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Complexation Reactions of Aluminum Ions with Polyamino Polycarboxylic Macrocycles in an Aqueous Solution

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The complex formation reactions of aluminum ions with polyamino polycarboxylic macrocycles (DOTA, TETA, PEPA, and HEHA) in an aqueous solution were investigated using a potentiometric method. At a pH higher than 5.00 the tetradecamer, $[Al_{14}(OH)_{34}]^{8+}$, was found to be the most consistent uncomplexed Al(III) species based on our experimental data. Under the experimental conditions employed, aluminum ions form solely 1 : 1 ratio complexes with all of the ligands studied. Polyaza rings of the ligands may act simply as a frame to constrain the carboxylate groups into a nearly spherical arrangement; DOTA, TETA, PEPA, and HEHA act as tetra-, penta-, and hexa-dentate ligands, respectively, wrapping themselves around the aluminum(III) ion.

Recently, numerous examples of aluminum-induced disorder in physiological processes have been reported and are widely recognized. This demands an understanding of how aluminum ions interact with compounds (ligands) in biological systems. The aluminum ion, whose accessible oxidation state in biological system is 3+, is a typical hard Lewis acid; its binding is primarily electrostatic. Accordingly, it is expected to complex with oxygen donor ligands, carboxylate and phosphate groups. For this reason, it would be worthwhile studying the complexation reactions of aluminum ions with polycarboxylate or phosphate anion ligands. We therefore decided to pursue an investigation concerning the complex formation equilibrium of aluminum ion with saturated polyaza macrocycles carrying an acetic acid group ($-CH_2COOH$) on each nitrogen atom, such as DOTA, TETA, PEPA, and HEHA (Fig. 1), and to determine their equilibrium constants using a conventional pH-metric method. The results were compared with those of alkaline earth metal(II) and lanthanide(III) complexes.

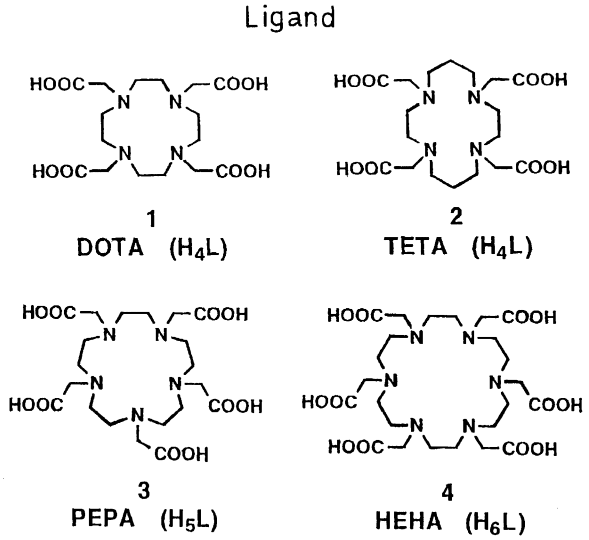

Fig. 1. Polyamino polycarboxylic macrocycles used in this study.

Experimental

Materials. The synthetic procedures of DOTA (H_4dota, [12]ane$N_4(CH_2COOH)_4$), TETA (H_4teta, [14]-ane$N_4(CH_2COOH)_4$), PEPA (H_5pepa, [15]ane$N_5(CH_2COOH)_5$), and HEHA (H_6heha, [18]ane$N_6(CH_2COOH)_6$) (Fig. 1) were reported in previous papers.[1—5] A stock solution of aluminum(III) perchlorate was prepared by dissolving a known weight of aluminum metal plate of 99.99% (Kanto) in hydrochloric acid, followed by repeated evaporation with perchloric acid. The free acid ($HClO_4$) in solution was previously determined by titration.[6] A carbon dioxide-free tetraethylammonium hydroxide ($(C_2H_5)_4NOH$) solution was stored in a paraffine-coated glass vessel under pure nitrogen. All other chemicals used were of analytical reagent grade (Aldrich or Dojin).

Equilibrium Constant Determinations. Potentiometric titrations for aluminum(III) complexes of $dota^{4-}$, $teta^{4-}$, $pepa^{5-}$, and $heha^{6-}$ were carried out in the same ways as described in previous papers.[5,7,8] All of the titrations were performed with a Mettler Automatic Titrator, using 0.500 mM ligand solutions containing equimolar aluminum ion ($M=1$ $mol\,dm^{-3}$), under a nitrogen or argon atmosphere. Three titrations were conducted for each system. The test-solution temperature was kept within ±0.05

°C, and the ionic strength (I) was adjusted to 0.20 with $NaNO_3$.

Since the formation kinetics of $pepa^{5-}$ and $heha^{6-}$ complexes is fairly fast, even at 25 °C, their formation constants could be determined very easily. On the other hand, in the DOTA and TETA systems a slow attainment of complexation equilibrium prevents any reliable determination of the formation constants. Thus, the formation constants for $dota^{4-}$ and $teta^{4-}$ complexes are less accurate than those of $pepa^{5-}$ and $heha^{6-}$ complexes. We allowed equilibration times of 500, 60, and 30 min after each addition of 0.100_0 M $(C_2H_5)_4NOH$ titrant in the cases of TETA, PEPA, and HEHA systems, respectively. For the DOTA system, since the equilibration took as long as 7 d, we barely obtained reproducible titrations. The protonation constants ($\boldsymbol{K}_i$) of $teta^{4-}$, $pepa^{5-}$, and $heha^{6-}$ anions used in this study were determined previously.[4] In the DOTA system the protonation constants determined by Stetter and Frank[1] at an ionic strength of 0.10 were corrected for an ionic strength 0.20 $mol\,dm^{-3}$ by using the activity coefficients of the ions derived from the Davies equation,[9] and were used in an analysis of the experimental data. Their logarithmic values were 11.08, 9.72, 4.42, and 4.38.

Results and Discussion

Although the aluminum(III) ion is perhaps the best-known example of metal-ion hydrolysis, there is little agreement in the literature on the formula of the species that are formed in an aqueous solution. At relatively low aluminum(III) ion concentrations it forms mononuclear OH^- complexes, and equilibria among them may be described by reactions 1, 2, and 3. By common consent we write reactions 1, 2, and 3 as follows:

$$\begin{aligned} &Al^{3+} + H_2O = [Al(OH)]^{2+} + H^+, \\ &K_1{}^{10)} = \frac{[Al(OH)^{2+}][H^+]}{[Al^{3+}]}(10^{-5.5}) \end{aligned} \tag{1}$$

$$\begin{aligned} &[Al(OH)]^{2+} + H_2O = [Al(OH)_2]^+ + H^+, \\ &K_2{}^{10)} = \frac{[Al(OH)_2^+][H^+]}{[Al(OH)^{2+}]}(10^{-5.6}) \end{aligned} \tag{2}$$

$$\begin{aligned} &[Al(OH)_2]^+ + 2H_2O = [Al(OH)_4]^- + 2H^+, \\ &K_3{}^{10)} = \frac{[Al(OH)_4^-][H^+]^2}{[Al(OH)_2^+]}(10^{-12.1}) \end{aligned} \tag{3}$$

As the pH of solution increases, the charge density of the Al^{3+} ion decreases due to hydrolysis, and aluminum begins to polymerize. Many investigators have proposed several polymeric hydroxoaluminum(III) species.[10] In 1965, J. Aveston mentioned that it is possible to give a satisfactory explanation for all of the experimental data obtained by ultracentifugation and acidity studies of the hydrolysis of the aluminum(III) ion in terms of only two polymerized species: a dimer ($[Al_2(OH)_2]^{4+}$) and a tridecamer ($[Al_{13}(OH)_{32}]^{7+}$).[6] Later, R. E. Mesmer and C. F. Baes, Jr.[11] examined the hydrolysis of aluminum(III) ions at higher temperature, where the kinetics are more favourable, using a hydrogen electrode concentration cell for precise acidity measurements; they drew the conclusion that the results could be best explained by assuming the formation of a dimer ($[Al_2(OH)_2]^{4+}$), a trimer ($[Al_3(OH)_4]^{5+}$) and a tetradecamer ($[Al_{14}(OH)_{34}]^{8+}$) instead. They determined the following least-squares refined formation constants for them:

$$\begin{aligned} &2Al^{3+} + 2H_2O = [Al_2(OH)_2]^{4+} \\ &\quad +2H^+, \ \log\beta_{2,2} = -7.45 \end{aligned} \tag{4}$$

$$\begin{aligned} &3Al^{3+} + 4H_2O = [Al_3(OH)_4]^{5+} \\ &\quad +4H^+, \ \log\beta_{3,4} = -13.36 \end{aligned} \tag{5}$$

$$\begin{aligned} &14Al^{3+} + 34H_2O = [Al_{14}(OH)_{34}]^{8+} \\ &\quad +34H^+, \ \log\beta_{14,34} = -110.45 \end{aligned} \tag{6}$$

Based on the foregoing discussion it is reasonable to assume that at a relatively low aluminum(III)-ion concentration it exists as a mixture of mononuclear OH^- complexes, $[Al_2(OH)_2]^{4+}$, $[Al_3(OH)_4]^{5+}$, and a tetradecamer ($[Al_{14}(OH)_{34}]^{8+}$) or a tridecamer ($[Al_{13}(OH)_{32}]^{7+}$). Calculations using the above six equilibrium constants show that in about 1 mM aluminum(III) aqueous solutions of pH lower than 3.90 aluminum(III) ions exist solely as a mixture of mononuclear complexes. At this pH region the concentrations of the dimer, trimer and tetradecamer (or tridecamer) were estimated to be only $4.2_5\times10^{-6}$, $1.6_1\times10^{-7}$, and $1.0_0\times10^{-20}$ $mol\,dm^{-3}$ (or $1.4_3\times10^{-19}$), respectively. On the other hand, in solutions having a pH higher than 5.00 almost all of the aluminum(III) ions exist as a tetradecamer (or tridecamer). At pH=5.00, 99.1 (or 96.4) per cent of the total aluminum ion exists as a tetradecamer (or tridecamer). Consequently, in the Al(III)-ligand (H_nL°) equimolar mixture solution having a pH lower than 3.90 the sum of the hydrogen ion and the tetraethylammonium ion ($(C_2H_5)_4N^+$ (from $(C_2H_5)_4NOH$)) concentrations at titration point a (where a represents the number of moles of $(C_2H_5)_4NOH$ added per mole of ligand) is given by (7), provided that only a 1 : 1 ratio complex of aluminum ion, AlL^{3-n} is formed during the titration:[4]

$$\begin{aligned} \alpha &= aC_L + [H^+] - [OH^-] \\ &= n[L^{n-}] + (n-1)[HL^{1-n}] + \cdots + [H_{n-1}L^-] \\ &\quad + n[AlL^{3-n}] + [Al(OH)^{2+}] + 2[Al(OH)_2{}^+] \\ &\quad + 4[Al(OH)_4{}^-] \end{aligned} \tag{7}$$

Here, C_L denotes the total concentration of the ligand, and is given by

$$C_L = [L]_f + [AlL^{3-n}]. \tag{8}$$

The concentration of the uncomplexed macrocyclic ligand ($[L]_f$) in Eq. 8 is given by

$$[\mathrm{L}]_\mathrm{f} = [\mathrm{L}^{n-}] + [\mathrm{HL}^{1-n}] + [\mathrm{H_2L}^{2-n}] + \cdots + [\mathrm{H}_n\mathrm{L}^\circ]. \tag{9}$$

The complex formation and acid-base equilibria involved during the titration at pH lower than 3.90 are defined by Eqs. 1, 2, 3, 10, and 11. In the following i=1, 2, ···, n:

$$\mathrm{Al}^{3+} + \mathrm{L}^{n-} = \mathrm{AlL}^{3-n},\ K_\mathrm{AlL} = \frac{[\mathrm{AlL}^{3-n}]}{[\mathrm{Al}^{3+}][\mathrm{L}^{n-}]} \tag{10}$$

$$\mathrm{H}_{i-1}\mathrm{L}^{i-n-1} + \mathrm{H}^+ = \mathrm{H}_i\mathrm{L}^{i-n},\ \boldsymbol{K}_i = \frac{[\mathrm{H}_i\mathrm{L}^{i-n}]}{[\mathrm{H}_{i-1}\mathrm{L}^{i-n-1}][\mathrm{H}^+]} \tag{11}$$

By combining the above eight equations one can derive

$$K_\mathrm{AlL}(n'C_\mathrm{L} - \alpha')^2(\alpha_\mathrm{H})_\mathrm{L} = (n'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H})(\alpha'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H}C_\mathrm{L}). \tag{12}$$

Here,

$$(\alpha_\mathrm{H})_\mathrm{L} = \frac{[\mathrm{L}]_\mathrm{f}}{[\mathrm{L}^{n-}]} = 1 + \boldsymbol{K}_1[\mathrm{H}^+] + \boldsymbol{K}_1\boldsymbol{K}_2[\mathrm{H}^+]^2 + \cdots + \boldsymbol{K}_1\boldsymbol{K}_2\cdots\boldsymbol{K}_n[\mathrm{H}^+]^n, \tag{13}$$

$$\beta_\mathrm{H} = n + (n-1)\boldsymbol{K}_1[\mathrm{H}^+] + \cdots + \boldsymbol{K}_1\boldsymbol{K}_2\cdots\boldsymbol{K}_{n-1}[\mathrm{H}^+]^{n-1}, \tag{14}$$

$$n' = n - \frac{\beta_\mathrm{OH}^\mathrm{Al}}{(\alpha_\mathrm{OH})_\mathrm{Al}}, \tag{15}$$

$$a' = a - \frac{\beta_\mathrm{OH}^\mathrm{Al}}{(\alpha_\mathrm{OH})_\mathrm{Al}}, \tag{16}$$

$$\alpha' = a'C_\mathrm{L} + [\mathrm{H}^+], \tag{17}$$

$$(\alpha_\mathrm{OH})_\mathrm{Al} = 1 + K_1/[\mathrm{H}^+] + K_1K_2/[\mathrm{H}^+]^2 + K_1K_2K_3/[\mathrm{H}^+]^4, \tag{18}$$

and

$$\beta_\mathrm{OH}^\mathrm{Al} = 4K_1K_2K_3/[\mathrm{H}^+]^4 + 2K_1K_2/[\mathrm{H}^+]^2 + K_1/[\mathrm{H}^+]. \tag{19}$$

Equation 12 clearly indicates that if the uncomplexed aluminum ion exists as a mixture of mononuclear OH^- complexes, that is, at a pH lower than 3.90, a plot of $(n'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H})\times(\alpha'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H}C_\mathrm{L})$ against $(n'C_\mathrm{L} - \alpha')^2(\alpha_\mathrm{H})_\mathrm{L}$ should give a straight line which passes through the point of origin; its slope gives the K_AlL value. When the uncomplexed aluminum ion exists solely as a tetradecamer or tridecamer, $[\mathrm{Al}_p(\mathrm{OH})_q]^{3p-q}$, Eq. 7 should be replaced by Eq. 20. Consequently, by applying the same treatment as employed above one can obtain

$$\alpha = n[\mathrm{L}^{n-}] + (n-1)[\mathrm{HL}^{1-n}] + \cdots + [\mathrm{H}_{n-1}\mathrm{L}^-] + \frac{q}{p}[\mathrm{Al}_p(\mathrm{OH})_q^{3p-q}] = \frac{\beta_\mathrm{H}}{(\alpha_\mathrm{H})_\mathrm{L}}[\mathrm{L}]_\mathrm{f} + \frac{q}{p}[\mathrm{Al}_p(\mathrm{OH})_q^{3p-q}] \tag{20}$$

$$\frac{K_\mathrm{AlL}}{(p\cdot\boldsymbol{K})^{1/p}K_\mathrm{w}^{q/p}} = \frac{[(\alpha - \frac{q}{p}C_\mathrm{L})(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H}C_\mathrm{L}][(n - \frac{q}{p}) - \frac{\beta_\mathrm{H}}{(\alpha_\mathrm{H})_\mathrm{L}}]^{1/p}}{[\mathrm{H}^+]^{q/p}} \times \frac{1}{(nC_\mathrm{L} - \alpha)^{(p+1)/p}}. \tag{21}$$

Here, $\boldsymbol{K} = \boldsymbol{\beta}_{p,q}/K_\mathrm{w}^q = [\mathrm{Al}_p(\mathrm{OH})_q^{3p-q}]/[\mathrm{Al}^{3+}]^p[\mathrm{OH}^-]^q$ and $K_\mathrm{w} = [\mathrm{H}^+][\mathrm{OH}^-]$ $(=10^{-13.79})$.

Equation 21 indicates that if the uncomplexed aluminum ion exists solely as a polynuclear OH^- complex, $[\mathrm{Al}_p(\mathrm{OH})_q]^{3p-q}$, i.e., at a pH higher than 5.00, a plot of $[(\alpha - qC_\mathrm{L}/p)(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H}C_\mathrm{L}][(n - q/p) - \beta_\mathrm{H}/(\alpha_\mathrm{H})_\mathrm{L}]^{1/p}/[\mathrm{H}^+]^{q/p}$ vs. $(nC_\mathrm{L} - \alpha)^{(p+1)/p}$ gives a straight line passing through the origin, and its slope gives $K_\mathrm{AlL}/(p\cdot\boldsymbol{K})^{1/p}\ K_\mathrm{w}^{q/p}$.

In about 1 mM aluminum solutions of pH between 3.90 and 5.00, aluminum(III) ions exists in the forms of $[\mathrm{Al(OH)}]^{2+}$, $[\mathrm{Al(OH)_2}]^+$, $[\mathrm{Al(OH)_4}]^-$, $[\mathrm{Al_2(OH)_2}]^{4+}$, $[\mathrm{Al_3(OH)_4}]^{5+}$, and $[\mathrm{Al}_p(\mathrm{OH})_q]^{3p-q}$ Consequently, it is almost impossible to derive a simple theoretical equation which correlates the a value with the hydrogen-ion concentration, such as Eqs. 12 and 21. Hence, at this pH region one can not analyze the experimental data graphically. For this reason we tried to analyze the experimental data at a pH lower than 3.90, as well as those at pH between 5.00 and 5.50, using theoretical Eqs. 12 and 21, respectively.

The titration curves of equimolar mixture solution of aluminum(III) and $\mathrm{H_4}$dota or $\mathrm{H_4}$teta ($\mathrm{H_4L^\circ}$) show one sharp break at a=4, suggesting the formation of a 1 : 1 ratio normal complex ($\mathrm{AlL^-}$). A typical titration curve obtained for the TETA system is reproduced in Fig. 2. Obviously, complex formation occurs at pH lower than 3.90. The titration curves for $\mathrm{H_6}$heha ($\mathrm{H_6L^\circ}$) solutions containing equimolar aluminum(III) ion gave two breaks, one very slight at a=5 and the other at a=6. A typical example is shown in Fig. 3. Those of $\mathrm{H_5}$pepa ($\mathrm{H_5L^\circ}$) solutions containing equimolar aluminum(III) ion also showed two breaks, one (very slight one) at a=4 and the other at a=5. In titrations of both PEPA and HEHA systems the second buffer region appears at pH in the neighborhood of 5.00.

The titration curves for the DOTA and TETA systems were analyzed using the experimental data at pH lower than 3.90 (in the region 4.0>a>2.5) by employing Eq. 12. Plots of $(4'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H})(\alpha'(\alpha_\mathrm{H})_\mathrm{L} - \beta_\mathrm{H}C_\mathrm{L})$ against $(4'C_\mathrm{L} - \alpha')^2(\alpha_\mathrm{H})_\mathrm{L}$ gave straight lines which pass through the point of origin. Here, 4′ is the n' value at n=4. A typical straight line obtained in the TETA system is reproduced in Fig. 4. Thus, the K_AlL values for the DOTA and TETA systems were determined from the gradients of the above-mentioned linear plots.

Taking into account the fact that the second pH buffer region appears in the neighborhood of pH= 5.00, and, hence, the uncomplexed aluminum(III) ion exists solely as a tetradecamer or a tridecamer, we analyzed the titration data in the second

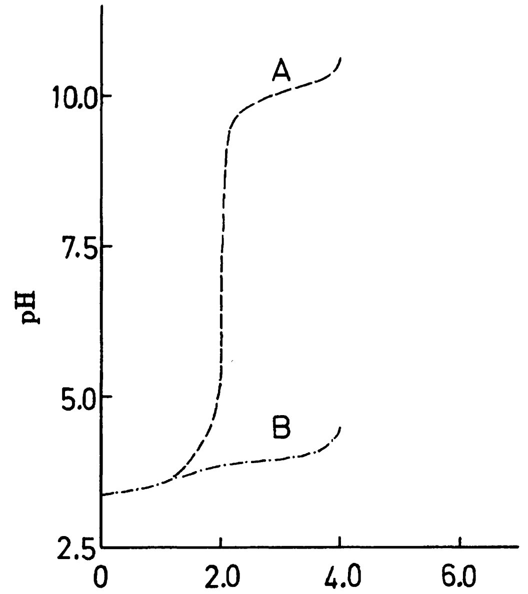

Fig. 2. Titration curve of equimolar mixture of [14]-aneN$_4$(CH$_2$COOH)$_4$(H$_4$teta) and aluminum(III) ions with (C$_2$H$_5$)$_4$NOH. I=0.20, 25 °C. (A) without aluminum(III) ion, (B) 0.500 mM aluminum(III) ion.

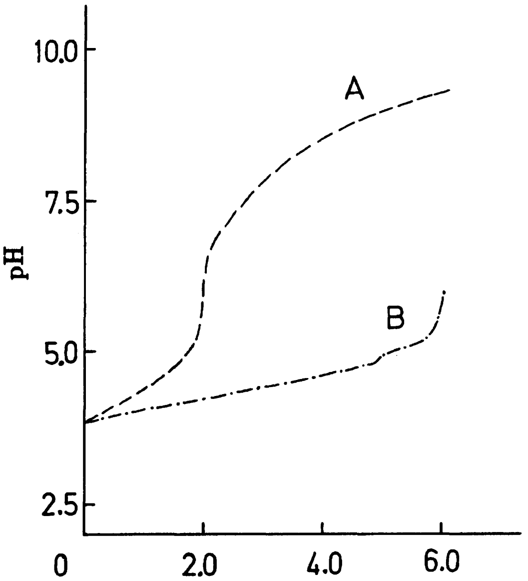

Fig. 3. Titration curve of equimolar mixture of [18]aneN$_6$(CH$_2$COOH)$_6$(H$_6$heha) and aluminum(III) ions with (C$_2$H$_5$)$_4$NOH. I=0.20, 25 °C. (A) without aluminum(III) ion, (B) 0.500 mM aluminum(III) ion.

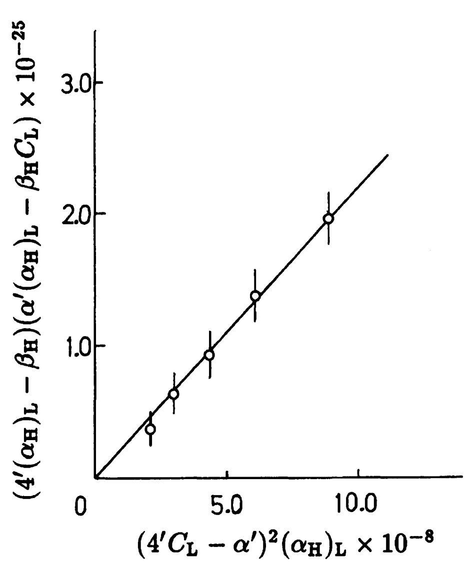

Fig. 4. Plots (with confidence limits) of $(4'(\alpha_H)_L - \beta_H)(\alpha'(\alpha_H)_L - \beta_H C_L)$ (Eq. 12) against $(4'C_L - \alpha')^2(\alpha_H)_L$. I=0.20, 25 °C. [14]aneN$_4$(CH$_2$COOH)$_4$-(H$_4$teta): 0.500 mM, aluminum(III) ion: 0.500 mM.

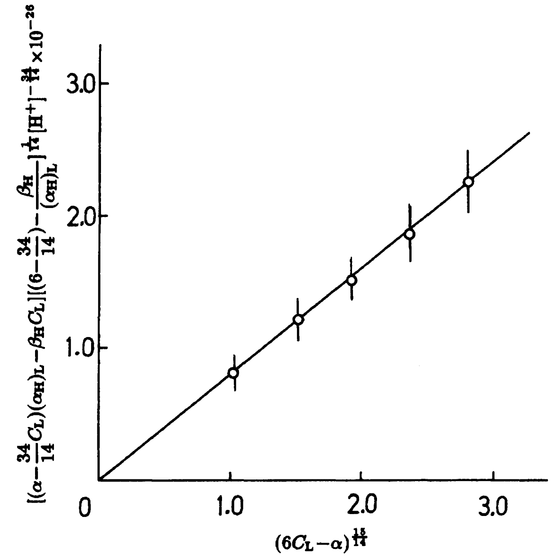

Fig. 5. Plots (with confidence limits) of $[(\alpha - 34C_L/14)(\alpha_H)_L - \beta_H C_L][6 - 34/14 - \beta_H/(\alpha_H)_L]^{1/14} \times [H^+]^{-34/14}$ against $(6C_L - \alpha)^{15/14}$. I=0.20, 25 °C. [18]aneN$_6$(CH$_2$COOH)$_6$(H$_6$heha): 0.500 mM, aluminum(III) ion: 0.500 mM.

buffer regions of the PEPA and HEHA systems using Eq. 21. In both systems plots of $[(\alpha - 34C_L/14)(\alpha_H)_L - \beta_H C_L][(n - 34/14) - \beta_H/(\alpha_H)_L]^{1/14}/[H^+]^{34/14}$ against $(nC_L - \alpha)^{15/14}$ only gave straight lines passing through the point of origin. A typical straight line obtained for the HEHA system is reproduced in Fig. 5. If the composition of polynuclear hydroxoaluminum(III) complex is given by $[Al_{13}(OH)_{32}]^{7+}$, as suggested by Aveston,[6] plots of $[(\alpha - 32C_L/13)(\alpha_H)_L - \beta_H C_L][(n - 32/13) - \beta_H/(\alpha_H)_L]^{1/13}/[H^+]^{32/13}$ against $(nC_L - \alpha)^{14/13}$ should give a straight line passing through the point of origin. The experimental data, however, did not obey this relation. As shown in Fig. 6, although plots (with confidence limits) of $[(\alpha - 32C_L/13)(\alpha_H)_L - \beta_H C_L][(6 - 32/13) - \beta_H/(\alpha_H)_L]^{1/13}[H^+]^{-32/13}$ against $(6C_L - \alpha)^{14/13}$ also gave a straight line, it does not pass through the point of origin. It is thus reasonable to consider that the polynuclear hydroxoaluminum(III) com-

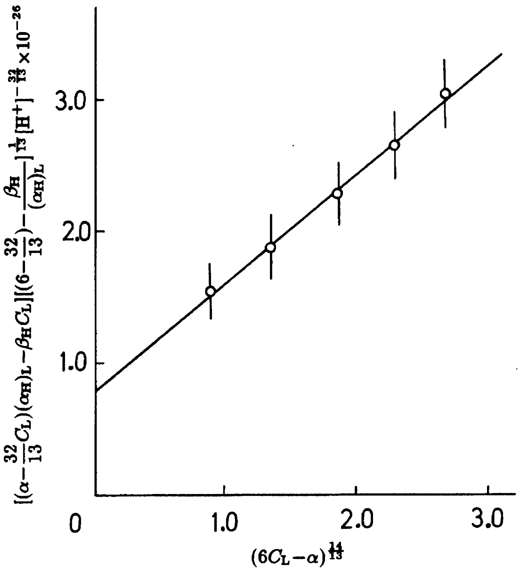

Fig. 6. Plots (with confidence limits) of $[(\alpha-32C_L/13)(\alpha_H)_L-\beta_H C_L][6-32/13-\beta_H/(\alpha_H)_L]^{1/13}\times[H^+]^{-32/13}$ against $(6C_L-\alpha)^{14/13}$. I=0.20, 25 °C. HEHA ([18]ane$N_6(CH_2COOH)_6$) system.

plex formed under the present experimental conditions is a tetradecamer, $[Al_{14}(OH)_{34}]^{8+}$. The K_{AlL} values for the PEPA and HAHA systems were determined based on the gradients of the linear relation between $[(\alpha-34C_L/14)(\alpha_H)_L-\beta_H C_L][(n-34/14)-\beta_H/(\alpha_H)_L]^{1/14}/[H^+]^{34/14}$ and $(nC_L-\alpha)^{15/14}$, and are summarized in Table 1, together with those for the DOTA and TETA systems along with those for the corresponding alkaline earth metal(II) and lanthanide(III) complexes.

Although monomeric aluminum complexes with coordination numbers of six and four are much more numerous, only a few complexes with a coordination number of five have been reported.[12)] In fact, in an aqueous solution the aquaaluminum(III) ion exists as the octahedral hexahydrate, $[Al(OH_2)_6]^{3+}$, and the hydroxo complex as tetrahedral $[Al(OH)_4]^-$.[13)] In general, the metal ion in macrocycle complexes is not located in the cavity of the macrocyclic polyamine when it is too large or too small to fit "exactly" in the cavity hole. However, in metal complexes of cyclic polyamines carrying an acetate group on each nitrogen atom, the metal ion is not incorporated into the macrocyclic ring, but prefers to remain outside of the ring cavity of the polyamine frame, even when its size is compatible with the polyamine ring cavity.[14)]

Table 1. Logarithmic Formation Constants I=0.20, 25 °C

Metal ion	log K_{ML}			
	DOTA	TETA	PEPA	HEHA
Mg(II)	11.03[1)]	3.02[1)]	$5.0_3\pm0.2_0$[a)]	—
Ca(II)	15.85[1)]	9.48[1)]	$8.7_7\pm0.2_0$[a)]	—
Sr(II)	12.86[1)]	6.15[1)]	$9.1_7\pm0.2_0$[a)]	—
Eu(III)	28.2[16)]	14.66[4)]	15.59[4)]	22.68[4)]
Tb(III)	28.6[16)]	14.81[4)]	15.91[4)]	23.15[4)]
Lu(III)	29.2[16)]	15.31[4)]	16.71[4)]	24.26[4)]
Al(III)	17.0±0.4	16.3±0.3	$16.1_0\pm0.2_0$	$22.0_9\pm0.2_0$

a) M. Kodama, unpublished data.

A stronger interaction of the aluminum(III) ion with a nitrogen donor site, as compared with a charged acetate group, seems unlikely, because the aluminum(III) ion is small and is typically a hard Lewis acid. As is clear from the foregoing discussion, it is reasonable to believe that the polyaza rings of the ligands studied simply act as frames to constrain the carboxylate groups into a nearly spherical arrangement; hence, dota^{4-}, teta^{4-}, pepa^{5-}, and heha^{6-} anions probably act as tetra$^-$, penta$^-$, and hexa-dentate ligands, respectively, wrapping themselves around the aluminum(III) ion, though these tetraamine, pentaamine and hexaamine ligands have eight, ten and twelve potential donor groups. The K_{AlL} values given in Table 1 show that the aluminum(III)–HEHA complex is 10^5—10^6 times more thermodynamically stable than those of tetraamine and pentaamine ligands. This can be explained well by assuming that the aluminum(III) ion forms a six-coordinate complex in reactions with these polyamino polycarboxylic macrocycles, and is bonded to their acetate groups. Because of its less-restricted flexibility of the cyclic ring, the polyaza ring of heha^{6-} does not prevent its six acetate groups to take favorable positions to interact with the aluminum(III) ion. Thus, all six acetate groups of the heha^{6-} anion may be available for use in bond formation with the aluminum(III) ion. The K_{AlL} value for the aluminum(III)–HEHA complex was determined at 25, 30, and 35 °C to obtain the thermodynamic parameters, ΔH and ΔS. The log K_{AlL} values found at 25, 30, and 35 °C were 22.0_9, 22.0_6, and 22.0_3, respectively. By using these log K_{AlL} values the ΔH value could be successfully determined from the linear relation between log K_{AlL} and the reciprocal temperature to be -11.7 ± 0.8 kJ mol^{-1}. Then, the ΔS value was estimated from the thus-determined ΔH value to be 383.3 ± 5.9 J K^{-1} mol^{-1} by employing the relation $\Delta S = 2.303R(\log K_{\mathrm{AlL}}+\Delta H/2.303RT)$. The net heat of metal complexation in an aqueous solution can be equated to the heats of the metal-donor group bonds minus the heats of the metal–water and the donor group–water bonds that must be broken. Furthermore, the release of water molecules from the metal ion and the donor groups yields a positive entropy of metal–donor bond formation, because the number of independent particles increases to an extent which can outweigh a simultaneous loss of configurational entropy and a consequent loss in the degree of freedom of the ligand itself in its complexation. Thus, the above-mentioned evidence that the formation reaction for the aluminum(III)–HEHA complex gives only a small negative enthalpy, but a large positive entropy, might lend strong support to our explanation. The small macrocyclic ligand, dota^{4-} anion, has a more rigidly constructed structure and adopts nearly the same conformation as that in a metal complex. Thus, as compared with the large flexible macrocycle system, little conformational freedom would be lost in its complexation reaction, producing a more favorable entropy effect.[15,16] This well explains why the dota^{4-} anion gave a more stable complex than did the pepa^{5-} anion, regardless of the fact that the dota^{4-} anion has a smaller number of acetate groups available for bond formation with the aluminum(III) ion than the pepa^{5-} anion. A similar trend in the magnitude of the K_{AlL} value also occurs in alkaline earth metal(II) and lanthanide(III) complexes.[4,16]

References

1) H. Stetter and W. Frank, *Angew. Chem.*, *Int. Ed. Engl.*, **15**, 686 (1976).

2) R. Delgado and J. T. R. F. Silva, *Talanta*, **29**, 815 (1982).

3) J. F. Desreux, *Inorg. Chem.*, **19**, 1319 (1980).

4) M. Kodama, T. Koike, A. B. Mahatma, and E. Kimura, *Inorg. Chem.*, **30**, 1270 (1991).

5) E. Kimura, H. Fujioka, A. Yatsunami, H. Nihira, and M. Kodama, *Chem. Pharm. Bull.*, **33**, 655 (1985).

6) J. Aveston, *J. Chem. Soc.*, **1965**, 4438.

7) M. Kodama, E. Kimura, and S. Yamaguchi, *J. Chem. Soc.*, *Dalton Trans.*, **1980**, 2536.

8) M. Kodama, H. Anan, T. Koike, and E. Kimura, *Bull. Chem. Soc. Jpn.*, **62**, 4044 (1989).

9) J. N. Butler, "Ionic Equilibrium," Addison-Wesley, Reading, Massachusetts (1964), p. 437.

10) H. Sigel (with A. Sigel), "Metal-Ions in Biological Systems," Marcel Dekker, Inc., New York (1988), Vol. 24, p. 64, and references therein.

11) R. E. Mesmer and C. F. Baes, Jr., *Inorg. Chem.*, **10**, 2290 (1971).

12) M. Dalibart and J. Derouault, *Coord. Chem. Rev.*, **74**, 1 (1986).

13) R. B. Martin, *Clin. Chem.* (*Winston-Salem, N C*), **32**, 1797 (1986).

14) H. Hofliger and T. A. Kaden, *Helv. Chim. Acta*, **62**, 683 (1979).

15) M. Kodama and E. Kimura, *J. Chem. Soc.*, *Dalton Trans.*, **1978**, 1081.

16) M. F. Loncin, J. F. Desreux, and E. Merciny, *Inorg. Chem.*, **25**, 2646 (1986).