallium(III) in a wide variety of metal chelates to polarize coordinated water in inverse proportion to the proton affinities or basicities in the coordinated ligands.

**Protonated Chelates.** The fact that the ligands used in this study possess many basic donor groups of varying degree of basicity and the fact that most of these ligands possess the dinegative phosphonate group result in the formation of many protonated metal chelate species in low- to medium-pH solutions. TPHA and EDTPO each form four protonated chelates having the general formula  $MH_iL$ , where  $i = 1, 2, 3,$  or  $4$ . TTHA and MSHBEDPO form three protonated species, while GDPO and HBIDPO form two protonated chelates, MHL and  $MH_2L$ . Finally, HEDPO and PMIDA form only a single such species, MHL.

The nature of protonated species formed by the Ga(III) chelate of EDDPO cannot be determined, since its solutions are turbid in the lower to mid pH region because of the formation of a precipitate of  $Ga(OH)_3$ . A calculation based on the pH measured at  $a = 0$  indicated complete gallium coordination, with  $\sim 2$  protons displaced from the ligand. This means that there are probably two protonated species formed in this metal chelate system,  $MH_2L$  initially and MHL at higher pH.

The protonated chelates of EDTPO formed at low pH are somewhat insoluble. At the beginning of the potentiometric titration ( $a = 0$ ) it appears that 4.12 mol of hydrogen ion/mol of ligand is displaced. When  $a = 4$  (at pH 2.9), the solution

becomes homogeneous. EDTPO was also reacted with 2 mol of Ga(III)/mol of ligand, but about 11 mol of base/mol of ligand was required to produce a clear, homogeneous solution. The pH was about 7.4 at this point. The equilibration time in this 2:1 system was much too long for reliable potentiometric measurement of hydrogen ion concentration within a reasonable length of time. However, it is apparent that a 2:1 binuclear complex forms in this system and that the complex is probably ligand bridged rather than hydroxo bridged. Solutions of the  $Ga^{III}$ -HBIDPO chelate are slightly turbid at low pH (1.8) but dissolve after a small amount of base is added, indicating the presence of several protonated forms of the chelate. All other chelate systems studied in this investigation were soluble throughout the entire accessible pH range.

The strong hydrolytic tendencies of gallium(III) were used to advantage in this work in the calculation of the normal stability constants. The uncertainties in the calculated values are due mainly to whatever uncertainties exist in the Ga(III) hydrolysis constants and, in particular, to the overall constant  $\beta_4^{hydr}$ . Uncertainties in  $\beta_1^{hydr}$ ,  $\beta_2^{hydr}$ ,  $\beta_3^{hydr}$  are not expected to have much influence on the results since gallium(III) is generally strongly bound to the ligand in the pH regions for which the mono-, di-, and trihydroxo complexes would be the main hydrolytic species. The value of the constant  $\beta_4^{hydr}$  is well-known, and the best value available in the literature<sup>9</sup> has been employed in the calculations.

With the information available at this point the probable coordinate bonding modes of the complexes formed in solution may be inferred, without definite implications concerning the structures and stereochemistry of the complexes. These conclusions are guided to some extent by the recent work on Ga(III) chelates of dihydroxyaromatic ligands<sup>2</sup> and by the information provided by Harris and Martell<sup>1</sup> on a wide variety of gallium chelates.

The triprotonated TTHA gallium(III) chelate,  $MH_3L$ , must be of the type indicated by 1, with the metal ion bound to a

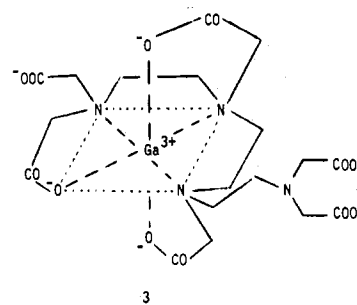
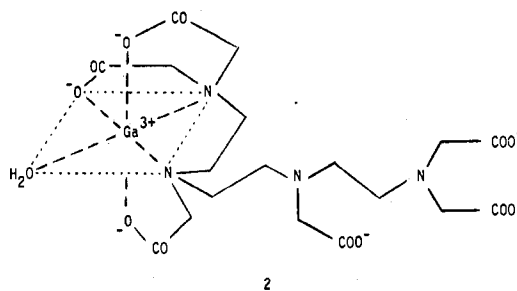
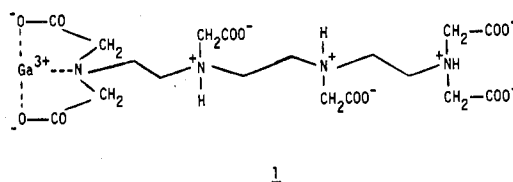
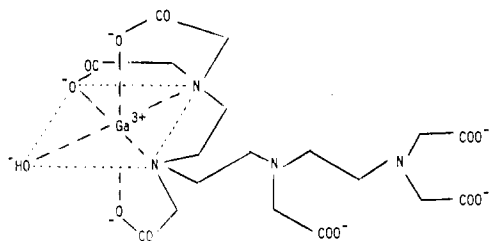


Table VI. Statistical Parameters for the Correlation of  $\log K_{\text{MOHL}}^{\text{H}}$  with  $\log K_{\text{ML}}$ 

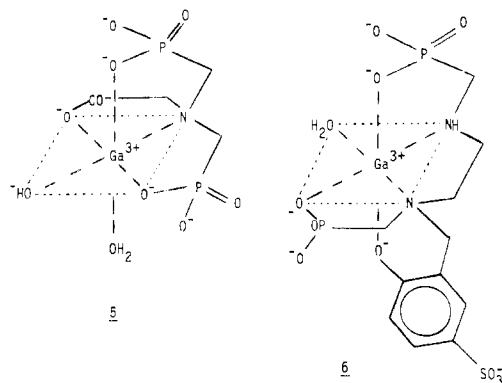
| ref       | slope <sup>a</sup> | intercept <sup>a</sup> | $\sigma_Y^b$ | var <sup>c</sup><br>(log $K_{\text{ML}}$ ) | var <sup>c</sup><br>(log $K_{\text{MOHL}}^{\text{H}}$ ) | $r^d$ |
|-----------|--------------------|------------------------|--------------|--|---|-------|
| this work | 0.37 (0.04)        | -1.2 (1.2)             | 0.54         | 22.3                                       | 3.28  | 0.95  |
| 1         | 0.31 (0.04)        | -0.7 (1.0)             | 0.56         | 19.1                                       | 2.25  | 0.93  |
| combined  | 0.37 (0.03)        | -1.5 (0.8)             | 0.61         | 38.4                                       | 5.62  | 0.97  |

<sup>a</sup> From Figure 3. <sup>b</sup>  $\sigma_Y$  = standard deviation in calculated  $Y$  values. <sup>c</sup> Variance. <sup>d</sup> Product moment correlation coefficient.

terminal terdentate iminodiacetate group and with the three protons bound to the three remaining basic nitrogen atoms, thus accounting for the magnitudes of the chelate protonation constants. Successive deprotonation of  $\text{MH}_3\text{L}$  to ultimately form  $\text{ML}$  involves wrapping the ligand around the gallium ion in such a manner as to coordinate the metal ion with a maximum number of oxygen donors but including the coordination of some of the basic nitrogens in order to form five-membered chelate rings. Possible coordinate bonding modes are indicated by formulas 2 and 3, but other arrangements are, of course, possible. The facile formation of the monohydroxo chelate  $\text{GaOHL}^{4-}$  seems to favor 2 over 3, since the former is converted to 4 by simple dissociation of a proton from the coordinated



4



5

6

water molecule. The coordinate bonding in formula 2 is favored over that in 3 because it indicates four coordinated oxygen donors, while in 3 only three such donor groups are utilized. Other possible conformations cannot be excluded for these systems, and a number of these species may be in mobile equilibrium, with those having the most favored coordination arrangements having the higher concentrations. At higher pH the metal chelate dissociates with concomitant formation of the more stable tetrahydroxogallate ion  $\text{Ga}(\text{OH})_4^-$ .

The properties of the  $\text{Ga}(\text{III})$  chelates of TPHA are apparently similar to those of TTHA, and the metal chelates formed are probably similar to those indicated by 1-4 with the exception that they contain one less aminoacetate moiety in the uncoordinated side chain.

The diphosphonate ligand GDPO forms a diprotonated complex of stoichiometry  $\text{GaH}_2\text{L}$ , resulting from combination of  $\text{GaL}^{2-}$  with two hydrogen ions and characterized by pro-

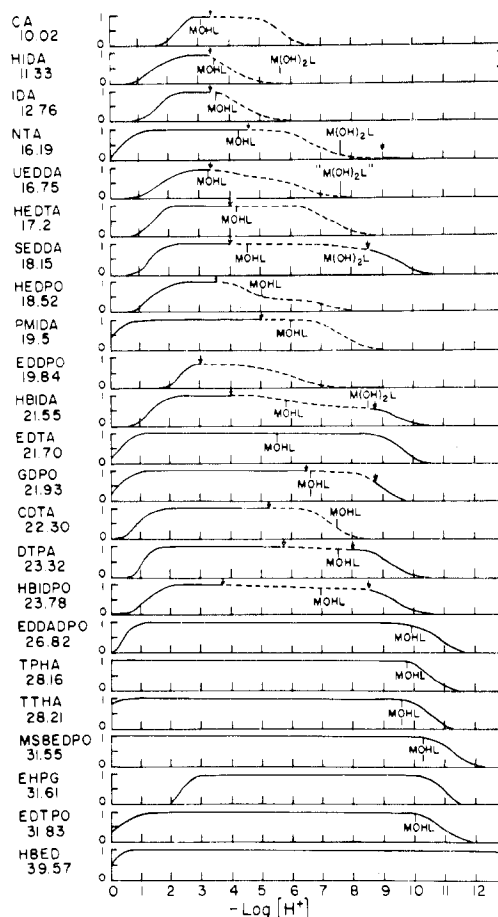


Figure 4. Calculated degree of formation of soluble gallium complexes as a function of  $-\log [\text{H}^+]$  for  $T_{\text{L}} = T_{\text{Ga}^{3+}} = 1.00 \times 10^{-3} \text{ M}$  and  $\mu = 0.10 \text{ M}$ . A broken line indicates that the concentration of free metal ion is fixed by the solubility product,  $K_{\text{sp}} = [\text{Ga}^{3+}][\text{OH}^-]^3 = 1.00 \times 10^{-37}$ , and is pinpointed by vertical arrows. Ligands taken from ref 1 are citric acid (CA), *N*-(hydroxyethyl)iminodiacetic acid (HIDA), iminodiacetic acid (IDA), nitrilotriacetic acid (NTA), *N,N*-ethylenediaminediacetic acid (UEDDA), *N*-(hydroxyethyl)-ethylenediamine-*N,N'*-triacetic acid (HEDTA), *N,N'*-ethylenediaminediacetic acid (SEDDA), *N*-(2-hydroxybenzyl)iminodiacetic acid (HBIDA), ethylenediaminetetraacetic acid (EDTA), cyclohexanediaminetetraacetic acid (CDTA), ethylene-1,2-bis(*o*-hydroxyphenylglycine) (EHPG), *N,N'*-bis(*o*-hydroxybenzyl)-ethylenediamine-*N,N'*-diacetic acid (HBED).

ton-association constants with logarithms of 4.09 and 2.51. These protons are most certainly coordinated to phosphonate groups, which in turn are coordinated to the metal ion through the unprotonated negative oxygen donor groups. In view of its high stability, it is probable that all donor groups in this terdentate ligand are coordinated to the metal ion. Additional coordinated water may be involved in the formation of the hydroxo chelate  $\text{Ga}(\text{OH})\text{L}^{3-}$ , as indicated in formula 5.

The ligand HEDPO is unique in the sense that it does not possess a tertiary nitrogen donor atom. Under conditions such that the hydroxyl group is not involved in metal coordination, this ligand may be considered the carbon analogue of pyrophosphate, and its complexes may be analogous to pyrophosphate complexes.

It is possible to postulate several alternate forms of the gallium(III) chelates of the remaining ligands and their protonated and hydroxo derivatives, but two (or three) in particular stand out as possessing extremely high stability constants: EDTPO ( $K_{\text{GaL}} = 31.83$ ) and MSBEPO ( $K_{\text{ML}} = 31.55$ ). Whether species  $\text{MH}_4\text{L}$  and other protonated EDTPO chelates of  $\text{Ga}(\text{III})$  are six coordinated or involve a lower

degree of metal ion coordination is a matter of speculation. It is fairly certain, however, that the normal chelate  $\text{GaL}^{5-}$  involves octahedral coordination. The fact that  $\log K_{\text{MOHL}}$  (10.06) is unusually high is due to the extremely high (-8) negative charge on the ligand, which tends to prevent hydroxide ion binding to the metal ion. Although the ligand MSHBEDPO has a somewhat lower negative charge in its fully deprotonated form, the stability constant of its  $\text{Ga(III)}$  chelate is higher than that of EDDPO. The  $\text{p}K$  of this chelate, corresponding to the formation of the monohydroxo species  $\text{Ga(OH)L}^{3-}$ , is also higher than that of the tetraphosphonate chelate. The higher stability of this chelate, represented by formula 6, and its lower tendency toward hydrolysis are due to the presence of the phenolate group, which binds the gallium(III) ion very strongly.

**Ligand Efficacy toward Binding of Trivalent Gallium.** Over 20 representative ligands for which reliable thermodynamic gallium(III) equilibrium constants are available have been selected for analysis of the species present in solution as a function of pH. For solutions  $1.00 \times 10^{-3}$  M in ligand and gallium(III) at  $\mu = 0.100$  and  $t = 25$  °C, a detailed species calculation as a function of  $-\log [\text{H}^+]$  was made. The calculations were carried out by taking into account the precipitation of  $\text{Ga(OH)}_3$ , whereby the concentrations of solution species were reduced by the quantity of solid phase that separated out in accordance to the solubility product for amorphous  $\text{Ga(OH)}_3$  ( $K_{\text{sp}} = [\text{Ga}^{3+}][\text{OH}^-]^3 = 1.00 \times 10^{-37}$ ).<sup>13</sup> A program, SPECIES, was written in these laboratories for the evaluation of all species present in a given equilibrium model and was modified to take into account the presence of one metal ion hydroxide separated as a solid phase. The simultaneous equations expressed in terms of equilibrium constants, hydrogen ion concentration, and stoichiometry are solved by iterative procedures (Newton-Rapson) to convergence. The solid-phase modification introduced consisted of a check of whether the  $K_{\text{sp}}$  of  $\text{Ga(OH)}_3$  had been exceeded. If it has been exceeded, the metal ion concentration is simply calculated directly from the  $[\text{OH}^-]$  and  $K_{\text{sp}}$ , and the fixed value of  $[\text{M}^{3+}]$  is used in the remaining computation of the species in equilibrium.

The results of these calculations are presented in Figure 4, in which the ligands are arranged in the order of decreasing magnitude of the stability constants of the unprotonated and unhydrolyzed metal chelates ML. The ordinate represents the

degree of formation of soluble gallium complexes in all its forms, including its protonated and hydroxo forms. Thus it is seen that throughout most of the accessible lower pH region gallium(III) is fully complexed. The detailed analysis of the various protonated forms, MHL,  $\text{MH}_2\text{L}$ , etc., that exist in the lower pH range may be calculated from the successive chelate protonation constants listed in Table II. The appearance of the precipitated hydroxide is indicated by an arrow followed by a broken line (which itself represents the degree of formation of soluble complexes), which is terminated by a second arrow, where applicable. The decrease in concentration of complexed species at high pH in the absence of precipitate is due to formation of the soluble tetrahydroxogallate complex,  $\text{Ga(OH)}_4^-$ .

The two most outstanding features of the data in Figure 4 are (1) the formation of the monohydroxo chelate,  $\text{M(OH)L}$ , at high pH in nearly all cases and (2) the breakdown of the hydroxo chelate at higher pH to gallate and free ligand. Evidently the former is a general reaction for all non-phenolic-type ligands while the latter is the essential consequence of the extremely high stability of  $\text{Ga(OH)}_4^-$ . The "effective" stability of this complex increases with the fourth power of the pH as the pH increases. The general shapes of the formation curves of  $\text{Ga(OH)}_4^-$  are therefore quite similar, and visual inspection of the extremities of these curves gives representations of the relative effectiveness of each ligand system in binding gallium(III).

While the ligands with the higher stability constants regulate the free  $\text{Ga(III)}$  at sufficiently low concentrations to prevent precipitation, the weaker complexes allow the  $K_{\text{sp}}$  of  $\text{Ga(OH)}_3$  to be exceeded to varying extents. It is to be noted that the drop-off at higher pH is due in many cases to both the precipitation of  $\text{Ga(OH)}_3$  and the formation of the tetrahydroxogallate anion. The soluble tetrahydroxo species finally predominates as the pH is further increased, so that ultimately all metal chelates and any precipitated hydroxide are fully converted to the amphoteric gallate anion.

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**Registry No.** TTHA, 869-52-3; TPHA, 3234-59-1; EDDADPO, 2310-83-0; GDPO, 2439-99-8; EDDPO, 1733-49-9; HEDPO, 2809-21-4; HBIDPO, 73199-04-9; EDTPO, 1429-50-1; PMIDA, 5994-61-6; MSHBEDPO, 73199-05-0.