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TETRAHEDRON

Synthesis and Stabilities of the Ga(III) and In(III) Chelates of A New Diaminodithiol Bifunctional Ligand

Yizhen Sun[a], Arthur E. Martell[a,*], Ramunas J. Motekaitis[a] and Michael J. Welch[b]

[a] *Department of Chemistry, Texas A&M University, College Station, Texas 77842-3012*
[b] *The Edward Mallinckrodt Institute of Radiology, Washington University, School of Medicine, St. Louis, MO 63110, USA*

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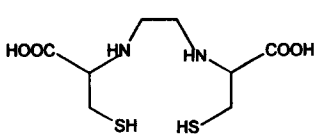
Abstract. The synthesis of a new bifunctional ligand 1-(4-carboxymethoxybenzyl)-N,N'-bis[(2-mercapto-2,2-dimethyl)ethyl]-1,2-ethylenediamine-N,N'-diacetic acid (B6SS) is described. It consists of substitution of a side-chain, a 4-carboxymethoxybenzyl group on a carbon atom of the ethylene-diamine moiety of a hexadentate ligand, 6SS, which has been found to have a very high affinity for In(III). Potentiometric determination of Ga(III) and In(III) chelate stabilities of the bifunctional ligand show that the side-chain on the ligand reduces the pM values about 2-4 log values.

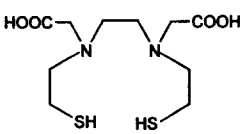
Keywords. Gallium(III) complexes, Indium(III)complexes, bifunctional ligand, diaminodithiol.

INTRODUCTION

There has been much interest in the use of bifunctional chelates for radiolabeling of proteins and antibodies with various radiometals and indium-111 is one of the most widely used radionuclides for this purpose. Numerous reports have been published about the design and synthesis of effective ligands for indium such as EDTA (pM = 22; pM is -log [In^{+3}] at pH = 7.4 with 100% excess of the ligand)[1] and DTPA (pM = 24.9).[1] In recent years, several ligands containing aminoethanethiol donor groups were found to possess strong affinity for In(III): EC (**1**) (pM = 28),[2] EDDASS (**2**) (pM = 30.4),[1] 6SS (**3**) (pM = 30.9)[3] and TACN-TM (**4**) (pM = 23.6).[4] Here we report the design and the synthesis of a derivative of 6SS, the ligand having the highest affinity for In(III), with a side chain of the type that might be used in a bifunctional ligand[5], 1-(4-carboxymethoxybenzyl)-N,N'-bis[(2-mercapto-2,2-dimethyl)ethyl]-1,2-ethylenediamine-N,N'-diacetic acid (B6SS, **5**).



EC, **1**



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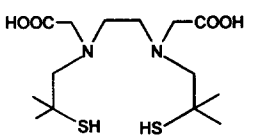
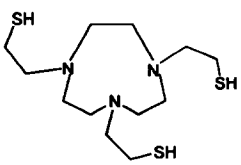
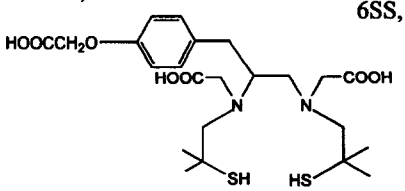


6SS, **3**



TACN-TM, **4**



B6SS, **5**

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PII: S0040-4020(98)00121-5

Since a covalent chain to be added to 6SS to produce B6SS could produce considerable steric strain as well as the possibility of additional metal coordination, the question of where to place it on the 6SS molecule was important. After consideration of several alternatives, on the basis of space-filling molecular models, it was decided that substitution on the carbon atom of the ethylenediamine moiety of the ligand would produce the least interference with the complex and therefore compound **5** was selected for synthesis and investigation. As a test of the effect of the side chain, the stabilities of the Ga(III) and In(III) chelates are determined and compared to those of 6SS (**3**).

RESULTS AND DISCUSSION

Synthetic Methods

The synthetic route for the preparation of B6SS is outlined in the Scheme. The synthetic method used for the preparation of compound **7** is similar to that of other tetramethyl-1,2-dithia-5,8-diazacyclodeca-4,8-dienes; here BSA was used for the temporary protection of the hydroxy group on the side chain. The three acetic acid groups were added as their *t*-butyl esters, since the tri-ester (compound **9**) was found to be easily purified by flash chromatography. In the last step there was considerable concern that the carboxymethoxy bond may also be attacked by Na/NH_3 (liq.). This undesirable side reaction was avoided through the modifications of controlled slight excess of Na metal and by the use of lower temperature and very short reaction time. With these precautions in place a reasonable yield was obtained.

Protonation Constants and Stability Constants

The protonation constants of B6SS are shown in Table 1. They were calculated from direct potentiometric p[H] measurements illustrated in Figure 1 since protonation reactions were observed to take place within the potentiometrically measurable pH range. The logarithms of the successive protonation constants were found to be 12.0, 11.7, 9.85, 3.89 and 2.9. In considering the nature of the donor groups involved in successive protonation reactions, it is helpful to compare them with the protonation constants of cysteine (10.29, 8.16 and 1.91)[7] , cystine (8.80 AND 8.03)[7], 6SS (11.11, 10.56, 8.99, 4.24, 2.7)[3] and 4-carboxymethoxytoluene (3.22).[7] The two higher values of the protonation constants of B6SS correspond to the mercapto groups; they are about 1 log unit higher than that of 6SS because of higher initial overall charge on the former ligand (L^{5-}) relative to the charge of the latter (L^{4-}). The fact that benzyl substituents tend to reduce the basicity of amino groups is reflected in the second amino protonation step (3.89 for B6SS *vs* 4.24 for 6SS). However the first amino protonation step is increased for B6SS over that of 6SS because of the difference in overall charge discussed above (9.85 for B6SS *vs* 8.99 for 6SS). While the fifth protonation step is obviously associated with one of the acetic acid groups in 6SS, it probably involves all three acetate groups present in B6SS. The intrinsic basicity of the carboxylate on the connecting arm of the bifunctional ligand is too close to the observed fifth protonation constant to make an exact judgment of the degree of formation of each microspecies. It should be noted, however, that an additional sixth protonation step is not possible in the measurable pH range.

Table 1. Protonation constants[a] of B6SS and 6SS; t = 25.0 °C, μ = 0.100 M KNO_3

Equilibrium quotient	B6SS[b]	6SS[c]
[HL]/[L][H]	12.0	11.11
$[H_2L]/[HL][H]$	11.7	10.56
$[H_3L]/[H_2L][H]$	9.85	8.99
$[H_4L]/[H_3L][H]$	3.89	4.24
$[H_5L]/[H_4L][H]$	2.9	2.7

[a] Charges of individual species are omitted. [b] σ_{fit} = 0.008; see Ref. 7 p.30. [c] Ref. 1.

The potentiometric pH profiles and stability constants for the complexes of In(III) and Ga(III) are shown in Fig. 1 and Fig. 2 and Table 2. In Table 2, for comparison, the published values for the same metal ions with 6SS are also indicated. It is quite clear that both In(III) and Ga(III) are very effectively chelated by B6SS and both metal ions form the same type of complexes. Of the two protonated chelates which form, one involves the protonation of the pendent arm.

Table 2. Equilibrium Constants[a] for In(III) and Ga(III) Complexes of B6SS and 6SS; t = 25.0 °C, μ = 0.100 M KNO_3.

Equilibrium quotient	B6SS	6SS[b]
	In(III)	
[ML]/[M][L]	40.0[c]	40.0
[MHL]/[ML][H]	3.2[d]	-
$[MH_2L]/[MHL][H]$	3.0[d]	-
[M(OH)L][H]/[ML]	-10.9[e]	-10.7
pM	28.6	30.9
	Ga(III)	
[ML]/[M][L]	38.4[f]	41.0
[MHL]/[ML][H]	3.6[g]	2.5
$[MH_2L]/[MHL][H]$	2.8[g]	-
[M(OH)L][H]/[ML]	-10.2[h]	-11.4
pM[i]	27.0	31.6

[a] Charges of individual species are omitted. [b] Ref. 3. [c] σ_{fit} = 0.10. [d] σ_{fit} = 0.010. [e] Estimated value. [f] σ_{fit} = 0.084. [g] σ_{fit} = 0.003. [h] Estimated value. [i] For 1.0 x10^{-3} M metal chelates, 100% excess ligand, and p[H] 7.4.

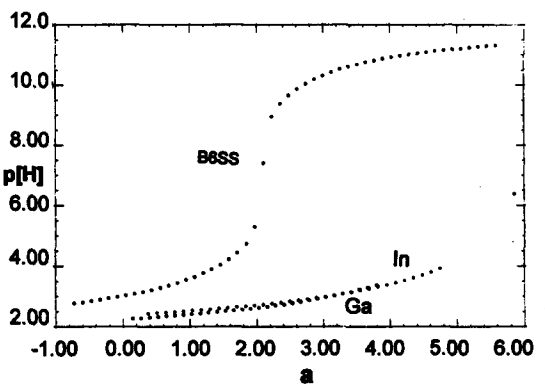


Figure 1. Potentiometric pH profiles of B6SS and its 1:1 metal complexes with In(III) and Ga(III) at μ = 0.10 M KNO_3, t = 25.0 °C. *a* = moles of base added per mole of ligand present. B6SS: T = 0.00156M. In: T_{B6SS} = 0.00133M; T_{In} = 0.00131M; Ga: T_{B6SS} = 0.00180 M; T_{Ga} = 0.00174 M. • p[H]; • p[H](In); ○ p[H](Ga).

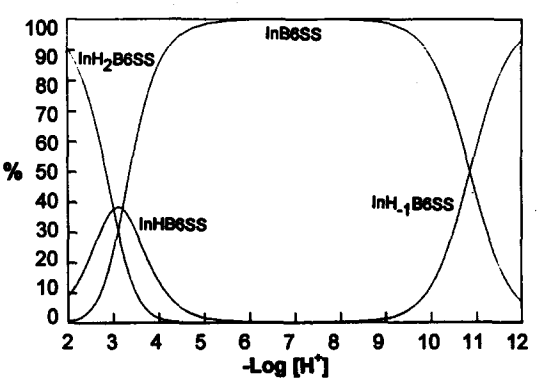


Figure 2 Species distribution curves of In(III)-B6SS. T_{B6SS} = 0.00133 M, $T_{In(III)}$ = 0.00131 M; μ = 0.10 M KNO_3, t = 25.0 °C. % equals per cent of species present, with 100% = 0.00131 M.

At titration concentratons (the initial metal ion concentration ~2 mmol) both In(III)-In(III) and Ga(III)-Ga(III) systems start to precipitate at pH 3.9 and 3.5; (and both become clear solutions at pH above 8.8), hence as shown in Figures 1 and 2, the titrations were discontinued before a = 5 (moles of base/mole of ligand). The two protonation constants of MOHL are estimated values. Nevertherless, at physiological pH the complexes exist 100% as ML^{2-} (Figure 2) and are characterized by very large pM values (28.6 for In(III) and 27.0 for Ga(III)). The pM values calculated in the manner indicated in the Experimental are listed for the Ga(III)and In(III) chelates of B6SS and 6SS in Table 2. Since the higher the value of pM the more stable the chelate complex, it is seen that the effect of the bifunctional covalent linkage is small, and the stabilities of all the chelates listed are very high. The slightly lower pM values for B6SS relative to 6SS, reflects only a small steric factor introduced by the presence of a connecting bridge on the backbone of the ligand. Therefore it is concluded that the connecting pendant arm has only a small, almost negligible influence on Ga(III) and In(III) affinities, and that ligand **5**, B6SS, is an excellent bifunctional agent for attaching Ga(III) and In(III)to proteins and peptides.

EXPERIMENTAL

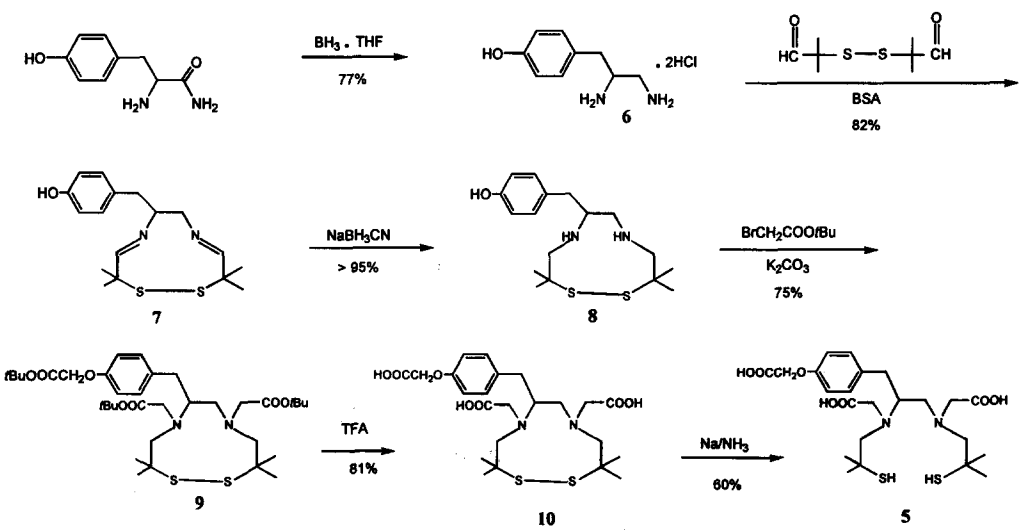
Materials and Methods

t-Butyl bromoacetate, sodium cyanoborohydride, bis(trimethylsilyl)acetamide(BSA) were obtained from Aldrich Chemical Co. and were used as supplied. 1-(4-Hydroxybenzyl)-1,2-ethylenediamine dihydrochloride salt[5] (**6**), 2,2'-dithio-bis(2-methyl-propanal)[6] were prepared by previously reported procedures.

The proton and carbon-13 NMR were recorded on a Varian XL-200 spectrometer operating at 200 MHz, and the chemical shifts are reported in ppm relative to tetramethylsilane in chloroform-d. The mass spectra were obtained with a VG analytical 70S high resolution double focusing magnetic sector spectrometer with an attached VG analytical 11/250J data system. Measurements were made by the Departmental mass spectrometry specialist, Dr. Lloyd W. Sumner. The C, H, N analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. The melting point was determined with a Fisher-Johns melting point apparatus and was uncorrected.

Synthetic Procedure

The route used for the synthesis of B6SS is shown in the Scheme.



6-(4-Hydroxybenzyl)-3,3,10,10-tetramethyl-1,2-dithia-5,8-diazacyclodeca-4,8-diene (7). Compound **6,** 2.53g (10.6 mmol), was placed in a two-necked flask attached to a vacuum line and the whole system was flushed several times with dry Ar. Bis(trimethylsilyl)acetamide (BSA), 20 mL (80.9 mmol) was added and this mixture was stirred at 30-35 °C for 30-40 min. until a clear solution was obtained. The trimethylsilyl chloride produced was removed by vacuum distillation at 40-60 mm Hg/25-30 °C for about 20 min. A solution of 2.18g (10.6 mmol) of 2,2'-dithiobis(2-methylpropanal)and 15 mL of dry benzene was added to the reaction mixture; which was then heated in a 55-65 °C bath for 1.5 hr and then cooled. The by-products, solvent and excess reagent were removed by vacuum distillation until the pressure and temperature reached 0.1 mm Hg and 90 °C. A pale yellow viscous liquid was obtained, to which 20 mL of absolute ethanol and one drop of concentrated hydrochloric acid was added. The reaction mixture was stirred at room temperature for 1 hr, and the solvents and by-products were removed by evaporation under reduced pressure. Another 20 mL absolute ethanol containing 5 drops of concentrated hydrochloric acid was added and the reaction mixture was stirred at room temperature for 16 hr. After the solution was cooled, a substantial quantity of white precipitate separated which was collected by filtration and washed with cold ethanol and ethyl ether ; and vacuum dried over P_2O_5 at room temperature for 16 hr. 1.96 g pure product was obtained. Another 0.96g product was obtained from the filtrate. The total yield was 2.92g (82%). M.p.= 216-219 °C (dec). ^{1}H NMR of compound **7** (in $CDCl_3$): 1.32-1.46 (m, 12H, methyl), 2.8-3.1 and 3.3-3.5 (m, 4H, methylenes), 3.9-4.0 (m, 1H, asymmetric CH-), 6.6-6.7 (d, 4H, arom.), 6.94 (s, 2H, N=CH-). ^{13}C NMR (in $CDCl_3$): 21.219, 21.286, 24.442 and 24.576. (methyl), 39.030 ($Me_2\underline{C}$-), 52.857, 53.013 and 65.664 (two -CH_2-), 74.136 (-CH-), 115.339 (arom. C-3), 29.867 (arom. C-1), 130.179 (arom. C-2), 154.777 (arom. C-4), 165.988 and 168.592 (two -CH=). FAB MS: [M+1] = 337. Anal. Calcd. for $C_{17}H_{24}N_2OS_2$·1/4 H_2O: C, 59.88; H, 7.19; N, 8.22. Found: C, 59.78; H, 7.37; N, 8.01.

6-(4-Hydroxybenzyl)-3,3,10,10-tetramethyl-1,2-dithia-5,8-diazacyclodecane (8). Sodium cyanoborohydride, 0.37 g (5.4 mmol) was added portionwise to a suspension of 2.58 g (7.67 mmol) of compound **7** in 45 mL of dry methanol in an ice-water bath. The pH of the reaction mixture was maintained at about 6.5 by the addition of a solution of methanol:conc.HCl (v/v) = 9:1; and it was then stirred at room temperature for 3 hr. More 9:1/methanol-HCl was added until pH of the solution became about 1.5. Water, 8 mL, was added and the reaction was rotavapped until water vapor appeared on the condenser. More water (12 mL) was added, and a 7 M NH_3-H_2O solution was used to neutralize the acid until the pH became 9.5. Chloroform (3/30 mL) was used to extract the product. The combined chloroform extracts were filtered and dried with anhydrous $MgSO_4$ for 16 hr. After the solvent was removed and the residue was dried at 0.1 mm Hg and 30 °C for 20 hr; 2.6 g of white glassy residue was obtained. Both NMR and elemental analysis showed it to be the pure product; the yield was nearly quantitative. ^{1}H NMR (in $CDCl_3$): 1.19-1.48 (m, 12H, methyl), 2.3-3.2 (m, 9H, -CH_2- and -CH-), 3.8-4.3 (b, HO- and NH), 6.69-6.7 (d, 2H, H-3 of phenyl), 6.89-7.1 (m, 2H, H-2 of phenyl). ^{13}C NMR (in $CDCl_3$): 26.986 and ect.(methyl), 39.155 ($Me_2\underline{C}$-), 50.327, 51.266, 52.079, 52.274, 56.771, 57.067 (-CH_2- and CH), 115.862 (C-3 of phenyl), 128.613 (C-1 of phenyl), 130.045 (C-2 of phenyl), 155.828 and 155.934 (C-4 of phenyl). FAB MS: [M+1] = 341. Anal. Calcd. for $C_{17}H_{28}N_2OS_2$·$CHCl_3$: C, 47.01; H, 6.36; N, 6.09. Found: C, 47.46; H, 6.63; N, 6.02.

6-(p-Carboxymethoxybenzyl)-3,3,10,10-tetramethyl-1,2-dithia-5,8-diazacyclodecane-N,N'-diacetic Acid Tri-t-butyl Ester (9). Compound **8**, 2.6g (7.6 mmol); *t*-butyl bromoacetate, 13.3g (68 mmol); potassium carbonate, 9.3g (6.7 mmol) and potassium iodide, 3.7g (2.2 mmol) were mixed with 150 mL of acetonitrile and were stirred at room temperature for 22 hr. The reaction mixture was filtered and the insoluble material was washed with dichloromethane. The combined filtrate and washings were rotavapped. A pale yellow oil was obtained, which was redissolved in 75 mL of dichloromethane and this solution was dried with anhydrous $MgSO_4$ for 16 hr. After evaporation of the solvent, 7g of pale yellow oil was obtained. This crude product was purified on silica gel 60. The impurities were removed by elution with hexane; after elution with benzene

3.9 g pure product was obtained by evaporation of the solvnt; the yield was 75%. ^{1}H NMR (in $CDCl_3$): 1.17-1.50 (m, 39H, methyl and *t*-butyl), 2.1-2.5 and 2.7-3.4 (m, 11H, CH_2-N- and CH-N-), 3.85-4.0 and 4.15-4.25 (m, 2H, CH_2- of benzyl), 6.7-6.85 (d, 2H, H-3 of phenyl), 7.1-7.15 (d, 2H, H-2 of phenyl). ^{13}C NMR (in $CDCl_3$): 25.241, 26.753, (methyl), 27.870 and 28.054 (the methyl of *t*-butyl), 33.036 and 32.414 (-C-Me_2),49.984 and 65.683 (-CH_2- of acetate) 53.668, 55.789, 58.861 and etc. (CH_2-N- and CH-N-), 80.392 and 80.602 (CH_2- of benzyl), 82.036 (-CH_2-O-), 114.286 (C-3 of phenyl), 130.081 (C-2 of phenyl), 132.937 (C-1 of phenyl), 156.036 (C-4 of phenyl), 167.960, 170.712 and 171.521 (the three carbonyls). FAB MS: [M+1] = 682. Anal. Calcd. for $C_{35}H_{58}N_2O_7S_2 \cdot 1/4H_2O$: C, 61.15; H, 8.58; N, 4.07. Found: C, 61.13; H, 8.25; N, 4.04.

6-(p-Carboxymethoxybenzyl)-3,3,10,10-tetramethyl-1,2-dithia-5,8-diazacyclodecane-N,N'-diacetic Acid (10). Compound **9**, 1.8g (2.6 mmol) was dissolved in 60 mL of trifloroacetic acid and was stirred at room temperature for 24 hr. The volatile material was removed by rotavaporation. To the residue, 100 mL water was added; 2.5M NaOH solution was used to dissolve the product (pH about 11). The solution was acidified with 2.5 M HCl until the pH of the solution became 1.5. It was allowed to stand at about 5 °C for 16 hr, filtered and washed with cold water, and vacuum dried over P_2O_5 at room temperature for 16 hr. 1.1g of pure product was obtained, the yield was 81%. ^{1}H NMR (in D_2O): 1.01-1.21 (m, 12H, methyl), 2.1-3.2 (m, 13H, CH_2-N-, CH-N-, CH_2- of benzyl), 4.29 (s, 2H, -CH_2O-), 6.69-6.75 and 7.02-7.06 (d, 4H, arom). FAB MS: [M+1] = 515. Anal. Calcd. for $C_{23}H_{34}N_2O_7S_2 \cdot 1/4H_2O$: C, 53.21; H, 6.70; N, 5.40. Found: C, 53.08; H, 6.49; N, 5.25.

1-(4-carboxymethoxybenzyl)-N,N'-bis[(2-mercapto-2,2-dimethyl)ethyl]-1,2-ethylenediamine-N,N'-diacetic acid (B6SS, 5). In a three-necked flask compound **10**, 0.257g (0.5 mmol) was dissolved in 4 mL of THF, the solution was cooled with a dry ice-*i*-PrOH bath and 10-12 mL of NH_3 (liquid) was added. Small pieces of Na (0.06-0.1g) were added under Ar gas until the blue color remained for about 10 min. Powdered dry NH_4Cl was added until the reaction solution became colorless. The NH_3 was removed by evaporation under reduced pressure. Degassed water, 2.0 mL, was added to dissolve the white residue; and 0.4 mL of 2.5M HCl was added; the pH was about 8-9. It was quickly filtered by aspirator, then acidified until the pH became 2.0. After filtration and washing with water and vacuum drying, 0.155g pure product was obtained, the yield was 60%. ^{1}H NMR (in D_2O-NaOD): 1.10-1.22 (m, 12H, methyl), 2.3-3.35 (m, 13H, CH_2-N-, CH-N- and CH_2- of benzyl), 4.30 (s, 2H, -CH_2O-), 6.77 and 7.10 (d, 4H, arom.). FAB MS: [M+1] = 516. Anal. Calcd. for $C_{23}H_{36}N_2O_7S_2 \cdot 1/3H_2O$: C, 52.87; H, 7.03; N, 5.36. Found: C, 52.72; H, 7.00; N, 4.99

Other Reagents and Standard Solutions

Stock solutios of In(III) and Ga(III) were prepared at about 0.02 M (with excess acid to prevent hydrolysis) from analytical grade chloride salts with demineralized water and were standardized by complexometric titration with EDTA and by cation exchange (Dowex 50W-X8 cation exchange resin, 20-50 mesh, hydrogen form).[9]

A carbonate-free solution of the titrant, KOH, was prepared by dilution of analytical concentrate "Dilut-It"™ (J. T. Baker Chemical Co.) with demineralized water under a stream of purified argon gas. The solution was standardized with potassium hydrogen phthalate, and the extent of the carbonate accumulation was checked periodically by titration with a standard hydrochloric acid solution.

Potentiometric equipment and measurements

A Corning pH/ion analyzer 250 instrument was used together with a Model S-30056-10C Sargent Welch glass electrode and a Fisher 13-639-52 calomel reference electrode. A completely sealed 75 mL glass-jacketed titration cell was used, and the temperature 25.0 ± 0.1 °C, was controlled with a Fisher Model 90 Refrigerated Bath. Atmospheric CO_2 was excluded from the cell during the titration by passing purified argon through the

experimental solution in the reaction cell. The standard base was delivered through a capillary tip just under the surface of the solution by means of a 10-mL capacity Metrohm piston-type burette.[8]

Prior to each potentiometric equilibrium study, a calibration of the pH meter and electrode system was made with standard dilute HCl solutions at ionic strength 0.10 M adjusted with KNO_3 in the thermostated cell at 25.0 °C, so as to read hydrogen ion concentration directly. Thus, the term p[H] in this work is defined as -log $[H^+]$. The value of $K_W = [H^+][OH^-]$ used in the computations was $10^{-13.78}$.[8] The 1:1 log formation constant of $InCl^{2+}$ is 2.3 at 20 °C (ionic strength 0.7), and that of $InNO_3^{2+}$ is only 0.18 under the same conditions.[7] Therefore in the present study, KNO_3 was used as the ionic medium in all systems at 0.10 M ionic strength.

The potentiometric equilibrium measurements were made on 40-50 mL of ligand solutions initially 1.56 x 10^{-3} M, first in the absence of metal ions and then in the presence of each metal ion for which ligand:metal ratios were about 1.03:1. The p[H] values were measured after equilibration with each addition of 0.100 mL increment of standard KOH solution. The protonation constants of the ligands were obtained directly from the pH titration data. The protonation constants and hydrolysis constants of all metal chelates were calculated from the original p[H] profiles by methods described elsewhere.[8] Because the degree of formation of In(III) and Ga(III) complexes, even at low pH, was too high for the determination of stability constants by use of direct potentiometry, the ligand-ligand competition method was performed. The stability constant of the In(III)-B6SS complex was determined by EDTA-B6SS competition and that of the Ga(III)-B6SS complex by B6SS-PLED competition.[1] The equilibria were confirmed by forward and back titrations. The protonation constants of B6SS and its stability constants of In(III) and Ga(III) were obtained from the experimental data with the aid of the BEST program.[8] The species distribution curves were calculated and plotted with SPE and SPEPLOT programs.[8]

The pM values (pM = -log [M]) were calculated at physiological p[H], 7.4, for 1.00 x10^{-3} M metal ion and 1.00 x 10^{-3} excess ligand (total ligand is 2.00 x 10^{-3} M).

The four successive proton dissociation constants for $Ga(III)_{aq}$ ion included in the calculations are $10^{-2.91}$, $10^{-3.70}$, $10^{-4.40}$ and $10^{-5.77}$.[7] The first proton dissociation constant. for $In(III)_{aq}$ is $10^{-4.28}$.[7] The protonation constants and formation constants used in the ligand-ligand competition experiments are shown in Table 3.[7]

Table 3. Protonation Constants[a] and Formation Constants Used in the Ligand-Ligand Competition Experiments

EDTA		PLED[b]	
Equilibrium Quotient	Log K	Equilibrium Quotient	Log K
[HL]/[H][L]	9.93[c]	[HL]/[H][L]	10.89
$[H_2L]/[HL][H]$	6.05[c]	$[H_2L]/[HL][H]$	10.28
$[H_3L]/[H_2L][H]$	2.68[c]	$[H_3L]/[H_2L][H]$	7.20
$[H_4L]/[H_3L][H]$	2.07[c]	$[H_4L]/[H_3L][H]$	5.73
[InL]/[In][L]	24.90[b]	$[H_5L]/[H_4L][H]$	3.26
[InHL]/[InL][H]	1.5[b]	$[H_6L]/[H_5L][H]$	2.31
		[GaL]/[Ga][L]	32.31
		[GaHL]/[GaL][H]	7.10
		$[GaH_2L]/[GaHL][H]$	6.2

[a] Charges of individual species are omitted. [b] Ref.78 [c] Determined in this work; μ = 0.100 M (KCl), t = 25. 0 °C.

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