2990 © 1994 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 67, 2990—2993(1994) [Vol. 67, No. 11

Thermodynamic Study of Formation Reactions of Mercury(II) Complexes with Polyamino Polycarboxylic Macrocycles

Mutsuo Kodama
Department of Chemistry, College of General Education, Hirosaki University, Bunkyo, Hirosaki 036

(Received May 20, 1994)

We have investigated the equilibria of complex formation reactions of mercury(II) ions with polyamino polycarboxylic macrocycles: DOTA (H_4dota, H_4L), TETA (H_4teta, H_4L), PEPA (H_5pepa, H_5L), and HEHA (H_6heha, H_6L) by employing a polarographic method. Under the experimental conditions employed, tetra-, penta-, and hexa-amine macrocycles: TETA, PEPA, and HEHA, were found to form 1 : 1 ratio protonated complexes as well as normal complexes, while the other tetra-amine macrocycle, DOTA, forms solely a 1 : 1 ratio normal complex, HgL^{2-}. Measurement of thermodynamic parameters, ΔH and ΔS, showed that the introduction of acetate groups into the polyaza frame gives rise to a greater increase in the entropy of reaction, but produces a less exothermic effect.

In our current efforts in searching for new chelating agents, we have synthesized the macrocyclic polyamines carrying an acetic acid moiety on each nitrogen atom, and studied their complexation reactions with lanthanide[1,2] and their clinical applications.[3] As a continuation of our investigation concerning the ligating properties of the macrocyclic polyamines carrying an acetic acid group ($-CH_2COOH$) on each nitrogen donor (polyamino polycarboxylic macrocycles), I am now studying the complexation behavior of DOTA (H_4dota, H_4L), TETA (H_4teta, H_4L), PEPA (H_5pepa, H_5L), and HEHA (H_6heha, H_6L) (Fig. 1) towards mercury (II) ions by employing a polarographic method, and will compare with that of the skelton cyclic polyamine ligand. The study will provide much information on the effects of acetate moiety introduction on the complexation of macrocyclic polyamines with metal(II) ions.

Experimental

All the macrocyclic polyamines and their derivatives carrying acetic acid groups as their HCl salts were prepared according to the methods described in the literature.[1,3—9]

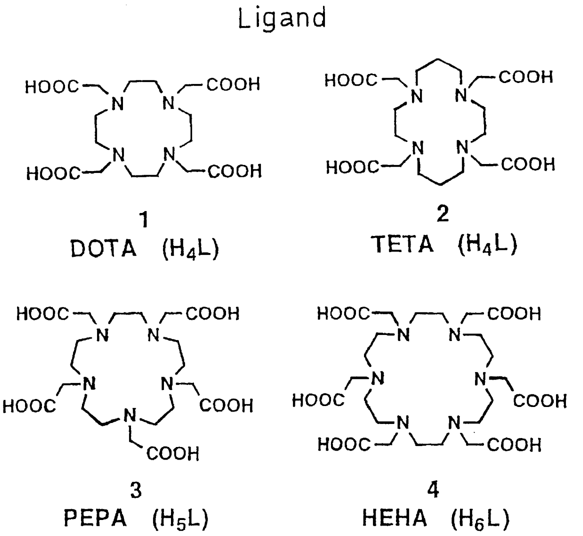

Fig. 1. Polyamino polycarboxylic macrocycles used in the present investigation.

The polarographic apparatus and experimental procedures used are the same as those applied to the mercury (II)–dioxopolyamine complex formation.[10]

The test solution temperature was kept constant within 0.1 °C, and ionic strength (I) was adjusted to 0.20 with $NaNO_3$. In the present study monochloroacetate ($2.9<pH<3.9$), acetate ($3.9<pH<5.8$), phosphate ($6.0<pH<7.9$), tris. ($7.0<pH<9.0$), and borate ($8.2<pH<10.3$) buffers were used to maintain the test solution pH constant. They manifested practically no effect on the half-wave potential of the anodic dissolution waves. All other chemicals used were of analytical reagent grade.

Results and Discussion

All the polyamino polycarboxylic macrocycles gave well defined anodic waves at the dropping mercury electrode (DME). Their limiting currents, i_l, were proportional to the bulk concentration of ligands and also to the square root of the effective pressure on the dropping mercury electrode. Furthermore, plots of $\log[i/(i_l-i)]$ against the DC potential, E, invariably gave straight lines with reciprocal slopes falling in the range of -29 to -32 mV over the entire pH range covered, showing a reversible two-electron oxidation at the DME. Here, i is the anodic current at DC potential E. The reversible nature of the electrode process was also confirmed by the AC polarographic method.[11]

As was mentioned by Reilley et al.,[12] the ethylenediamine-N,N,N', N'-tetraacetic acid, EDTA (H_4edta, H_4L'), also gives a single well-defined anodic wave at DME, with the half-wave potential $(E_{1/2})_{L'}$, expressed by Eq. 3 in Ref. 5, which was derived on the reasonable assumption that the diffusion coefficients of Hg(II)–EDTA complex and of various forms of protonated $edta^{4-}$ are equal to one another. The half-wave potential, $(E_{1/2})_L$, for PEPA shifted to more negative values on increasing the solution pH. At pH's higher than 8.00 the A value calculated with the aid of the following relation (Eq. 1) was almost constant (Fig. 2). Here, $(\alpha_H)_L$, is the (α_H) value of EDTA system,[5] and

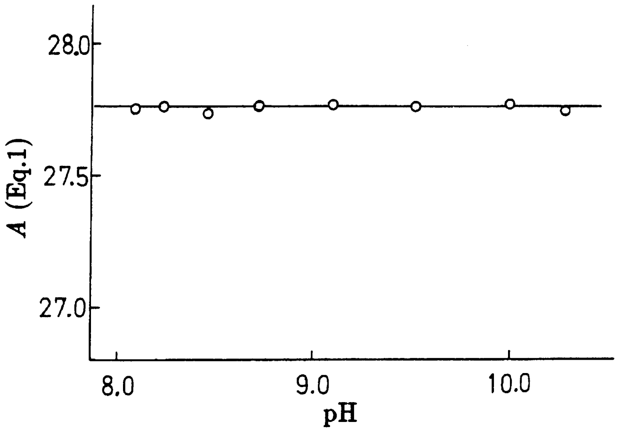

Fig. 2. Plots of A (Eq. 1) against pH. [15]-ane$N_5(CH_2COOH)_5$: 0.40 mM, borate: 0.030 M, $I=0.20$, 25 °C, 1 M=1 mol dm^{-3}.

$(\alpha_H)_L$, the (α_H) value of PEPA defined as $1+K_1[H^+]+K_1K_2[H^+]^2\cdots+K_1K_2K_3K_4K_5[H^+]^5$. K_i is the i-th protonation constant of quinquevalent PEPA anion, [15]-aneN_5 $(-CH_2COO)_5^{5-}$ (L^{5-}). At the pH region from 4.00 to 6.00, plots of antilog A against the hydrogen ion concentration, $[H^+]$, gave a straight line with an intercept of finite value (Fig. 3). At pH's lower than 4.00 the plots of antilog $A/[H^+]$ against $[H^+]$, then, gave a straight line with an intercept of finite value (Fig. 4). All of the above findings are evidently consistent with the following theoretical equation derived for the reversible two-electron oxidation at DME, corresponding to the electrode reaction (3).

$$A = \frac{(E_{1/2})_{L'} - (E_{1/2})_L}{0.0296} + \log K_{HgL'} + \log(\alpha_H)_L - \log(\alpha_H)_{L'} \qquad (1)$$

$$(E_{1/2})_L = \varepsilon^{\circ}_{Hg} + 0.0296 \log f_{Hg^{2+}} - 0.0296 \log K_{HgL} \times (1+K_1^H[H^+]+K_1^HK_2^H[H^+]^2+\cdots)/(\alpha_H)_L \qquad (2)$$

$$Hg + H_jL^{j-5} \rightleftharpoons \begin{cases} HgL^{3-} + jH^+ + 2e^- \\ HgHL^{2-} + (j-1)H^+ + 2e^- \\ HgH_2L^- + (j-2)H^+ + 2e^- \end{cases} \qquad (3)$$

Here, K_{HgL} is the formation constant of Hg(II)–PEPA complex, HgL^{3-}, K_j^H, the j-th protonation constant of HgL^{3-}; the definitions of other symbols used in Eq. 2 were given in the previous paper.[5] Hence, the half-wave potential difference between EDTA and PEPA system, $\Delta E_{1/2}$, is given by the relation (4). The $(E_{1/2})_{L'}$ value used was determined at pH=5.75, where the mercury (II) ion forms solely a normal complex, $HgL'^{\,2-}$, with edta^{4-} anion,

$$\begin{aligned}\Delta E_{1/2} &= (E_{1/2})'_L - (E_{1/2})_L \\ &= 0.0296[\log K_{HgL}(1+K_1^H[H^+]+K_1^HK_2^H[H^+]^2+\cdots) \\ &\quad -\log K_{HgL'} + \log(\alpha_H)_{L'}/(\alpha_H)_L] \qquad (4)\end{aligned}$$

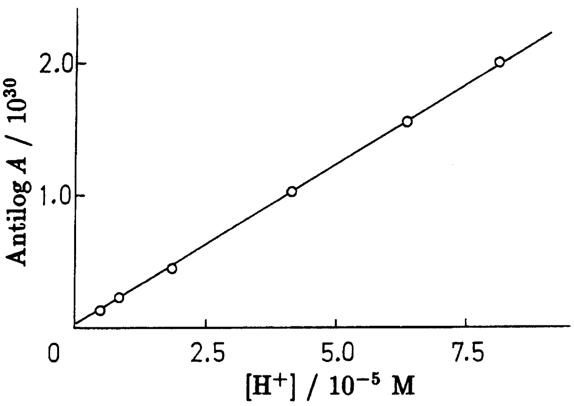

Fig. 3. Plots of antilog A (Eq. 5) against the hydrogen ion concentration, $[H^+]$. 6.00>pH>4.00.

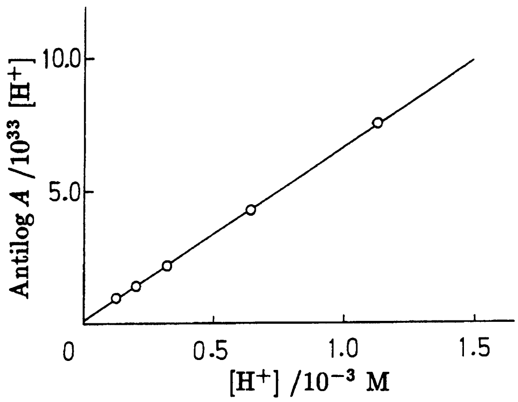

Fig. 4. Plots of antilog $A/[H^+]$ (Eq. 6) against $[H^+]$. 3.90>pH>2.90.

One can easily rearrange Eq. 4 to Eq. 5.

$$\begin{aligned}&K_{HgL}(1+K_1^H[H^+]+K_1^HK_2^H[H^+]^2+\cdots) = \\ &\quad \text{Antilog}\left[\frac{\Delta E_{1/2}}{0.0296} + \log K_{HgL'} + \log(\alpha_H)_L - \log(\alpha_H)_{L'}\right] \\ &\quad (= \text{Antilog}\,A) \qquad (5)\end{aligned}$$

When the Hg (II)–PEPA complex exists solely as HgL^{3-}, in other words, at pH's higher than 8.00, the antilog A value can be equated to K_{HgL}. When the monoprotonated complex, $HgHL^{2-}$, as well as HgL^{3-} is formed, i.e. at the pH range from 4.00 to 6.00, the left-hand side of Eq. 5 is simplified to $K_{HgL}+K_{HgL}K_1^H[H^+]$. Furthermore, when the equilibrium concentration of HgL^{3-} is negligible as compare with those of $HgHL^{2-}$ and HgH_2L^-, that is, at pH's lower than 4.00, the Eq. 5 can be rewritten as:

$$K_{HgL}K_1^H + K_{HgL}K_1^HK_2^H[H^+] = \frac{\text{Antilog}\,A}{[H^+]} \qquad (6)$$

As is clear from the foregoing discussion, we can evaluate the K_{HgL} value for the Hg(II)–PEPA complex from the antilog A value in Fig. 2. Next, we determined the $K_{HgL}K_1^H$ value from the slope of the straight line in Fig. 3. The intercept of the straight line in Fig. 3 showed a fairly good agreement with the antilog A value

Table 1. Logarithmic Equilibrium Constants (I=0.20, 25 °C)

Ligand	$\log K_{\mathrm{HgL}}$	$\log K_1^{\mathrm{H}}$	$\log K_2^{\mathrm{H}}$	$\log K_3^{\mathrm{H}}$
[12]aneN$_4$[4]	25.5	—	—	—
[12]aneN$_4$(CH$_2$COO)$_4^{4-}$	$26.4_1 \pm 0.2_0$	—	—	—
[14]aneN$_4$[4]	23.0	—	—	—
[14]aneN$_4$(CH$_2$COO)$_4^{4-}$	$25.7_1 \pm 0.2_0$	$4.6_4 \pm 0.2_1$	—	—
[15]aneN$_5$[4]	28.5	6.0_2	—	—
[15]aneN$_5$(CH$_2$COO)$_5^{5-}$	$27.7_6 \pm 0.2_2$	$6.6_3 \pm 0.2_2$	$5.4_4 \pm 0.3_3$	—
[18]aneN$_6$	$29.1_0 \pm 0.2_4$	$7.8_5 \pm 0.2_4$	$5.8_5 \pm 0.3_5$	—
[18]aneN$_6$(CH$_2$COO)$_6^{6-}$	$25.2_7 \pm 0.2_0$	$8.0_5 \pm 0.2_4$	$6.5_3 \pm 0.3_3$	$5.2_9 \pm 0.4_4$

in Fig. 2. The $K_{\mathrm{HgL}}K_1^{\mathrm{H}}K_2^{\mathrm{H}}$ value was then determined from the slope of the straight line given in Fig. 4. Of course, its intercept agreed well with the slope of the straight line in Fig. 3.

In an identical manner to that applied to the Hg(II)–PEPA complex, we analyzed the complex formation reactions of mercury(II) ions with [12]aneN$_4$(CH$_2$COO)$_4^{4-}$ (DOTA anion), [14]aneN$_4$(CH$_2$COO)$_4^{4-}$ (TETA anion), and [18]aneN$_6$(CH$_2$COO)$_6^{6-}$ (HEHA anion), and determined the equilibrium constant graphically. All the equilibrium constants thus determined were listed in Table 1, together with those of the corresponding cyclic polyamine complexes. The linear plots of $\log K_{\mathrm{HgL}}$ for all the polyamino polycarboxylic macrocycles against the reciprocal of temperature permit us to estimate the thermodynamic parameters, ΔH and ΔS, for the 1 : 1 ratio normal complexes (Fig. 5). Results obtained are also summarized in Table 2, together with those for the corresponding polyamine system.

When charged and highly hydrated acetate groups partake in the metal bonding, they generally release more molecules of water upon chelation than do the noncharged amino groups. Furthermore, in smaller macrocycles which might have more rigidly constructed structure than the larger macrocycles, less conformational freedom would be lost in their complexation reactions. These processes would account for very important portions of the larger entropy of reaction in a smaller macrocycle ligand. However, in a smaller macrocycle, because of its rigid structure, the Hg(II)–N donor bond formation may create a severe strain and thus will give a less favorable ΔH value. On the other hand, in the larger macrocycles, with increasing the size of macrocyclic ring more conformational freedom would be lost in its complex formation reaction. However, the expansion of the macrocyclic ring makes the easy access of nitrogen donor atoms to the larger Hg(II) ion possible, and hence a stronger Hg(II)–donor bond is formed, producing a favorable exothermic heat of reaction.

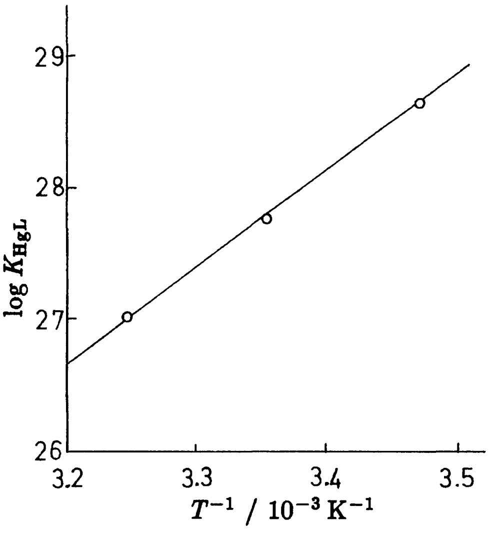

Fig. 5. van't Hoff plots of stability constant for Hg(II)–[15]aneN$_5$(CH$_2$COO)$_5^{5-}$ complex.

In the complexes of polyamino polycarboxylic macrocycles, irrespective of their cavity size, metal ions are not incorporated into the macrocyclic ring, but prefer to remain outside of the cavity.[13] Therefore, it is very natural to consider that in the smaller macrocycle system which has fewer nitrogen donors available for the bond formation, more acetate groups might be used in forming the Hg(II) chelates, producing a more favorable entropy effect. In the larger macrocycles having more nitrogen donors, on the other hand, only a few Hg(II)–O bondings are formed, and hence, the major part of all acetate groups remain unbound, giving a less favorable entropy effect.

The large protonation constants in Table 1 support the tentative conclusion that in the protonated complex the nitrogen donor is preferably protonated, rather than the carboxylate group.

From the foregoing discussion and the fact that the larger macrocycle has a greater number of nitrogen donors available for the bond formation with Hg(II) ion and the heat of formation of Hg(II)–N bond is more exothermic than that of Hg(II)–O bond,[14] one can easily understand why the formation reactions of larger macrocycle chelates are more exothermic than those of smaller macrocycle chelates, but can produce only a small positive entropy or vice versa (Table 2).

Of course, a chelating agent which produces a large exothermic heat of reaction as well as a large positive entropy of reaction can form a thermodynamically stable chelate. But the chelating agent which produces an exothermic reaction may very often tend

Table 2. Thermodynamic Parameters for Hg(II) Complexes

Ligand	$\log K_{\mathrm{HgL}}$	$-\Delta H/\mathrm{kJ\ mol^{-1}}$	$\Delta S/\mathrm{J\,K^{-1}\,mol^{-1}}$
$[12]\mathrm{aneN}_4^{4)}$	25.5	98.7	159
$[12]\mathrm{aneN_4(CH_2COO)_4^{4-}}$	$26.4_1 \pm 0.2_0$	85.8 ± 1.3	218 ± 13
$[14]\mathrm{aneN}_4^{4)}$	23.0	138	-21
$[14]\mathrm{aneN_4(CH_2COO)_4^{4-}}$	$25.7_1 \pm 0.2_0$	$123._4 \pm 1._3$	79 ± 8
$[15]\mathrm{aneN_5}$	28.5	$147._3 \pm 1._3$	51 ± 8
		$(137)^{4)}$	$(84)^{4)}$
$[15]\mathrm{aneN_5(CH_2COO)_5^{5-}}$	$27.7_6 \pm 0.2_2$	$128._4 \pm 1._3$	101 ± 8
$[18]\mathrm{aneN_6}$	$29.1_0 \pm 0.2_4$	$156._1 \pm 1._3$	34 ± 6
$[18]\mathrm{aneN_6(CH_2COO)_6^{6-}}$	$25.2_7 \pm 0.2_0$	$121._3 \pm 1._3$	77 ± 8

to lower the entropy of reaction or vice versa. Hence, the most stable metal chelate probably will result from a compromise between ΔH and ΔS values. Thus, $[15]\mathrm{aneN_5(CH_2COO)_5^{5-}}$ (*pepa*$^{5-}$ anion) forms the most thermodynamically stable Hg(II) complex among the polyamino polycarboxylic macrocycles studied in this report. In the $[12]\mathrm{aneN_4(CH_2COO)_4^{4-}}$ system the stabilization by the large ΔS term is to some extent offset by the less favorable heat of reaction, suggesting that the small size macrocycle can accommodate the larger metal ion such as Hg(II) ion only with a large strain. But, by virtue of the large entropy effect, the introduction of acetate groups can enhance certainly the affinity of 12-membered tetraaze cyclic moiety towards the Hg(II) ion. Although the introduction of acetate groups into the skelton 18-membered hexa-amine frame also produces a favorable entropy effect, this effect is counterbalanced by the smaller exothermic effect as compared with the skelton macrocyclic hexaamine. Thus, in the case of $[18]\mathrm{aneN_6}$ system the introduction of acetate groups into the polyamine frame rather lowers the thermodynamic stability of the Hg(II) complex. A similar explanation can be offered for the $[15]\mathrm{aneN_5}$ system.

The 14-membered tetraamine (cyclam, $[14]\mathrm{aneN_4}$) ligands may be exceptional in that they always show a smaller entropy gain as compared with the 12-membered tetra-amine and 15-membered penta-amine systems. At present, I can not offer a satisfactory, explanation for this. A free cyclam is considered to have a stronger tendency to adapt square planar configuration and less solvated.[15] This may be the main reason why they show smaller entropy gains in the complex formation reaction. Although the results were not shown in this report, the K_{ML} values of Zn(II), Cd(II), and Pb(II) complexes also exhibit a similar trend and experience a certain metal(II) ion size effect.

The present author expresses his deep gratitude to Professor. E. Kimura, Hiroshima University, School of Medicine, for the kind donation of pure macrocyclic ligands.

References

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

2) M. Kodama, A. B. Mahatma, T. Koike, and E. Kimura, *Bull. Chem. Soc. Jpn.*, **63**, 2639 (1990).

3) E. Kimura, H. Fujioka, A. Yatsunami, H. Nihira, and M. Kodama, *Chem. Pharm. Bull.*, **32**, 625 (1985).

4) M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, **1978**, 104.

5) M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, **1976**, 2335.

6) M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, **1980**, 2356.

7) E. Kimura, T. Koike, M. Yamaoka, and M. Kodama, *J. Chem. Soc., Chem. Commun.*, **1985**, 1341.

8) L. Y. Martin, L. J. Dehayes, L. J. Zompa, and D. H. Bush, *J. Am. Chem. Soc.*, **96**, 4046 (1974).

9) J. E. Richman and T. J. Atkins, *J. Am. Chem. Soc.*, **96**, 2269 (1974).

10) M. Kodama and E. Kimura, *Bull. Chem. Soc. Jpn.*, **62**, 3093 (1989).

11) M. Senda, M, Senda, and I. Tachi, *J. Electrochem. Soc. Jpn.*, **27**, 83 (1959).

12) C. N. Reilley, W. G. Scribner, and C. Temple, *Anal. Chem.*, **28**, 450 (1956).

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

14) J. A. Partridge, J. J. Christensen, and R. M. Izatt, *J. Am. Chem. Soc.*, **88**, 1649 (1966).

15) F. P. Hinz and D. W. Margerum, *Inorg. Chem.*, **13**, 2941 (1974).