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## Stability Constants of Divalent Transition and Trivalent Lanthanide Metal Ion Complexes of Macrocyclic Triazatri(Methylacetic Acid)

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The azacrown compound, 1,7-dioxa-4,10,13-triazacyclopentadecane-*N,N',N''*-tri(methyl-acetic acid)( $N_3O_2$ -tri(methylacetic acid)) was synthesized by modified procedure of Krespan. Potentiometric method has been used to determine the protonation constants of  $N_3O_2$ -tri(methylacetic acid) and stability constants of complexes on the divalent transition metal ions ( $Co^{2+}$ ,  $Ni^{2+}$ ,  $Cu^{2+}$ , and  $Zn^{2+}$ ) and trivalent metal ions ( $Ce^{3+}$ ,  $Eu^{3+}$ ,  $Gd^{3+}$ , and  $Yb^{3+}$ ) with  $N_3O_2$ -tri(methylacetic acid). The stability constants for the complexes of the divalent transition metal ions studied in the present work with  $N_3O_2$ -tri(methylacetic acid) were 11.4 for  $Co^{2+}$ , 11.63 for  $Ni^{2+}$ , 13.51 for  $Cu^{2+}$ , and 11.65 for  $Zn^{2+}$ , respectively. Thus, the order of the stability constants for complexes on the transition metal ions with  $N_3O_2$ -tri(methylacetic acid) was shown  $Co^{2+} < Ni^{2+} < Cu^{2+} > Zn^{2+}$  as same as the order of Irving-Williams series. The stability constants of  $Ce^{3+}$ ,  $Eu^{3+}$ ,  $Gd^{3+}$ , and  $Yb^{3+}$  trivalent lanthanide metal ion complexes of  $N_3O_2$ -tri(methylacetic acid) were, respectively, 11.26 for  $Ce^{3+}$ , 11.56 for  $Eu^{3+}$ , 11.49 for  $Gd^{3+}$ , and 11.80 for  $Yb^{3+}$ . The values of the stability constants on trivalent metal ions with the ligand are increasing according to increase atomic number, due to increase acidity. But the value of stability constant of  $Gd^{3+}$  ion is less than the value of  $Eu^{3+}$  ion. This disordered behavior is also reported by Moeller.

### Introduction

There have been considerable interest in the synthesis of macrocyclic ligands which show high selectivity for a particular metal ion in the complex formation, since such ligands can be used in the fields of biochemistry, hydrometallurgy, and waste treatment.<sup>1-5</sup> The stability constants of the metal ions with macrocyclic ligands were determined by various methods.<sup>6-9</sup>

Delgado *et al.*<sup>10</sup> determined the stability constants of comp-

lexes of some divalent and trivalent metal ions with a series of macrocyclic ligands having acetate groups as N-pendant arms. These series of ligands provide an opportunity to study the influence of size of the macrocyclic ring and the increasing number of donor atoms on the stability and selectivity of metal complexes. The metal ions studied include the divalent metal ions, such as  $Co^{2+}$ ,  $Ni^{2+}$ ,  $Cu^{2+}$ ,  $Zn^{2+}$ ,  $Ca^{2+}$ ,  $Pb^{2+}$ , and trivalent metal ions, such as  $Al^{3+}$ ,  $Ga^{3+}$ ,  $Fe^{3+}$ ,  $In^{3+}$ , and  $Gd^{3+}$ . These series of ligands also provide an opportunity to compare the affinities of the metal ions studied here with those of the parent *N,N',N''*-triazacyclononane-triacetic acid (NOTA),  $N_3O$ -triacetic acid, and  $N_3O_2$ -triacetic acid, especially

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those reported by Clarke and Martell,<sup>11</sup> and by Hana and Takamoto,<sup>12a</sup> and by Krespan.<sup>12b</sup>

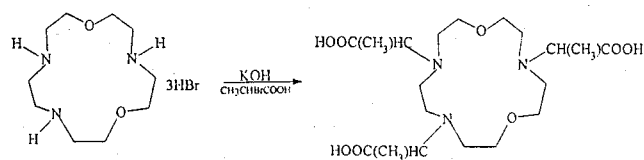
Of the ligands of N<sub>3</sub>O-triacetic acid, N<sub>3</sub>O<sub>2</sub>-triacetic acid, and N<sub>3</sub>O<sub>3</sub>-triacetic acid have been studied previously.<sup>9-11</sup> In this work, the protonation constants of the ligand, N<sub>3</sub>O<sub>2</sub>-tri(methylacetic acid), and the stability constants of complexes of some transition metal ions (Co<sup>2+</sup>, Ni<sup>2+</sup>, Cu<sup>2+</sup>, and Zn<sup>2+</sup>) and lanthanide metal ions (Ce<sup>3+</sup>, Eu<sup>3+</sup>, Ga<sup>3+</sup>, and Yb<sup>3+</sup>) with this macrocyclic ligand were determined.

## Materials and Methods

**Chemicals and Apparatus.** 2-Bromopropionic acid, toluenesulfonyl chloride, 2-(2-aminoethoxy) ethanol, 2-(2-chloroethoxy)ethanol, ethylenediamine, phosphorous tribromide, Dowex 1×8 ion exchange resin, and silica gel (200-400 mesh, 60 Å) were obtained from Aldrich Chemical Co. and were used as reagent without further purification. Dowex 1×8 resin was treated with 2 M KOH to convert it to the OH<sup>-</sup> form. 1,7-Dioxa-4,10,13-triazacyclopentadecane trihydrobromide was prepared by previously reported procedures.<sup>12-15</sup>

The proton NMR was recorded on a Varian T-60 spectrometer, and the chemical shifts are reported in ppm relative to tetramethylsilane. C, H, and N analyses were performed by using Perkin Elmer 240A.

**Synthesis of 1,7-Dioxa-4,10,13-Triazacyclopentadecane-N,N',N''-Tri(methylacetic acid).** The synthetic route is shown in Scheme 1. Ground KOH (87% pellets, 0.77 g (12 mmol) were added to suspension of 1.84 g (4 mmol) of 1,7-dioxa-4,10,13-triazacyclopentadecane trihydrobromide and 40 mL of absolute ethanol, and the mixture was stirred at room temperature for 1 h. The KBr was removed by filtration, and solvents were removed by vacuum distillation. The white residue obtained was dissolved in 20 mL of water. 2-Bromopropionic acid of 2.02 g (13.2 mmol) was dissolved in 20 mL of ice cold water (1-2 °C). A solution of 1.7 g of KOH (87%) in 20 mL of water was added dropwise to potassium 2-bromopropionate at 2-5 °C until pH of the solution became 12.0. 1,7-Dioxa-4,10,13-triazacyclopentadecane and Br(CH<sub>3</sub>)CHCOOK solutions were mixed and heated to 40-42 °C. The rest of the KOH aqueous solution described above was used to maintain the pH of the reaction solution at 11.5-12.0. The reaction solution was kept at 40-42 °C for 5 h, and then at room temperature for 16 h. It was neutralized to pH 9.0 with 6 M HCl, and then concentrated to 5-10 mL. The resulting solution was loaded on a Dowex 1×8 ion exchange resin in the OH<sup>-</sup> form in a column with 15 mm×300 mm. It was eluted successively with 200 mL of water, 200 mL of 0.01 M HCl, and 300 mL of 0.1 M HCl. The eluate with pH=3.0 contained the pure ligand. After elution with 100 mL of 0.2 M HCl, tri-HCl salt was



Scheme 1. Synthetic route of N<sub>3</sub>O<sub>2</sub>-tri(methylacetic acid).

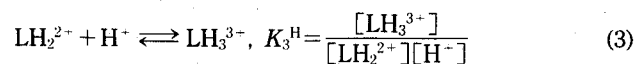
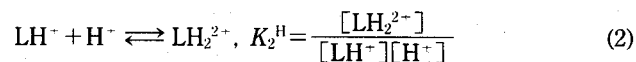
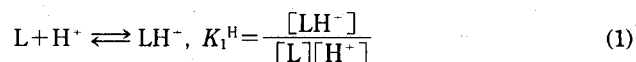
obtained; total yield 60%, <sup>1</sup>H NMR in D<sub>2</sub>O-NaOD, pD=13.2, 3.57 (t, 8H, -CH<sub>2</sub>-O-CH<sub>2</sub>-), 3.23 and 3.15 (two singlets, 6H, -CH<sub>2</sub>-COO-), 2.73 (two triplets, 8H, -O-CH<sub>2</sub>-CH<sub>2</sub>-N-), 2.64 (s, 4H, -N-CH<sub>2</sub>-CH<sub>2</sub>-N-), 2.41-2.7 (t, 9H, -CH<sub>3</sub>). Anal. calcd. for C<sub>9</sub>H<sub>35</sub>N<sub>3</sub>O<sub>3</sub>HCl: C, 42.04; H, 7.05; N, 7.74; Cl, 19.59. Found: C, 41.58; H, 7.25; N, 7.81.

**Other Reagents and Standard Solution.** Transition metal ion solutions were prepared at about 0.025 M from the analytical grade of chloride or perchlorate salts with demineralized water, and were standardized by titration with Na<sub>2</sub>H<sub>2</sub>EDTA (disodium salt of ethylenediamine tetraacetic acid).<sup>16</sup> Lanthanide metal ion (Ce<sup>3+</sup>, Eu<sup>3+</sup>, Gd<sup>3+</sup>, and Yb<sup>3+</sup>) solutions were prepared from the analytical grade of metal oxide with perchloric acid, and were standardized by titration with Na<sub>2</sub>H<sub>2</sub>EDTA. The stock solution of ligand, N<sub>3</sub>O<sub>2</sub>-tri(2-methylacetic acid) was prepared with demineralized water, and was standardized by complexometric titration with cupric perchlorate.<sup>16</sup>

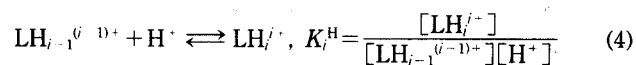
**Potentiometric Equipment and Measurements.** For the potentiometric titrations a Beckmann Model φ71 pH meter was used. The measurements of protonation constants of the ligand were made on 25 mL of the ligand solution (2.50×10<sup>-3</sup> M), and were made using standard 0.0491 M NaOH solution at an ionic strength adjusted to 0.10 M sodium perchloric acid in thermostated electrode at 25.0±0.1 °C. The value<sup>17</sup> of Kw=[H<sup>-</sup>][OH<sup>-</sup>] used in the computations was 10<sup>-13.80</sup>. The protonation constants (K<sub>i</sub><sup>H</sup>=[H<sub>i</sub>L]/[H<sub>i-1</sub>L][H]) were calculated by fitting the potentiometric data to the PKAS program.<sup>17</sup> The stability constants of metal ions with the ligand were determined 25 mL which in valued 0.025 M each metal ion and ligand, and was titrated standard 0.0491 M NaOH solution at an ionic strength adjusted to 0.10 M sodium perchloric acid. The stability constants of various species formed in the aqueous solution were obtained from the experimental data with the aid of the BEST program.<sup>17</sup> The initial computations were obtained in the form of over all stability constants (β) values: β=[M<sub>m</sub>L<sub>l</sub>H<sub>h</sub>]/[M]<sup>m</sup>[L]<sup>l</sup>[H]<sup>h</sup>. Differences between the various logβ's provide the stepwise formation and protonation reaction constants.

## Results and Discussion

**Protonation Constants.** In the present study, KCl is used as the ionic medium at 0.10 M ionic strength. The protonation of N<sub>3</sub>O<sub>2</sub>-tri(methylacetic acid) will be get same as the following protonation constants (K<sub>i</sub><sup>H</sup>=[H<sub>i</sub>L]/[H]<sup>i</sup>) were calculated by fitting



⋮



the potentometric data to the PKAS program. The values

**Table 1.** Protonation constants ( $\log K_i^H$ ) of  $N_3O_2$ -tri(methylacetic acid),  $N_3O$ -triacetic acid, and  $N_3O_2$ -triacetic acid in aqueous solutions

Equilibrium Quotient	Protonation Constant ( $\log K_i^H$ )		
	$N_3O$ -triacetic acid <sup>a</sup>	$N_3O_2$ -triacetic acid <sup>a</sup>	$N_3O_2$ -tri(methyl acetic acid)
	0.10 M KCl, 25 °C		0.10 M NaClO <sub>4</sub> , 25 °C
$[HL^+]/[L][H^+]$	11.24	9.55	8.10
$[H_2L_2^+]/[HL^+][H^+]$	7.76	8.92	7.48
$[H_3L^{3+}]/[H_2L^{2+}][H^+]$	4.00	4.51	4.97
$[H_4L^{4+}]/[H_3L^{3+}][H^+]$	2.59	1.59	4.70

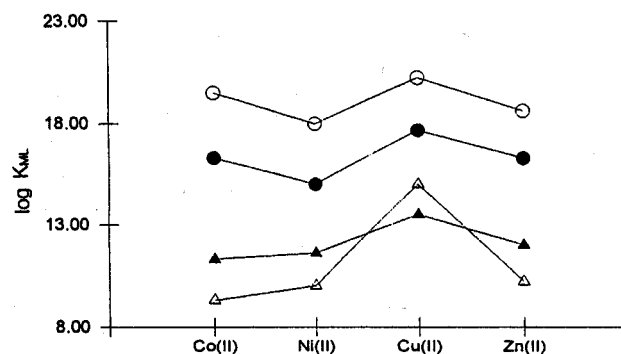
<sup>a</sup>Reference 10**Table 2.** Stability constants for metal complexes of macrocyclic ligand with several divalent transition metal ions

Cation	Quotient	Stability Constant ( $\log K_{ML}$ )			
		$N_3O$ triacetic acid [12] <sup>a</sup>	$N_3O_2$ triacetic acid [15] <sup>b</sup>	$N_3O_3$ triacetic acid [18] <sup>b</sup>	$N_3O_2$ tri(methylacetic acid) [15]
		0.10 M KCl 25 °C			0.10 M NaClO <sub>4</sub> 25 °C
Co <sup>2+</sup>	$[ML]/[M][L]$	19.54	16.38	9.33	11.40
Ni <sup>2+</sup>	$[ML]/[M][L]$	18.04	14.94	9.84	11.63
Cu <sup>2+</sup>	$[ML]/[M][L]$	20.17	17.54	14.88	13.51
Zn <sup>2+</sup>	$[ML]/[M][L]$	18.66	16.38	9.89	11.65

<sup>a</sup>Reference 18;  $\mu=0.10$  M (Me)<sub>4</sub>NNO<sub>3</sub>, <sup>b</sup>Reference 10

of the protonation constants obtained can be seen in the Table 1, together with the values determined in the previous work for  $N_3O$ -triacetic acid<sup>13</sup> and  $N_3O_2$ -triacetic acid.<sup>18</sup> Amorim *et al.*<sup>18</sup> reported that NMR spectroscopy titration has shown that the two higher values of the protonation constants correspond to the protonation of nitrogen atoms, but the third and fourth correspond to the protonation of the carboxylate groups for the  $N_3O$ -triacetic acid. Therefore, the protonation constants of two nitrogen atoms for  $N_3O_2$ -tri(methylacetic acid),  $\log K_1^H$  and  $\log K_2^H$  were determined each 8.10 and 7.48, and the protonation constants correspond to two carboxylate groups,  $\log K_3^H$ , and  $\log K_4^H$  were determined each 4.97 and 4.70. Table 1 shows that the stepwise protonation constants for  $N_3O$ -triacetic acid,  $N_3O_2$ -triacetic acid, and  $N_3O_2$ -tri(methylacetic acid) changing from ring size and the substituents. In the  $N_3O_2$ -tri(methylacetic acid) containing 15-membered ring the nitrogen atoms are separated by longer chains ( $-\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$ ), and the ring is less rigid because of large size of the macrocycle, compared with 12-membered  $N_3O$ -triacetic acid. All nitrogen atoms are protonated before the carboxylate groups, as the electrostatic repulsions between the positive charge on the nitrogen atoms are weaker than those of the 12-membered macrocycle. As usual the protonation of carboxylate groups linked to protonated nitrogen atoms corresponds to  $\log K$ 's of around 2 or less.

Compared with the protonation constants of  $N_3O_2$ -triacetic acid differ from those of  $N_3O_2$ -tri(methylacetic acid) obtained from the present experiment were different. In this case, the first and second constants correspond to protonation of the neighboring N atoms, therefore two N atoms of  $N_3O_2$ -

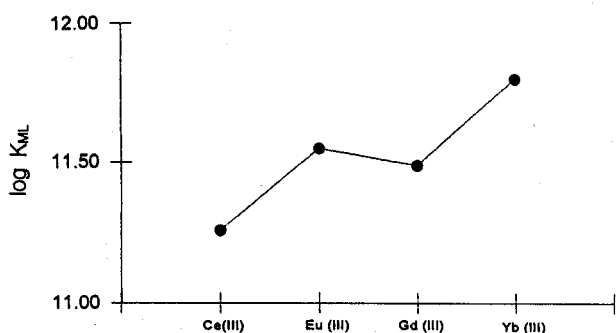
**Figure 1.** Variation of the stability constants,  $\log K_{ML}$  for metal complexes of macrocyclic ligands with divalent transition metal ions. ○;  $N_3O$ -triacetic acid, ●;  $N_3O_2$ -triacetic acid, △;  $N_3O_3$ -triacetic acid, ▲;  $N_3O_2$ -tri(methylacetic acid). The data taken from Table 2.

tri(methylacetic acid) effect on protonation steric hindrance of methyl groups. But the third constant can not be inferred from the potentiometric determinations only. The value of  $K_4^H$  corresponding to the protonation of the carboxylate group has more effect on methyl groups of  $N_3O_2$ -tri(methylacetic acid).

**Stability Constants of Divalent Transition Metal Ions.** In Table 2 and Figure 1 are shown the stability constants for the complexes of the divalent transition metal ions ( $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Zn}^{2+}$ ) studied in the present work with  $N_3O_2$ -tri(methylacetic acid). In Table 2, the published values for the same set of metal ions with ligands  $N_3O$ -tria-

**Table 3.** Stability constants for metal complexes of  $N_3O_2$ -tri(methylacetic acid) with several trivalent lanthanide metal ions ( $\mu = 0.10$  M  $NaClO_4$ ,  $t = 25$  °C)

Cation	Stability Constant ( $\log K_{ML}$ )
$Ce^{3+}$	11.26
$Eu^{3+}$	11.55
$Gd^{3+}$	11.49
$Yb^{3+}$	11.80

**Figure 2.** Variation of the stability constants,  $\log K_{ML}$  for metal complexes of  $N_3O_2$ -tri(methylacetic acid) with trivalent lanthanide metal ions.

cetic acid,  $N_3O_2$ -triacetic acid, and  $N_3O_3$ -triacetic acid are as so indicated comparison. The ligand will form several complex species, according to constant calculated by BEST program: all of them form ML, some form protonated and hydroxocomplex species. For all the ML complexes formed with divalent metal ions, the values of stability constants decrease with increase of ring size, in spite of the increase of the number of oxygen donor atoms and the increase of overall basicity.

The stability constants of  $N_3O_2$ -triacetic acid with transition metal ions are larger than those of  $N_3O_2$ -tri(methylacetic acid). They are on account of geometric configuration and the first protonation constant of ligand. Generally, the order of stability constants of transition metal ions with most of ligand was reported with  $Co^{2+} < Ni^{2+} < Cu^{2+} > Zn^{2+}$  by Irving-Williams. As shown in Figure 1, it was contrary to the stability order of Irving-Williams for  $N_3O_2$ -triacetic acid, but for  $N_3O_2$ -tri(methylacetic acid) agree with stability order.

**Stability Constants of Trivalent Lanthanide Metal Ions.** The stability constants of complexes formed by  $N_3O_2$ -tri(methylacetic acid) with  $Ce^{3+}$ ,  $Eu^{3+}$ ,  $Gd^{3+}$ , and  $Yb^{3+}$  have been determined, in 0.10 M  $NaClO_4$  ionic medium at 25 °C according to the BEST program.<sup>17</sup> The values obtained can be seen in Table 3 and Figure 2. The logarithm stability constant,  $\log K_{ML}$  of complexes forms by  $N_3O_2$ -tri(methylacetic acid) with  $Ce^{3+}$ ,  $Eu^{3+}$ ,  $Gd^{3+}$ , and  $Yb^{3+}$  have been determi-

ned with 11.26 for  $Ce^{3+}$ , 11.56 for  $Eu^{3+}$ , 11.69 for  $Gd^{3+}$ , and 11.80 for  $Yb^{3+}$ . The values of the stability constants on trivalent metal ions with the ligand are increasing according to increase atomic number, due to increase acidity and charge density of lanthanide. But the value of stability constant of  $Gd^{3+}$  ions is less than that of  $Eu^{3+}$  ion. This disorder behavior is also reported by Moeller.<sup>19</sup>

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