Gallium and Indium Complexes of Bis(amino thiol) (N_2S_2) Ligands

Yong Yong Zheng,[1a] Sunita Saluja,[1a] Glenn P. A. Yap,[1b] Michael Blumenstein,[1a] Arnold L. Rheingold,[1b] and Lynn C. Francesconi*,[1a]

Chemistry Departments Hunter College of the City University of New York, New York, New York 10021, and University of Delaware, Newark, Delaware 19716

Received November 30, 1995[⊗]

Three methods have been developed to prepare gallium and indium complexes of three tetradentate N_2S_2 ligands of the general formula $M(N_2S_2)R$ (M = Ga, In; R = Cl, Br, SCN, $O_2CC_6H_5$-*O*,*O*′). The ancillary ligand (Cl, SCN, $O_2CC_6H_5$-*O*,*O*′) was varied with the tetradentate ligand BAT-TM. X-ray crystallography shows that the coordination geometry about the d^{10} metal ion is influenced by the steric requirements of the ligands. X-ray crystallography of four molecules results in the following data: GaCl(BAT-TM) (**1**), formula = $C_{10}H_{22}ClGaN_2S_2$, space group = *Pnma*, a = 12.387(4) Å, b = 21.116(6) Å, c = 5.986(2) Å, V = 1565.8(9) Å^3, Z = 4; InCl(BAT-TM) (**2**), formula = $C_{10}H_{22}ClInN_2S_2$, space group = *Pnma*, a = 12.968(9) Å, b = 29.29(1) Å, c = 5.866(2) Å, V = 1620(2) Å^3, Z = 4; InNCS(BAT-TM) (**3**), formula = $C_{11}H_{24}ClInN_3S_3$, space group = *Pbca*, a = 11.812(3) Å, b = 11.679(3) Å, c = 24.238(9) Å, V = 3449.7 (17) Å^3, Z = 8; In(O,O′-$O_2CC_6H_5$)(BAT-TM) (**4**), formula = $C_{19}H_{29}O_2InN_2S_2$, space group = $P2_1/n$, a = 10.783(2) Å, b = 18.708(4) Å, c = 12.335(4) Å, V = 2321.7(9) Å^3, Z = 4. Proton NMR studies show that the complexes are stable in solution; in polar solvents such as acetonitrile, for certain molecules, two metal−ligand complexes are observed. Similarly, two metal−ligand complexes are seen in NMR data taken in 80% acetonitrile/20% D_2O (pD = 4.6) mixture. HPLC studies (acetonitrile/50 mM sodium acetate, pH = 4.6) show that the lipophilicity of the ligand determines the retention time of the complex.

Introduction

Routine applications of gallium and indium radiopharmaceuticals include the use of ^{67}Ga citrate for tumor and abcess imaging,[2,3] and the use of ^{111}In for leukocyte labeling for imaging sites of infection and inflammation and ^{111}In DTPA for evaluation of cerebral spinal fluid pathways.[2] Currently, ^{67}Ga citrate is one of the most versatile radiopharmaceuticals available to the nuclear physician and oncologist for the initial staging and following up of patients with cancer.[3] Both ^{67}Ga and ^{111}In are reactor produced and decay by emitting a γ-ray of suitable energy for imaging using Single Photon Emission Computed Tomography (SPECT) techniques.

Another radioisotope of gallium, ^{68}Ga, is a short-lived positron emitting radionuclide, available from a parent/daughter generator system.[4] The parent radioisotope, ^{68}Ge, has a 275 day half-life, convenient for delivery and use at a remote site. The 68 min half-life of the ^{68}Ga daughter is suitable for radiopharmaceutical synthesis and limits the radiation dose to the patient. Thus, the ^{68}Ge/^{68}Ga generator may offer a convenient source of positron-emitting ^{68}Ga radiopharmaceuticals for positron emission tomography (PET) imaging in institutions which do not have an on site cyclotron.[5]

To be useful as radiopharmaceuticals to target organs, gallium and indium compounds must be either thermodynamically stable toward hydrolysis at physiological pH or kinetically stable within the time frame of the nuclear medicine procedure. In addition, the potential transchelation of Ga(III) and In(III) complexes *in vivo* by transferrin (transferrin has two high affinity binding sites for Ga: log K_1 = 20.3 and log K_2 = 19.3)[6] requires that thermodynamically and/or kinetically inert complexes be developed for radiopharmaceutical applications.

A number of hexadentate ligands with donor sets N_3X_3 (X = O, S)[7−14] and N_2O_4[15−17] and ligand systems with O_6[18−20] donor sets form thermodynamically stable complexes with gallium(III) and indium(III). Some gallium complexes with N_3O_3 and N_2O_4 donor sets show promise as myocardial imaging agents.[14,17] The tracer gallium and indium complexes of most of these ligand systems also show high *in vitro* and *in vivo* stability.

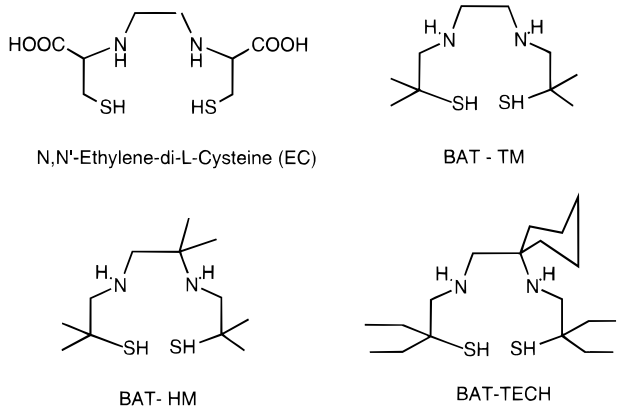
^{67}Ga and ^{68}Ga and ^{113}In complexes of N_2S_2 ligands show high myocardial uptake,[21,22] suggesting that the gallium and indium complexes of N_2S_2 ligands may be kinetically inert and do not

⊗ Abstract published in *Advance ACS Abstracts,* October 1, 1996.

(1) (a) Hunter College of the City University of New York. (b) University of Delaware.
(2) Jurisson, S.; Berning, D.; Jia, W.; Ma, D. *Chem. Rev.* **1993**, 1137.
(3) Macapinlac, H. A.; Scott, A. M.; Larson, S. M.; Divgi, C. R.; Yeh, S. D. J.; Goldsmith, S. J. *Nucl. Med. Biol.* **1994**, *21*, 731.
(4) Green, M. A.; Welch, M. *J. Nucl. Med. Biol*., **1989**, *16*, 435.
(5) Deutsch, E. *J. Nucl. Med.* **1993**, *34*, 1132.
(6) Harris, W. R.; Pecoraro, V. L. *Biochemistry* **1983**, *22*, 292.
(7) Moore, D. A.; Fanwick, P. E.; Welch, M. J. *Inorg. Chem.* **1989**, *28*, 1504.
(8) Craig, A. S.; Parker, D.; Adams, H.; Bailey, N. A. *J. Chem. Soc., Chem. Commun.* **1989**, 1793.
(9) Liu, S.; Wong, E.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1993**, *32*, 4268.
(10) Liu, S.; Wong, E.; Karunaratne, V.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1993**, *32*, 1756.
(11) Liu, S.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1992**, *31*, 5400.
(12) Moore, D. A.; Fanwick, P. E.; Welch, M. J. *Inorg. Chem.* **1990**, *29*, 672.
(13) Bossek, U.; Hanke, D.; Wieghardt, K.; Nuber, B. *Polyhedron* **1993**, *12*, 1.
(14) (a) Green, M. A.; Welch, M. J.; Mathias, C. J.; Fox, K. A. A.; Knabb, R. M.; Huffman, J. C. *J. Nucl. Med.* **1985**, *26*, 170. (b) Green, M. A.; Mathias, C. J.; Neumann, W. L.; Fanwick, P. E.; Janik, M.; Deutsch, E. A. *J. Nuc. Med.* **1993**, *34*, 228−233.
(15) Riley, P. E.; Pecoraro, V. L.; Carrano, C. J.; Raymond, K. N. *Inorg. Chem.* **1983**, *22*, 3096.
(16) Motekaitis, R. J.; Sun, Y.; Martell, A. E.; Welch, M. J. *Inorg. Chem.* **1991**, *30*, 2737.
(17) Green, M. A.; Mathias, C. J.; Tsang, B. W. *J. Nucl. Med.* **1993**, *34*, 1127.
(18) Nelson, W. O.; Karpishin, T. B.; Rettig, S. J.; Orvig, C. *Inorg. Chem.* **1988**, *27*, 1045.
(19) Clevette, D. J.; Lyster, D. M.; Nelson, W. O.; Rihela, T.; Webb, G. A.; Orvig, C. *Inorg. Chem.* **1990**, *29*, 667.
(20) Kappel, M. J.; Pecoraro, V. L.; Raymond, K. N. *Inorg. Chem.* **1985**, *24*, 2447.

S0020-1669(95)01535-7 CCC: $12.00

Chart 1



decompose and subsequently exchange with serum proteins to an appreciable extent. The stability constants, log *K*, for Ga(III) and In(III) complexes of the tetradentate ligand, tetramethylbis(aminoethanethiol) (BAT-TM, Chart 1) have been determined recently to be 24.73 and 27.34, respectively.[23] In a recent multifaceted study[24] incorporating molecular mechanics, stability constant measurements, crystallography, radiochemistry, and *in vivo* biodistribution studies, the ligand *N*,*N*′-ethylenedi-L-cysteine, EC, shown in Chart 1 was found to form stable complexes with Ga(III) and In(III).

We are interested in using the N_2S_2 ligand framework as a base upon which to design future gallium and indium radiopharmaceuticals. The basic N_2S_2 ligand framework is shown in Chart 1, where BAT-TM, BAT-HM, and BAT-TECH are the ligands used in this study. These open-chain N_2S_2 ligands display versatility in the structures which they adopt when complexed to a variety of metal ions.[25] Also, importantly, Ga(III) and In(III), d^{10} metal ions derive no ligand field stabilization energy benefits by assuming certain geometries. The combination of these two parameters may augur well for the design of new molecules. Given that the stability of the molecule is insured by correct placement of donor atoms, the shape, size, and topology of the resulting molecule will be dependent only on the steric requirements of the ligand. To develop a model for potential ligands for gallium(III) and indium(III) based on the N_2S_2 backbone, we have investigated the preparation, solution properties, and structures of gallium and indium complexes of simple tetradentate N_2S_2 ligands where a fifth ligand is varied. We report the results of our study here.

Experimental Section

General Comments. The ligands, BAT-TM and BAT-HM, were synthesized according to literature procedures.[26] The ligand BAT-TECH was a gift from Professor Hank F. Kung. Stock solutions of $GaCl_3$ were prepared by dissolving a weighed amount of gallium metal in concentrated HCl, followed by diluting to a known volume. The concentration of gallium was checked by complexometric titration using xylenol orange as an indicator. $Ga(NO_3)_3 \cdot 9H_2O$ was purchased from Alfa and used as received. An aqueous solution of $InCl_3$ was prepared by dissolving $InCl_3 \cdot 4H_2O$ (Alfa) in HCl; the concentration was checked in the same fashion as for $GaCl_3$. $In(NO_3)_3 \cdot 3H_2O$ was purchased from Aldrich and used as received. All solvents were reagent grade and were used without additional purification. Distilled, deionized water was used throughout. Infrared spectra were measured from KBr pellets on a Perkin-Elmer 1615 Fourier transfer infrared spectrophotometer. Mass spectra for compounds **1**, **2**, **7**, **8**, and **9** were measured on a Hewlett-Packard 5989A quadrupole mass spectrometer. Samples were run using electron impact ionization at 70 eV. Samples were introduced via a heated filament on a Scientific Instrument Services direct exposure probe. HPLC measurements were made on a Hamilton PRP-1 column, 25 cm, using a RAININ Dynamax system; the detector was a Dynamax Model UV-1 UV−visible detector, and the software used was the Dynamax HPLC Method Manager. NMR spectra were run on a Varian Unity Plus 500 MHz spectrometer. The COSY spectra were run in absolute value mode.

Synthesis of Compounds. GaCl (BAT-TM), 1. To an aqueous solution of BAT-TM·2HCl (10 mL, 0.12 g, 0.388 mmol) was added $GaCl_3$ (0.353 mL, 1.098 M, 0.388 mmol). A 1 N solution of NH_4OH (3.7 mL, 3.7 mmol) was added until pH = 3. The volume of the solution was reduced to 2 mL with heating to precipitate a solid. The solid was filtered, washed with water, and recrystallized from CH_2Cl_2/hexane. The fine needle-like crystals were dried at 100 °C in vacuo. A suitable single crystal was grown from CH_3CN/H_2O. Anal. Calcd for $C_{10}H_{22}N_2S_2ClGa$: C, 35.35; H, 6.48; N, 8.25; S, 18.85; Cl, 10.46. Found: C, 35.17; H, 6.50; N, 8.17; S, 18.77; Cl, 10.35. MS: *m*/*z* = 338/340 M^+, 301/303 $M^+ - Cl$. IR (cm^{-1}): 3213, 3177 (sh, N−H), 1631 (m, N−H).

InCl(BAT-TM), 2. To an aqueous solution of BAT-TM·2HCl (5 mL, 0.218 g 0.70 mmol), $InCl_3$ (0.72 mL, 0.9747 M, 0.702 mmol) was added. Ammonium hydroxide (1 N, 5.2 mL, 5.2 mmol) was added until pH = 2.88. Ethanol (25 mL) was added, and the solution was heated. The volume of the solution was reduced to ca. 2 mL, and a white solid precipated. The solid was filtered, washed with water, and recrystallized from CH_2Cl_2/hexane. The fine needle-like crystals were dried at 100 °C in vacuo. A suitable single crystal was grown from CH_3CN/H_2O. Anal. Calcd for $C_{10}H_{22}N_2S_2ClIn$: C, 31.21; H, 5.72; N, 7.28; S, 16.64; Cl, 9.23. Found: C, 31.40; H, 5.67; N, 7.16; S, 16.54; Cl, 9.17. MS: *m*/*z* = 384/386 M^+, 349/351 $M^+ - Cl$. IR (cm^{-1}): 3224, 3176 (sh, N−H), 1625 (m, N−H).

InNCS(BAT-TM), 3. $In(NO_3)_3 \cdot 5H_2O$ (0.39 g, 1.0 mmol) and KNCS (0.30 g, 0.31 mmol) were added to 15 mL of water. The solution was extracted with Et_2O (3 × 20 mL), and the organic layer was dried with Na_2SO_4. The ether solution of $In(NCS)_3$ was mixed with the free base, BAT-TM (0.224 g, 0.9 mmol), in 15 mL of Et_2O. A solid formed immediately; the solid was filtered and recrystallized from 15 mL of CH_3CN. Anal. Calcd for $C_{11}H_{22}N_3S_3In$: C, 32.43; H, 5.41; N, 10.32; S, 23.59. Found: C, 32.53; H, 5.56; N, 10.18; S, 23.38. IR (cm^{-1}): 3224.9, 3183 (m, N−H), 1627 (m, N−H), 2068.2 (s, NCS).

In($O_2CC_6H_5$-*O*,*O*′)(BAT-TM), 4. To 10 mL of ethanol containing 0.24 g (1.0 mmol) of BAT-TM ligand was added 0.39 g (1.0 mmol) of $In(NO_3)_3 \cdot 5H_2O$. To the resulting cloudy solution were added 50 mL of water and 0.14 g (1.0 mmol) of $C_6H_5CO_2NH_4$, and the solution was heated at 70−80 °C for 20 min to form a clear solution. The volume of the solution was reduced to 20 mL by stirring and heating at 100 °C. Ammonium hydroxide (1 N, 3.2 mL, 3.2 mmol) was added until the pH of the solution was 3.0 and a white precipitate formed. The solid was filtered and recrystallized from CH_3CN. Single crystals were grown from a CH_3CN/H_2O solvent system. Anal. Calcd for $C_{17}H_{27}N_2S_2O_2In \cdot CH_3CN$: C, 44.62; H, 5.87; N, 8.22; S, 12.52. Found: C, 44.11; H, 5.97 N, 8.32; S, 12.45. IR (KBr pellet, cm^{-1}): 3226.9 (s, NH), 3060.3 (w, aromatic), 1704.1 (s, C═O), 1600.6 (s, aromatic), 1537.9 (m, COO), 1404 (s, COO).

GaNCS(BAT-TM), 5. To the free base BAT-TM (0.235 g, 1 mmol) dissolved in 5 mL of ethanol, was added $Ga(NO_3)_3 \cdot H_2O$ (0.270 g, 1.0 mmol), followed by the addition of 5 mL of water. The slightly cloudy solution was heated (80 °C) for 20 min resulting in a clear, colorless solution. Solid KNCS (0.098 g, 1 mmol) was added, followed by the dropwise addition of ammonium hydroxide (3.0 mL, 1 N, 3 mmol) until the pH = 3.0. A white solid precipitated and was filtered, washed with water, and recrystallized from CH_3CN. Mass Spectroscopy, FAB

(21) Kung, H. F.; Liu, B. L.; Mankoff, D.; Kung, M.-P.; Billings, J. J.; Francesconi, L.; Alavi, A. *J. Nucl. Med.* **1990**, *31*, 1635.
(22) Liu, B.-L.; Kung, H. F.; Jin, Y. T.; Zhu, L.; Meng, M. *J. Nucl. Med.* **1989**, *30*, 367.
(23) Sun, Y.; Anderson, C. J.; Pajeau, T. S.; Reichert, D. E.; Hancock, R. D.; Motekaitis, R. J.; Martell, A. E.; Welch, M. J. *J. Med. Chem.* **1996**, *39*, 458.
(24) (a) Anderson, C. J.; John, C. S.; Li, Y. J.; Hancock, R. D.; McCarthy, T. J.; Martell, A. E.; Welch, M. J. *Nucl. Med. Biol.* **1995**, *22*, 165. (b) Li, Y.; Martell, A. E.; Hancock, R. D.; Reibenspies, J. H.; Anderson, C. J.; Welch, M. J. *Inorg. Chem.* **1996**, *35*, 404.
(25) Francesconi, L. C. Manuscript in preparation.
(26) (a) D'Amico, J. J.; Dahl, W. E. *J. Org. Chem.* **1975**, *40*, 1224. (b) Corbin, J. L.; Work, D. E. *J. Org. Chem.* **1976**, *41*, 489.

Table 1. Crystallographic Data for **1**−**4**

	1	**2**	**3**	**4**
		(a) Crystal Parameters		
formula	$C_{10}H_{22}ClGaN_2S_2$	$C_{10}H_{22}ClInN_2S_2$	$C_{11}H_{24}InN_3S_3$	$C_{19}H_{29}InN_3O_2S_3$
fw	339.6	384.7	409.3	510.4
cryst syst	orthorhombic	orthorhombic	orthorhombic	monoclinic
space group	*Pnma*	*Pnma*	*Pbca*	$P2_1/n$
a, Å	12.387(4)	12.968(9)	11.812(3)	10.783(2)
b, Å	21.116(6)	21.29(1)	11.679(3)	18.708(4)
c, Å	5.986(2)	5.866(2)	24.238(9)	12.335(4)
β, deg				111.09(2)
V, Å^3	1565.8(9)	1620(2)	3349.7(17)	2321.7(9)
Z	4	4	8	4
cryst dimens, mm	0.24 × 0.26 × 0.28	0.26 × 0.32 × 0.34	0.22 × 0.24 × 0.44	0.38 × 0.40 × 0.40
cryst color	colorless	colorless	colorless	colorless
D(calc), g cm^3	1.441	1.590	1.618	1.460
μ(Mo, Kα), cm^{-1}	21.74	18.77	17.68	12.15
temp, K	296	296	296	298
T(max)/*T*(min)	1.3	1.2	1.2	1.7
		(b) Data Collection		
diffractometer		Siemens P4		
monochromator		graphite		
radiation		Mo Kα (λ = 0.710 73 Å)		
2θ scan range, deg	4.0−52.0	4.0−45.0	4.0−50.0	4.0−62.0
no. of rflns collcd	1840	1300	3407	8039
no. of indpt rflns	1568	1088	2948	7693
no. of indpt obsd rflns $F_o \geq n\sigma(F_o)$	911 (n = 5)	808 (n = 4)	1801 (n = 4)	5427 (n = 4)
		(c) Refinement[a]		
R, %	4.99	4.96	4.06	4.34
R_w, %	6.07	6.44	4.68	5.25
Δ/σ (max)	0.07	0.07	0.00	0.01
$\Delta(\rho)$, e Å^{-3}	0.59	1.04	0.58	0.82
N_o/N_v	10.7	9.5	11.0	22.2
GOF	1.3	1.5	1.0	1.1

[a] Quantity minimized = $\sum w\Delta^2$; $R = \sum\Delta/\sum(F_o)$; $R_w = \sum\Delta w^{1/2}/\sum(F_o w^{1/2})$, $\Delta = |(F_o - F_c)|$.

positive ions: M$^{\bullet}$ + 1, *m*/*z* = 362; M$^{\bullet}$ + 1 − SCN, *m*/*z* = 303. Anal. Calcd for $C_{11}H_{22}N_3S_3Ga$: C, 36.46; H, 6.08; H, 6.08; N, 11.60; S, 26.52. Found: C, 36.49; H, 5.93; N, 11.50; S, 26.35. IR (cm^{-1}): 3174.1 (m, NH), 2067.2 (s, NCS),

Ga(O$_2$CC$_6$H$_5$-*O,O′*)(BAT-TM), 6. To the free base BAT-TM (0.24 g, 1 mmol) in 5 mL of ethanol, $Ga(NO_3)_3{\cdot}H_2O$ (0.28 g, 1 mmol) was added, followed by the addition of 10 mL of water. The slightly cloudy solution was heated (80 °C) for 30 min resulting in a clear, colorless solution. Ammonium benzoate (0.14 g, 1 mmol) was then added. A white precipitate formed on cooling the solution to room temperature (25 °C). The final pH was 3.8. The solid was filtered, washed with water, and recrystallized from CH_3CN. Anal. Calcd for $C_{17}H_{27}N_2S_2O_2Ga{\cdot}0.5\,CH_3CN$: C, 48.54; H, 6.40; N, 7.86; S, 14.38. Found: C, 48.78; H, 6.33 N, 7.37; S, 13.90. IR (KBr pellet, cm^{-1}): 3216.3 (m, NH), 3055.0 (w, aromatic), 1707.8 (s, C═O), 1625.8, 1601.5, 1566.5.

GaCl(BAT-HM), 7. This compound was prepared in a similar fashion as compound **2**. Anal. Calcd for $C_{12}H_{26}N_2S_2ClGa$: C, 39.18; H, 7.07; N, 7.62; S, 17.41; Cl, 9.66. Found: C, 39.18; H, 7.10; N, 7.65; S, 17.37; Cl, 9.58. MS: *m*/*z* 366/368 M$^+$, 331/333 M$^+$ − Cl. IR (cm^{-1}): 3213, 3166 (sh, N−H), 1631 (m, N−H).

InCl(BAT-HM), 8. This compound was prepared in a similar fashion as compound **2**. Anal. Calcd for $C_{12}H_{26}N_2S_2ClIn{\cdot}0.25CH_2Cl_2$: C, 33.95; H, 6.12; N, 6.46; S, 14.70; Cl, 12.29. Found: C, 34.04; H, 6.26; N, 6.37; S, 14.56; Cl, 12.63. MS: *m*/*z* 412/414 M$^+$, 377/379 M$^+$ − Cl. IR (KBr pellet, cm^{-1}): 3172 (N−H), 1628 (m, N−H).

InCl(BAT-TECH), 9. The ligand BAT-TECH·2HCl (0.107 g, 0.247 mmol) was dissolved in 15 mL of water. A solution of $InCl_3$ (0.253 mL, 0.9747 M, 0.247 mmol) was added dropwise. The pH of the resulting cloudy solution was 1.0. The solution cleared up after adding 10 mL of ethanol. The volume of the solution was reduced to 5 mL by heating, and a precipitate formed. The solid was filtered and recrystallized from CH_2Cl_2/ethanol. IR (KBr pellet, cm^{-1}): 3237.1 (w, NH), 1634 (m, NH). Anal. Calcd for $C_{19}H_{28}N_2S_2ClIn$: C, 44.84; H, 7.47; N, 5.51; S, 12.59; Cl, 6.98. Found: C, 44.92; H, 7.49; N, 5.43; S, 12.49; Cl, 7.03. MS: m/z = 508.

Collection and Reduction of Crystallography Data. Crystal, data collection, and refinement parameters are given in Table 1. Suitable crystals were selected and mounted with epoxy cement on thin glass fibers. The unit-cell parameters were obtained by the least-squares refinement of the angular settings of 24 relfections (20° ≤ 2θ ≤ 24°).

The systematic absences in the diffraction data are consistent for both space groups $Pna2_1$ and *Pnma* for **1** and **2**, and uniquely *Pbca* for **3**, and $P2_1/n$ for **4**. The *E*-statistics suggested the centrosymmetric option for **1** and **2**, which yielded chemically reasonable results of refinement. The structures were solved using direct methods, completed by subsequent difference Fourier syntheses and refined by full-matrix least-squares procedures. Semiempirical absorption corrections were applied.

Molecules of the isomorphous compounds **1** and **2** are located on mirror planes with one carbon atom disordered with 50/50 distribution over two positions, C(3) and C(3′). An acetonitrile solvent molecule was located in the asymmetric unit in **4**. All non-hydrogen atoms were refined with anisotropic displacement coefficients. Hydrogen atoms were treated as idealized contributions except those on disordered carbon atoms which were ignored.

All software and sources of the scattering factors are contained in the SHELXTL PLUS (4.2) program library (G. Sheldrick, Siemens XRD, Madison, WI).

Results and Discussion

(A) Synthesis of Compounds. Three synthetic methods, shown in Scheme 1, were used to prepare compounds **1**−**9**. Compounds **1**, **2**, **7**, **8**, and **9** were prepared by method 1; in this method, an aqueous solution of the metal chloride was reacted with the HCl salt of the ligand in water. Increasing the pH to ca. 3, by addition of base, resulted in formation of a precipitate. The precipitate was recrystallized from organic solvents. In the preparation of compound **9**, a precipitate of the complex occurred at ca. pH = 1. The gallium analog of

Scheme 1

Method 1:

$$MCl_3\ (M=Ga,In) + N_2(SH)_2 \cdot 2HCl \xrightarrow{pH=3} MCl(N_2S_2)$$

Method 2:

$$M(NO_3)_3\ (M=Ga,In) + N_2(SH)_2 + NH_4R \xrightarrow{pH=3} MR(N_2S_2)$$

Method 3:

$$In(NO_3)_3 + 3\ KSCN \xrightarrow{Et_2O} In(SCN)_3 + N_2(SH)_2 \longrightarrow InSCN(N_2S_2)$$

compound **9** was prepared by method 1;[27] however, as in the case of compounds **1**, **2**, **7**, and **8**, the pH was increased to 3 before precipitation of white solid occurred. The formation and precipitation of InCl BAT-TECH, **9**, at pH = 1 from the aqueous solution may reflect the stability at low pH and the lipophilicity of this compound. A unique feature of this method is the preparation of neutral, organic soluble indium and gallium complexes from completely aqueous precursors. These molecules may serve as starting reagents for exploration of the reactivities of the M−R(N_2S_2) (M = Ga(III), In(III); R = Cl or other ancillary ligand) species in organic solution.

Method 2 (Scheme 1) used the metal nitrate salts in a reaction with the free base of the ligand and the ammonium salt of the R group (SCN or benzoate) in an aqueous/ethanol solvent system. The pH was increased to ca. 3 using ammonium hydroxide to form the neutral M(R)(N_2S_2) species. In the third method, indium(III) nitrate and potassium isothiocyanate were reacted to form the $In(SCN)_3$ species, which was extracted into ether, in the initial step. This species was reacted with the free base form of the ligand dissolved in ether to form the neutral In(SCN) (N_2S_2) complex (**3**), which precipitated from solution. In the first two methods, the pH was controlled at or below 3. The metal hydroxides generally form at or slightly above pH = 3.[28] Elemental analysis, mass spectroscopy, infrared spectroscopy, and X-ray crystallographic data are consistent with the formulations. These air-stable compounds are soluble in methanol and acetonitrile and the more lipophilic analogs are soluble in chloroform.

(B) Spectroscopy. Generally, for all complexes, strong peaks are observed in the infrared spectra at 3300−3500 cm^{-1}; these are attributed to N−H stretches of the coordinated secondary amine groups. Peaks found at ca. 1650 cm^{-1} are consistent with the amine bending frequencies. For the SCN derivatives, we also observed a strong peak at 2068 cm^{-1} which is attributed to the N-bound SCN stretching frequency.[29] Chemical ionization mass spectrometry shows clearly the parent ions for the MCl(N_2S_2) species and the M − Cl fragmentation species. However, neither chemical ionization nor electron ionization mass spectrometry shows the parent ions or fragments, reflecting the loss of the ancillary ligands, for the SCN or benzoate species. It appears that FAB mass spectrometry may be useful for these species; the parent ion $M^{+\bullet}$ at m/z = 362 and $M^{+\bullet}$ − SCN at m/z = 304, was observed for Ga(SCN)BAT-TM (**5**) in the FAB positive ion spectrum.

(C) X-ray Crystallography. Compounds **1**−**4** were examined by X-ray crystallography. Figures 1−3 show ORTEP diagrams for molecules **1**, **3** and **4**, respectively. A figure for **2**, essentially similar to **1**, is provided as Supporting Information (Figure S1). The atomic coordinates and equivalent isotropic displacement coefficients for molecules **1**−**4** are shown in Table 2. Table 3 shows selected bond lengths, and Table 4 shows selected bond angles for the molecules. Tables S1−S4 show all of the bond lengths and bond angles for compounds **1**−**4**, Table S5 gives the anisotropic displacement coefficients for **1**−**4**, and Table S6 shows the H atom coordinates and isotropic displacement coefficients.[30]

Molecules **1** and **2** are isomorphous. The Ga−N, Ga−S, and Ga−C bond lengths are in the range observed for recently

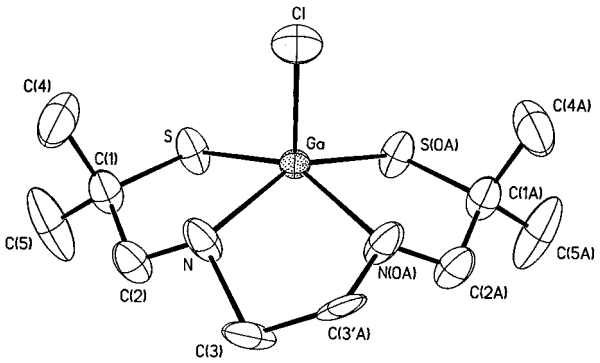


Figure 1. ORTEP diagram of GaCl(BAT-TM), **1**. Atom C(3) is disordered over two sites in a 50/50 ratio. The mirror plane generates the connecting atoms for each. Only one such combination is shown in the figure.

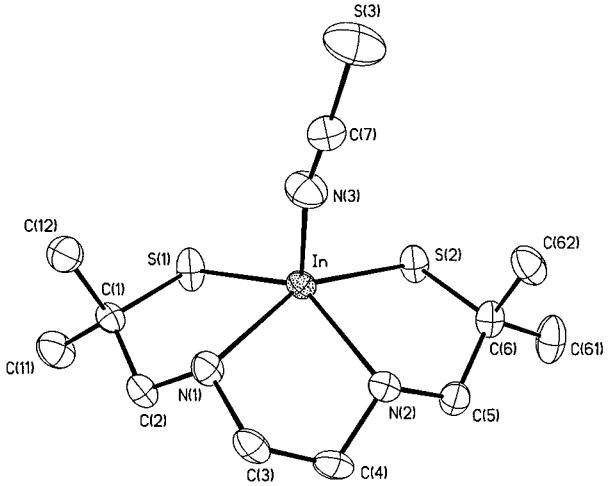


Figure 2. ORTEP diagram of InNCS(BAT-TM), **3**.

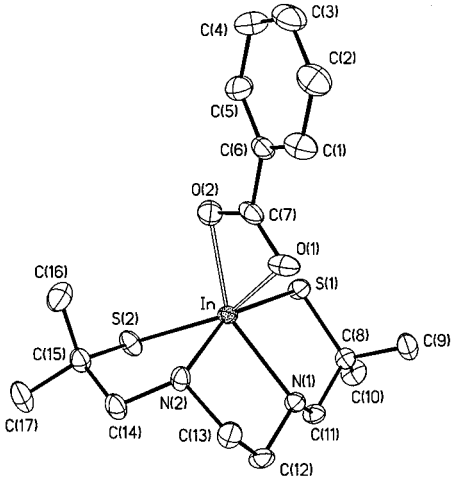


Figure 3. ORTEP diagram of In($O_2CC_6H_5$-*O*,*O*′)(BAT-TM), **4**.

(27) Francesconi, L. C.; Liu, B.-L.; Billings, J. J.; Carroll, P. J.; Graczyk, G.; Kung, H. F. *J. Chem. Soc., Chem. Commun.* **1991**, 94.

(28) (a) Taylor, M. J. *Compr. Coord. Chem.* **1987**, *3*, 105. (b) Tuck, D. G. *Compr. Coord. Chem.* **1987**, *3*, 153.

(29) (a) Patel, S. J.; Sowerby, D. B.; Tuck, D. G. *J. Chem. Soc. A* **1967**, 1187. (b) Patel, S. J.; Tuck, D. G. *Can. J. Chem.* **1969**, *47*, 229. (c) Habeeb, J. J.; Tuck, D. G. *J. Chem. Soc., Dalton Trans.* **1973**, 96.

(30) Supporting Information.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients ($Å^2 \times 10^3$) for Molecules **1**−**4**

	x	*y*	*z*	*U*(eq)[a]
		GaCl(BAT-TM) (**1**)		
Ga	972.2(8)	7500	2630(2)	38(1)
S	797(2)	6683(9)	157(3)	71(1)
N	1920(5)	6853(3)	4582(12)	72(3)
C(1)	1363(7)	6050(4)	1831(14)	68(3)
C(2)	2228(7)	6311(4)	3346(14)	72(3)
C(3)	3016(18)	7202(18)	5346(62)	88(11)
C(3′)	2639(16)	7162(18)	6062(58)	72(10)
C(4)	480(9)	5739(5)	3268(21)	142(6)
C(5)	1818(11)	5556(5)	350(19)	154(7)
Cl	−434(2)	7500	4986(4)	68(1)
		InCl(BAT-TM) (**2**)		
In	787.9(6)	7500	2436(2)	39(1)
S	689(2)	6585(2)	−81(5)	69(1)
N	1844(6)	6834(4)	4544(14)	58(3)
C(1)	1325(12)	6019(5)	1777(18)	68(4)
C(2)	2173(10)	6312(6)	3173(19)	69(4)
C(3)	2571(19)	7192(12)	6076(34)	54(9)
C(3′)	2875(17)	7225(11)	4931(36)	44(8)
C(4)	526(12)	5731(7)	3410(23)	122(7)
C(5)	1770(13)	5499(7)	323(26)	132(8)
Cl	−581(3)	7500	5193(6)	70(2)
		InSCN(BAT-TM) (**3**)		
In	2235.9(4)	495.3(4)	1377.4(2)	38(1)
S(1)	2246(2)	−694(2)	2186.8(8)	59(1)
S(2)	1644(2)	−702(2)	604.3(9)	53(1)
N(1)	3534(5)	1566(5)	1883(3)	45(2)
N(2)	3408(5)	1296(5)	733(2)	39(2)
C(1)	3115(6)	204(6)	2640(3)	39(3)
C(2)	4007(7)	838(6)	2312(3)	47(3)
C(3)	4388(7)	2086(7)	1517(3)	48(3)
C(4)	4518(6)	1453(7)	987(4)	53(3)
C(5)	3436(7)	589(7)	234(3)	48(3)
C(6)	2281(7)	174(6)	55(3)	46(3)
C(11)	3716(8)	−578(8)	3037(4)	71(4)
C(12)	2349(7)	1020(7)	2950(3)	60(3)
C(61)	2415(9)	−615(8)	−440(3)	77(4)
C(62)	1508(7)	1178(7)	−88(3)	63(3)
S(3)	−653(2)	3408(2)	1271(2)	92(1)
C(7)	347(7)	2501(7)	1357(3)	48(3)
N(3)	1035(6)	1847(6)	1433(3)	64(3)
		In($O_2CC_6H_5$)(BAT-TM) (**4**)		
In	6858.5(2)	2322.1(1)	6454(2)	28(1)
S(1)	7759(1)	1767(5)	8405.6(8)	39(1)
S(2)	8757.2(9)	2647.2(6)	5903.4(8)	42(1)
N(1)	6192(3)	1164(2)	5945(3)	32(1)
N(2)	5753(3)	2382(2)	4415(3)	33(1)
C(1)	2766(5)	3600(3)	6544(4)	58(2)
C(2)	1915(5)	4073(3)	6781(5)	62(2)
C(3)	2405(5)	4647(3)	7492(5)	62(2)
C(4)	3751(5)	4764(3)	7962(5)	67(2)
C(5)	4618(5)	4292(2)	7715(4)	53(2)
C(6)	4125(4)	3704(2)	7011(3)	41(1)
C(7)	5049(4)	3186(2)	6769(3)	44(2)
C(8)	7409(3)	813(2)	8004(3)	35(1)
C(9)	6164(4)	578(3)	8241(4)	50(2)
C(10	8601(4)	373(2)	8758(4)	52(2)
C(11)	7217(4)	692(2)	6729(3)	36(1)
C(12)	5932(4)	1070(2)	4692(3)	42(1)
C(13)	5071(4)	1679(2)	4029(3)	42(1)
C(14)	6682(4)	2550(2)	3809(3)	42(1)
C(15)	7803(4)	3055(2)	4485(3)	38(1)
C(16)	7283(5)	3776(2)	4648(5)	59(2)
C(17)	8739(5)	3122(3)	3810(4)	59(2)
O(1)	4649(3)	2582(2)	6350(3)	50(1)
O(2)	6253(3)	3368(2)	7011(3)	55(1)
C(101)	7440(5)	3796(3)	343(4)	53(2)
N(100)	8189(4)	4234(3)	473(5)	72(2)
C(100)	6484(6)	3225(3)	162(6)	86(3)

[a] Equivalent isotropic *U* defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

reported five- or six-coordinate gallium, nitrogen, and sulfur compounds.[7,8,12,27] The corresponding bond lengths for indium(III) compounds, **2**−**4**, are also in the range observed for other five- or six-coordinate indium complexes with nitrogen and sulfur donor atoms.[13,17,31−33] Comparison of the bond distances (Table 3) shows that the M−N and M−S bond distances increase by 0.175 and 0.16 Å, respectively, on going from Ga^{3+}

Table 3. Selected Bond Lengths (Å) for **1**−**4**

	GaCl(BAT-TM) (**1**)		
Ga−S	2.283(2)	Ga−N	2.147(7)
Ga−Cl	2.241(3)	Ga−S(OA)	2.284(2)
Ga−N(OA)	2.147(7)		
	InCl(BAT-TM) (**2**)		
In−S	2.440(7)	In−N	2.322(10)
In−Cl	2.394(7)	In−S(OA)	2.440(7)
In−N(OA)	2.322(10)		
	InSCN(BAT-TM) (**3**)		
In−S(1)	2.411(2)	In−N(3)	2.127(7)
In−S(2)	2.446(2)	C(7)−N(3)	1.130(11)
In−N(1)	2.331(6)	S(3)−C(7)	1.601(9)
In−N(2)	2.291(6)		
	In($O_2CC_6H_5$)(BAT-TM) (**4**)		
In−S(1)	2.477(1)	In−O(1)	2.390(3)
In−S(2)	2.454(1)	In−O(2)	2.247(3)
In−N(1)	2.298(3)	C(7)−O(1)	1.252(5)
In−N(2)	2.367(3)	C(7)−O(2)	1.270(6)

Table 4. Selected Bond Angles (deg) for **1**−**4**

	GaCl(BAT-TM)(**1**)		
S−Ga−N	85.6(2)	N−Ga−N(OA)	79.0(4)
N−Ga−Cl	94.7(2)	S(OA)−Ga−N(OA)	85.6(2)
N−Ga−S(OA)	152.3(2)	Ga−S−C(1)	99.3(3)
S−Ga−N(OA)	152.3(2)	Ga−N−C(3)	108.9(14)
Cl−Ga−N(OA)	94.7(2)	Ga−N−C(3′)	113.0(15)
S−Ga−Cl	109.5(1)	Ga−N−C(2)	112.2(5)
S−Ga−S(OA)	98.1(1)	C(2)−N−C(3)	106.9(13)
Cl−Ga−S(OA)	109.5(1)	C(2A)−N(OA)−C(3′A)	122.0(13)
	InCl(BAT-TM) (**2**)		
S−In−N	82.1(3)	S(OA)−In−N(OA)	82.1(3)
N−In−Cl	94.7(3)	In−N−C(2)	110.6(7)
N−In−S(OA)	146.7(3)	In−N−C(3′)	104.6(9)
S−In−N(OA)	146.7(3)	In−N−C(3)	112.0(11)
Cl−In−N(OA)	94.7(3)	C(2)−N−C(3)	122.5(12)
S−In−Cl	111.4(2)	C(2)−N−C(3′)	103.6(11)
S−In−S(OA)	105.7(2)	In−S−C(1)	98.4(4)
Cl−In−S(OA)	111.4(2)		
N−In−N(OA)	75.1(5)		
	InSCN(BAT-TM) (**3**)		
S(1)−In−S(2)	107.5(1)	S(1)−In−N(1)	82.8(2)
S(2)−In−N(1)	154.3(2)	S(1)−In−N(2)	142.3(2)
S(2)−In−N(2)	83.1(2)	N(1)−In−N(2)	75.2(2)
S(1)−In−N(3)	112.3(2)	S(2)−In−N(3)	106.4(2)
N(1)−In−N(3)	90.4(3)	N(2)−In−N(3)	98.3(3)
In−S(1)−C(1)	99.5(2)	In−S(2)−C(6)	97.1(2)
In−N(1)−C(2)	108.5(4)	In−N(1)−C(3)	110.6(4)
C(2)−N(1)−C(3)	114.2(6)	In−N(2)−C(4)	107.8(5)
In−N(2)−C(5)	110.5(4)	C(4)−N(2)−C(5)	113.6(6)
In−N(3)−C(7)	166.0(7)		
	In($O_2CC_6H_5$)(BAT-TM) (**4**)		
S(1)−In−S(2)	107.4(1)	C(7)−O(1)−In	88.4(3)
S(2)−In−N(1)	111.6(1)	C(7)−O(2)−In	94.5(3)
S(2)−In−N(2)	81.1(1)	O(1)−C(7)−O(2)	120.7(4)
S(1)−In−N(1)	81.1(1)	S(2)−In−O(2)	103.4(1)
S(1)−In−N(2)	157.5(1)	S(2)−In−O(1)	148.2(1)
N(1)−In−N(2)	76.5(1)	S(1)−In−O(2)	97.1(1)
O(1)−In−O(2)	56.3(1)	S(1)−In−O(1)	99.9(1)
C(14)−N2−C(13)	111.6(3)	N(1)−In−O(1)	88.3(1)
C(11)−N1−C(12)	115.4(3)	N(1)−In−O(2)	143.9(1)
In−S(1)−C(8)	99.9(1)	N(2)−In−O(1)	79.7(1)
In−S(2)−C(15)	97.4(1)	N(2)−In−O(2)	101.1(1)

(31) Maecke, H. R.; Riesen, A.; Ritter, W. *J. Nucl. Med.* **1989**, *30*, 1235.
(32) Riesen, A.; Kaden, T. A.; Ritter, W.; Macke, H. R. *J. Chem. Soc., Chem. Commun.* **1989**, 450.

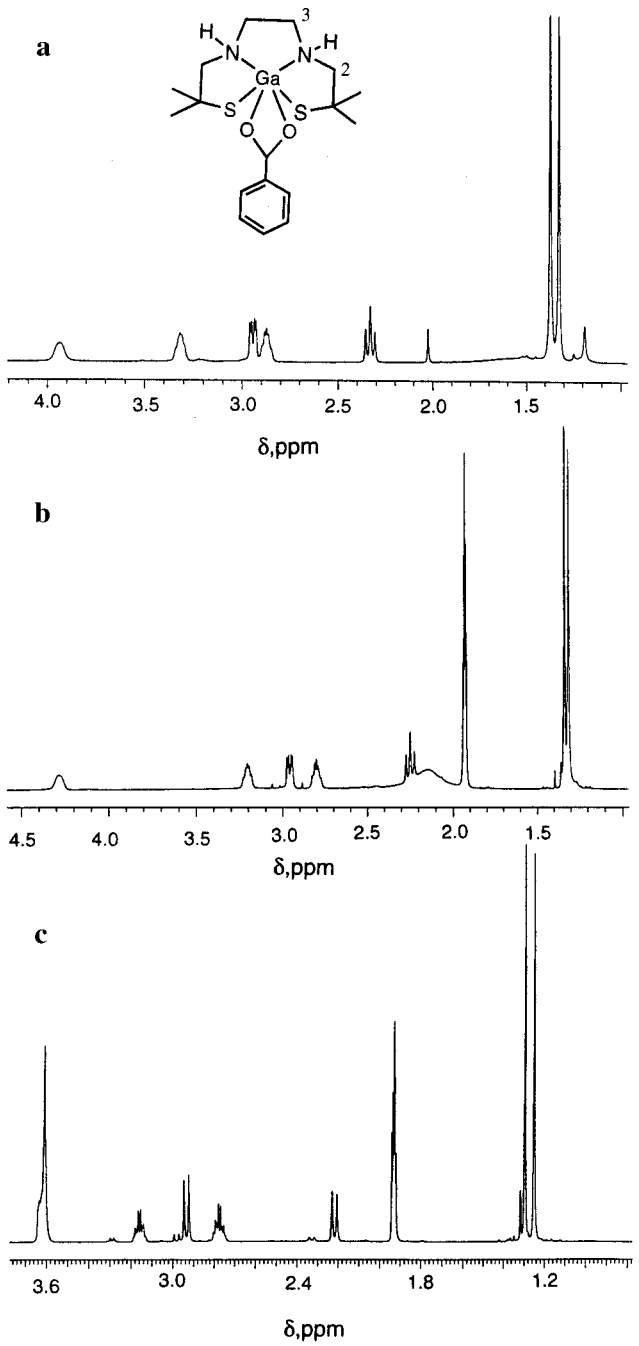


Figure 4. ^{1}H NMR data (500 MHz) for Ga($O_2CC_6H_5$-*O,O′*)(BAT-TM), **6**, measured in (a) $CDCl_3$, (b) CD_3CN, and (c) 80% CD_3CN/20% D_2O (pD = 4.6).

to In^{3+}. This trend is consistent with the larger ionic radius of In(III) (0.55 Å for Ga(III), 0.80 Å for In(III) in an octahedral coordination environment).[34] A comparison of the overall structure and M−N and M−S bond lengths in M(TS-TACN) (M = Ga(III), In(III)) compounds)[12,13] reveals the same trend. In these six-coordinate molecules, the hexadentate ligand, TACN-TS, provides a *fac*-N_3S_3 donor set around the metal(III) ion; the M−N and M−S bond distances increase by 0.189 and 0.172 Å, respectively, on going from Ga^{3+} to In^{3+}. This trend has also been observed in isostructural M(xanthine)$_3$ (M = Ga-

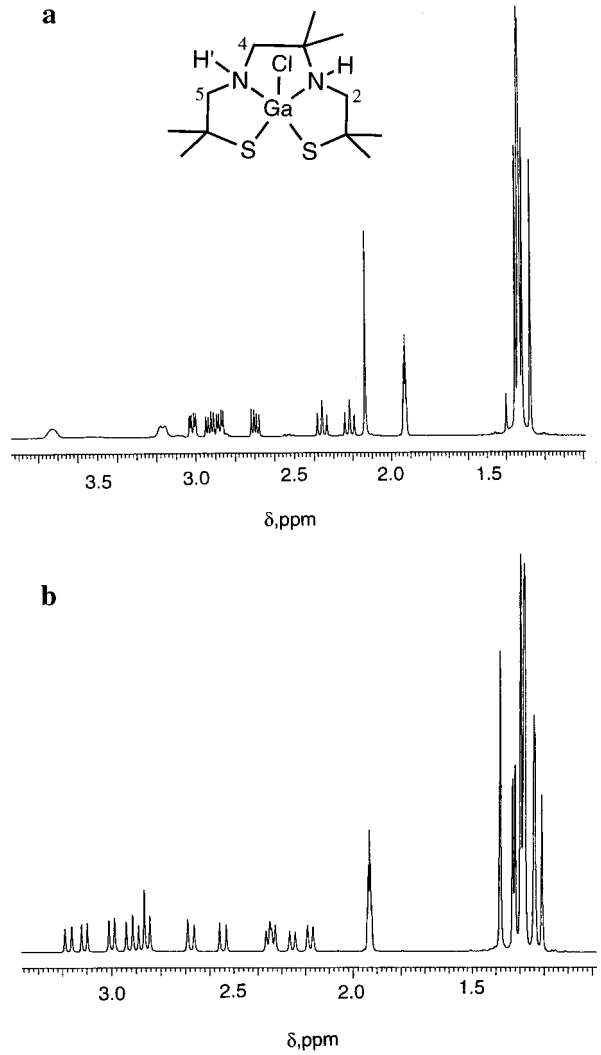


Figure 5. ^{1}H NMR data (500 MHz) for GaCl(BAT-HM), **7**, measured in (a) CD_3CN and (b) 80% CD_3CN/20% D_2O (pD = 4.6).

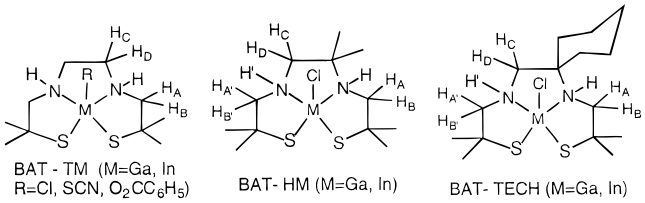
(III), In(III)) complexes.[33a] The metal ions in molecules **1** and **2** are in square pyramidal coordination geometries with the N_2S_2 ligand forming the base of the square pyramid and the Cl as the apical ligand. The nitrogen and sulfur atoms show no deviation from the best least squares plane calculated for the two N and two S atoms for **1** and **2**. The metal atom deviations from the N,S planes for **1** and **2** are 0.4961 and 0.6005 Å, respectively. The methylene carbon atoms of the ethylene diamine backbone C(3) and C(3A) have 50/50 probability in positions C(3′) and C(3A′) of the puckered five-membered ring.

The ORTEP diagram of In(SCN)BAT-TM (**3**) (Figure 2) shows that the indium(III) is in a distorted square pyramidal coordination geometry with the N_2S_2 ligand forming the base and the SCN bound through the nitrogen atom forming the apical ligand. The deviation from the best least-squares plane for the two nitrogen and two sulfur atoms are 0.11 Å for the sulfur atoms and 0.15 Å for the N atoms; the indium metal is 0.5421 Å out of the plane. The In−N(3) (NCS) bond is 2.127(7) Å which is consistent with the range of In−N bond lengths observed in $[In(NCS)_6]^{3-}$.[35] The bond angle In-N3-C7 is 166.0(7)°.

The indium(III) atom is coordinated to the benzoate and BAT-TM ligands in a distorted octahedral coordination environment

(33) (a) Hoskins, B. F.; Tiekink, E. R. T.; Vecchiet, R.; Winter, G. *Inorg. Chim. Acta* **1984**, *90*, 197. (b) Hauser, P. J.; Bordner, J.; Schriener, A. F. *Inorg. Chem.* **1973**, *12*, 1347. (c) Harrowfield, J. McB.; Pakawatchai, C.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1983**, 1109. (d) Einstein, F. W. B.; Jones, R. D. G. *J. Chem. Soc. A* **1971**, 2762. (e) Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1982**, *21*, 2379.
(34) Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *A32*, 761.
(35) Einstein, F. W. B.; Gilbert, M. M.; Tuck, D. G. *Acta Crystallogr.* **1976**, *B32*, 2234.

Table 5. NMR Spectroscopic Data for Selected Compounds



Ga(BAT-TM)($O_2CC_6H_5$), **6**, in $CDCl_3$

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
1.326	6[H]	s	methyl		2.942	2[H]	dd	H_B	$J_{HB-NH} = 4.5$
1.373	6[H]	s	methyl		3.314	2[H]	m	H_D	
2.331	2[H]	t	H_A	$J_{HA-HB} = 12$, $J_{HA-NH} = 1\ 2$	3.94	2[H]	br	NH	
2.872	2[H]	m	H_C		7.30−8.10	5[H]	m	aromatic	

In(BAT-TECH)Cl, **9**, in $CDCl_3$

δ, ppm	int	mult	assign	δ, ppm	int	mult	assign
1.70	6[H]	m	methyl	2.470	1[H]	br	NH′
1.95	6[H]	m	methyl	2.575	1[H]	t	H_C
1.3−1.8	18[H]	m	methylene	2.796	1[H]	dd	H_D
2.08	1[H]	t	H_A	2.934	1[H]	dd	H_B
2.16	1[H]	br	NH	3.076	1[H]	dd	$H_{B'}$
2.31	1[H]	t	$H_{A'}$				

Ga(BAT-TM)($O_2CC_6H_5$), **6**, in CD_3CN

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (100%)					
1.316	6[H]	s	methyl		2.958	2[H]	dd	H_B	$J_{HB-NH} = 5$
1.339	6[H]	s	methyl		3.204	2[H]	m	H_D	
2.247	2[H]	t	H_A	$J_{HA-HB} = 12$, $J_{HA-NH} = 12$	4.285	2[H]	br	NH	
2.800	2[H]	m	H_C		7.1−7.5	5[H]	m	aromatic	

Ga(BAT-TM)($O_2CC_6H_5$), **6**, in 80% CD_3CN/20% D_2O (pD = 4.6)

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (95%)					
1.251	6[H]	s	methyl		2.771	2[H]	m	H_C	
1.295	6[H]	s	methyl		2.934	2[H]	d	H_B	
2.212	2[H]	d	H_A	$J_{HA-HB} = 12$	3.159	2[H]	m	H_D	
				Minor Species (5%)					
1.2	6[H]	s	methyl		2.8	2[H]	m	H_C	
1.316	6[H]	s	methyl		2.980	2[H]	d	H_B	
2.33	2[H]	d	H_A	$J_{HA-HB} = 11.5$	3.29	2[H]	d	H_D	

Ga(BAT-TM)NCS, **5**, in CDCN

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (65%)					
1.286	6[H]	s	methyl		2.94	2[H]	dd	H_B	$J_{HB-NH} = 5$
1.32	6[H]	s	methyl		3.08	2[H]	m	H_D	
2.20	2[H]	t	H_A	$J_{HA-HB} = 12.5$, $J_{HA-NH} = 24$	3.88	2[H]	br	NH	
2.77	2[H]	m	H_C						
				Minor Species (35%)					
1.275	6[H]	s	methyl		3.00	2[H]	dd	H_B	J_{HB-NH}=4.5
1.364	6[H]	s	methyl		3.30	2[H]	m	H_D	
2.24	2[H]	t	H_A	J_{HA-HB}=12, J_{HA-NH}=12	3.68	2[H]	br	NH	
2.64	2[H]	m	H_C						

Ga(BAT-TM)NCS, **5**, in 80% CD_3CN/20% D_2O (pD = 4.6)

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (60%)					
1.236	6[H]	s	methyl		2.76	2[H]	m	H_C	
1.285	6[H]	s	methyl		2.93	2[H]	d	H_B	
2.18	2[H]	d	H_A	$J_{HA-HB} = 11.5$	3.07	2[H]	m	H_D	
				Minor Species (40%)					
1.236	6[H]	s	methyl		2.63	2[H]	d	H_C	$J_{HC-HD} = 8.5$
1.335	6[H]	s	methyl		3.01	2[H]	d	H_B	
2.23	2[H]	d	H_A	$J_{HA-HB} = 11.5$	3.30	2[H]	d	H_D	

Table 5 (Continued)

Ga(BAT-HM)Cl, **7**, in CD_3CN

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (>98%)					
1.2−1.35	18[H]	m	methyl		2.93	1[H]	dd	H_D	$J_{HD-HC} = 13$, $J_{HD-NH'} = 6.5$
2.215	1[H]	t	H_A	$J_{HA-HB} = 12$, $J_{HA-NH} = 12$	3.01	1[H]	dd	$H_{B'}$	$J_{HB'-HA'} = 12$, $J_{HB'-NH'} = 4.5$
2.357	1[H]	t	$H_{A'}$	$J_{HA'-HB'} = 12$, $J_{HA'-NH'} = 12$	3.17	1[H]	br,d	NH	
2.70	1[H]	dd	H_C	$J_{HC-HD} = 13$, $J_{HC-NH'} = 6.5$	3.73	1[H]	br,d	NH′	
2.89	1[H]	dd	H_B	$J_{HB-NH} = 5.5$					

Ga(BAT-HM)Cl, **7**, in 80% CD_3CN/20% D_2O (pD = 4.6)

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Species 1 (50%)					
1.20−1.35	18[H]	m	methyl		2.855	1[H]	d	H_B	$J_{HB-HA} = 11.5$
2.18	1[H]	d	H_A	$J_{HA-HB} = 11.5$	2.927	1[H]	d	H_D	$J_{HD-HC} = 13$
2.34	1[H]	d	$H_{A'}$	$J_{HA'-HB'} = 11$	2.993	1[H]	d	$H_{B'}$	$J_{HB'-HA'} = 11$
2.68	1[H]	d	H_C	$J_{HC-HD} = 13$					
				Species 2 (50%)					
1.20−1.35	18[H]	m	methyl		2.877	1[H]	d	$H_{B'}$	$J_{HB-HA'} = 11.5$
2.254	1[H]	d	H_A	$J_{HA-HB} = 11.5$	3.109	1[H]	d	H_B	$J_{HB-HA} = 11.5$
2.353	1[H]	d	$H_{A'}$	$J_{HA'-HB'} = 11.5$	3.176	1[H]	d	H_D	$J_{HD-HC} = 14.5$
2.545	1[H]	d	HC	$J_{HC-HD} = 14$					

Ga(BAT-TM)Cl, **1**, in CD_3CN

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (85%)					
1.34	6[H]	s	methyl		2.94	2[H]	dd	H_B	$J_{HB-HA} = 11.5$; $J_{HB-NH} = 5.0$ Hz
1.38	6[H]	s	methyl		3.06−3.10	2[H]	m	H_D	
2.24	2[H]	t	H_A	$J_{HA-HB} = 11.5$, $J_{HA-NH} = 11.5$	3.69	2[H]	br	NH	
2.76−2.80	2[H]	m	H_C						
				Minor Species (15%)					
1.29	6[H]	s	methyl		2.97	2[H]	dd	H_B	$J_{HB-HA} = 11$ Hz
1.31	6[H]	s	methyl		3.06−3.10	2[H]		H_D	
2.24	2[H]		H_A		3.60	2[H]	br	NH	
2.73	2[H]	br	H_C						

Ga(BAT-TM)Cl, **1**, in 80% CD_3CN/20% D_2O (pD = 4.6)

δ, ppm	int	mult	assign	J_{H-H}, Hz	δ, ppm	int	mult	assign	J_{H-H}, Hz
				Major Species (70%)					
1.25	6[H]	s	methyl		2.77	2[H]	m	H_C	
1.27	6[H]	s	methyl		2.92	2[H]	d	H_B	
2.214	2[H]	d	H_A	$J_{HA-HB} = 11$	3.08	2[H]	m	H_D	
				Minor Species (30%)					
1.38	6[H]	s	methyl		2.72	2[H]	d	H_C	$J_{HC-HD} = 8.5$
1.41	6[H]	s	methyl		2.97	2[H]	d	H_B	
2.28	2[H]	d	H_A	$J_{HA-HB} = 11$	3.28	2[H]	d	H_D	

in the molecule In($O_2CC_6H_5$-*O*,*O*′)(BAT-TM) (**4**). The benzoate ligand binds in a bidentate fashion to the metal ion and the BAT-TM ligand distorts to accommodate the steric requirements of the benzoate ligand, specifically the acute O(2)−In−O(1) angle of 56.3°. Deviation of the nitrogen and sulfur atoms from a least-squares plane constructed from the two nitrogen and two sulfur atoms is significant (0.42, 0.36 Å for S(1) and S(2), respectively, and 0.62, 0.56 Å for N(1) and N(2), respectively). The indium−oxygen bond lengths are unequal with In−O(1) significantly larger than In−O(2) in complex **4** and significantly larger than those for carboxylate moieties bound to indium(III) in a similar bidentate fashion[36]. The indium−oxygen bond lengths in **4** are slightly longer than those found in the literature for carboxylate moieties bound to indium(III) in a monodentate fashion.[31,32] In general, M−L bond lengths increase as the bite angle of a chelating ligand becomes smaller.[37] The indium−sulfur bond distances in **4** are significantly larger than those in molecules **2** and **3**, while the average In−N distance in **4** is consistent with those found in molecules **2** and **3**.

(D) NMR Spectroscopy. NMR spectroscopic data were collected in $CDCl_3$ for the three lipophilic complexes, M($O_2CC_6H_5$-*O*,*O*′)(BAT-TM) (M = In, Ga) and InCl(BAT-TECH) (**4**, **6**, and **9**) which are soluble in this solvent. Also, NMR data for the nine compounds were taken in CD_3CN and CD_3CN/D_2O (pD = 4.6, uncorrected). Selected NMR data are tabulated in Table 5. All NMR data are given in Table S7.[30] Figures 4−7 show one-dimensional and two-dimensional spectra of selected molecules.

The NMR spectrum of the BAT-TM ligand, measured in $CDCl_3$, shows four resonances at 2.75 ppm (intensity 4, methylene protons), 2.57 ppm (intensity 4, methylene protons), 1.73 ppm (intensity 4, NH,SH), and 1.33 ppm (intensity 12, CH_3). Typically, upon metal complexation, the methylene resonances shift downfield and show splitting patterns due to the diastereotopic protons. Figure 4 shows NMR data for Ga(O,O-$O_2CC_6H_5$)(BAT-TM) (**6**) taken at room temperature in $CDCl_3$ (Figure 4a), in CD_3CN (Figure 4b), and in a 80% CD_3CN/20%/D_2O mixture (Figure 4c). These data are tabulated

(36) (a) Einstein, F. W. B.; Gilbert, M. M.; Tuck, D. G. *J. Chem. Soc., Dalton Trans.* **1973**, 248. (b) Hausen, H.-D. *J. Organomet. Chem.* **1972**, *39*, C37. (c) Khan, M. A.; Peppe, C.; Tuck, D. G. *Acta Crystallogr.* **1983**, *C39*, 1339.

(37) Hancock, R. D.; Martell, A. E. *Chem. Rev.* **1989**, *89*, 1875.

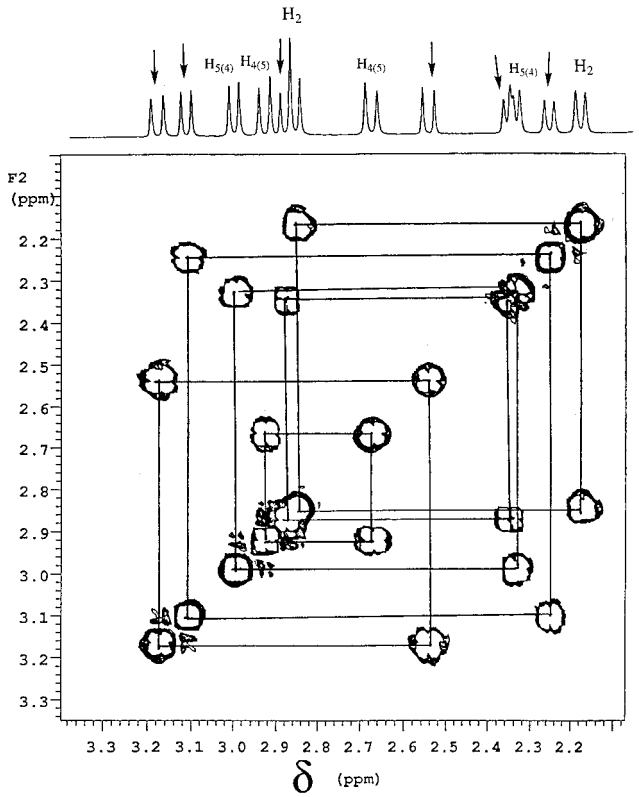


Figure 6. COSY NMR data (500 MHz) for GaCl(BAT-HM), **7**, measured in 80% CD_3CN/20% D_2O (pD = 4.6). The arrows mark the resonances assigned to the second species.

in Table 5. It is clear from Figure 4a that the molecule Ga($O_2CC_6H_5$-*O,O′*)(BAT-TM) (**6**) assumes a symmetrical structure in the chloroform solution and one species is present in solution; one amine hydrogen is observed at 3.98 ppm, an AB pattern is observed for protons at carbon 2, and an AA′XX′ pattern is observed for protons at carbon 3. The molecule Ga($O_2CC_6H_5$-*O,O′*)(BAT-TM) (**6**) also adapts a symmetrical structure in acetonitrile solution (Figure 4b, Table 5), and again, one species is observed in this solution. Addition of D_2O, as shown in Figure 4c, however, results in a small amount (5%) of a new species, also showing planar symmetry, forming in solution and a simplification of the spectrum, due to the exchange of NH protons.

Six resonances, accounting for all six of the methylene protons of the backbone in the molecule GaCl(BAT-HM), **7**, are seen in acetonitrile solution and primarily one species is present in solution (Figure 5a and Table 5). The assignments were made from the one-dimensional and COSY spectra (Figure S2[30]). From these experiments, one cannot distinguish the protons on C4 and C5. The MCl(BAT-HM) (compounds **7** and **8**) and M(BAT-TM)−benzoate (compounds **4** and **6**) (M = Ga(III), In(III)) derivatives show primarily (>90%) one species in acetonitrile solution.

The addition of D_2O to the acetonitrile results in an increase in the minor species to ca. 30−50% for the MCl(BAT-HM) (**7**, **8**) (M = Ga(III), In(III)) derivatives. The NMR spectrum of GaCl(BAT-HM), **7**, in CD_3CN/D_2O (shown in Figure 5b) is simplified due to lack of NH coupling to the six methylene protons of the backbone of the BAT-HM ligand. Furthermore, *12* doublets of equivalent intensity are observed in the NMR spectrum of **7** in CD_3CN/D_2O (Figure 5b), suggesting 50% formation of a separate species in this solution. The COSY spectrum for **7**, taken in CD_3CN/D_2O, is shown in Figure 6. The resonances assigned to the new species are designated by arrows in the figure.

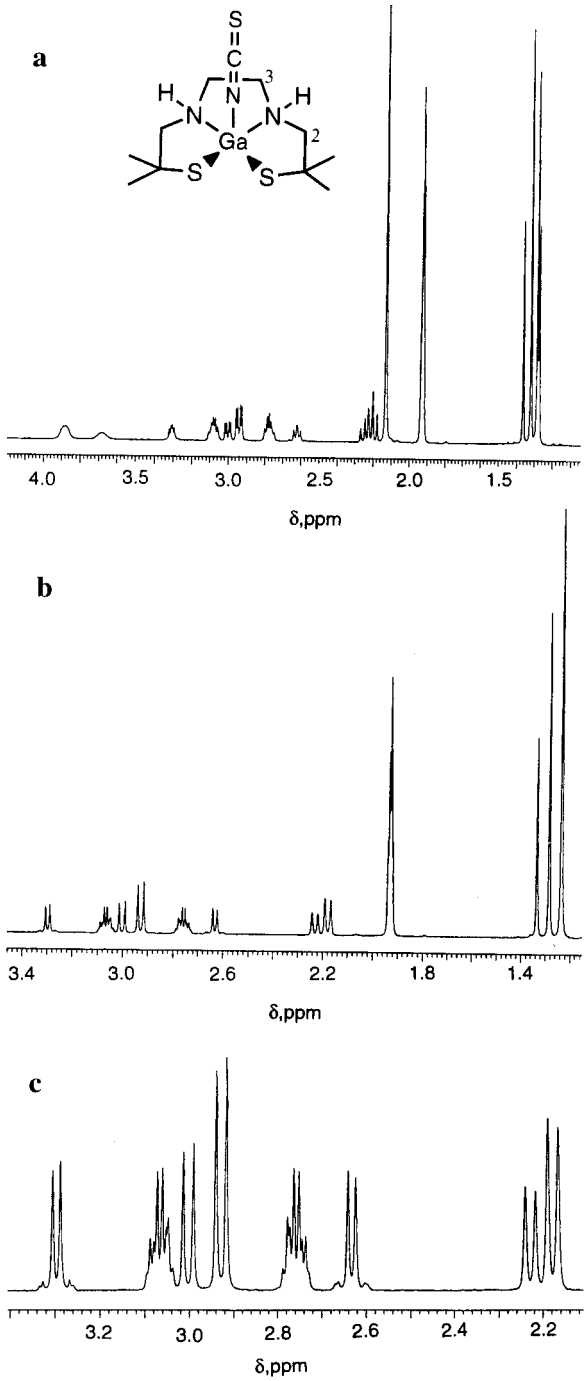


Figure 7. ^1H NMR data (500 MHz) for Ga(NCS)(BAT-TM), **5**, measured in (a) CD_3CN and (b) 80% CD_3CN/20% D_2O (pD = 4.6). Spectrum c is an expansion of the methylene region of spectrum b.

The M(BAT-TM)Cl (compounds **1** and **2**) and M(BAT-TM)-SCN (compounds **3** and **6**) derivatives show two separate and identifiable species (major species, ca. 60−80%; minor species, 40−20%) in acetonitrile solution. The one-dimensional NMR spectrum for Ga(BAT-TM)NCS, **6**, in acetonitrile is shown in Figure 7a. The presence of two species can often be deduced by the resonances in the methyl region. Two main peaks, assigned to the methyl groups of the major species, are observed along with two peaks of less intensity signifying the minor species. The pattern of peaks in the methylene region indicates that, in each species, the metal ion is bound to the ligand. The COSY spectrum for **6**, taken in acetonitrile, shown in Figure S3,[30] illustrates the cross peaks between the amine protons of both species and their respective methylene protons. One can deduce from the NMR data that for the two species in

Table 6. HPLC Data for Representative Compounds[a]

compound	retention time, min	compound	retention time, min
GaCl(BAT-TM) (**1**)	3.12	GaCl(BAT-HM) (**7**)	3.53
InCl(BAT-TM) (**2**)	3.25	InCl(BAT-HM) (**8**)	3.93
In(SCN)(BAT-TM) (**3**)	3.04	GaCl(BAT-TECH)	7.74
In($O_2CC_6H_5$)(BAT-TM) (**4**)	3.21	InCl(BAT-TECH) (**9**)	9.11

[a] Conditions used: Hamilton PRP-1 column, 25 cm; mobile phase, 90% CH_3CN/10% 50 mM ammonium acetate; pH = 4.6; flow rate 1.00 mL/min; detection UV, 250 nm.

acetonitrile solution (1) the N_2S_2 ligand is bound to the metal ion and (2) the BAT-TM derivatives show a plane of symmetry in solution.

The addition of D_2O (pD = 4.6) to the CD_3CN mimics the mobile phase used in our HPLC experiments and has the advantage of simplifying the spectra due to elimination of the broad resonances of the nitrogen atoms and their coupling to the four adjacent methylene protons. Further, the addition of D_2O often results in an increase in the minor species to ca. 30−50% upon addition of D_2O in the M(BAT-TM)-Cl (**1**, **2**) and M(BAT-TM)SCN (**3**, **6**) derivatives. Figure 7b shows the one dimensional spectrum for Ga(NCS)(BAT-TM) (**6**) in CD_3CN/D_2O (pD = 4.6); an expansion of the methylene region is shown in Figure 7c. The chemical shift assignments are given in Table 5. Figure S4 shows the COSY spectrum for and GaNCS(BAT-TM) (**6**) in CD_3CN/D_2O. Although, we cannot, with these experiments, unambiguously identify the ancillary ligands for both species, it is obvious that each species involves metal−tetradentate N_2S_2 binding; the presence or absence of the ancillary ligands or solvent is in question.

E. HPLC Data. HPLC data for all of the molecules are tabulated in Table 6. For all of the HPLC work, the column used is a Hamilton PRP-1 column, 25 cm, and the mobile phase used is 90% CH_3CN/10% 50 mM ammonium acetate, pH = 4.6, with a flow rate of 1 mL/min. Detection is by ultraviolent absorption at 250 nm. From Table 6, it is clear that the metal ion influences the retention time. GaCl(BAT-HM) and GaCl-(BAT-TECH) have significantly shorter retention times than the indium analogs. The N_2S_2 ligand also influences the retention time; the increasing lipophilicity of the ligand results in an increase in the retention time. The HPLC traces for InCl(BAT-TM), InCl(BAT-HM), and InCl(BAT-TECH) are compared in Figure 8. The ancillary ligand (Cl, SCN, or benzoate), however, appears *not* to influence the retention time. Examination of the indium BAT-TM series in Table 6, shows that the retention times are not affected by the Cl, SCN, or benzoate ligands. Hydrolysis of the ancillary ligand in the acetonitrile/water mobile phase may be occurring, resulting in the observed HPLC measurements, which reflect the $M(N_2S_2)^+$ species.

Isolation and crystallization of $M^{III}N_2S_2$ compounds may require the complexation of an ancillary (axial) ligand to form a neutral compound. The $[M^{III}N_2S_2]^+$ core itself may be quite stable. The stability of this unit may be inferred from observation of the HPLC data in acetonitrile/acetate buffer (pH = 4.6) where the retention time of the complex is apparently determined by the lipophilicity of the N_2S_2 ligand. Also, the addition of water to NMR solvents results, for all compounds, in the delineation of a separate species in which the metal is complexed to the ligand. Finally, the stability constants, log *K*, for Ga(III) and In(III) complexes of BAT-TM have been measured to be 24.73 and 27.34, respectively,[23] further corroborating the stability of the $[M^{III}N_2S_2]^+$ unit.

In gallium (III) and indium (III) complexes of BAT ligands, the steric requirements of the ligand(s) determines the coordination geometry about the metal ion and the geometry of the N_2S_2 ligand. In the molecules, InCl(BAT-TM) (and the Ga analog)

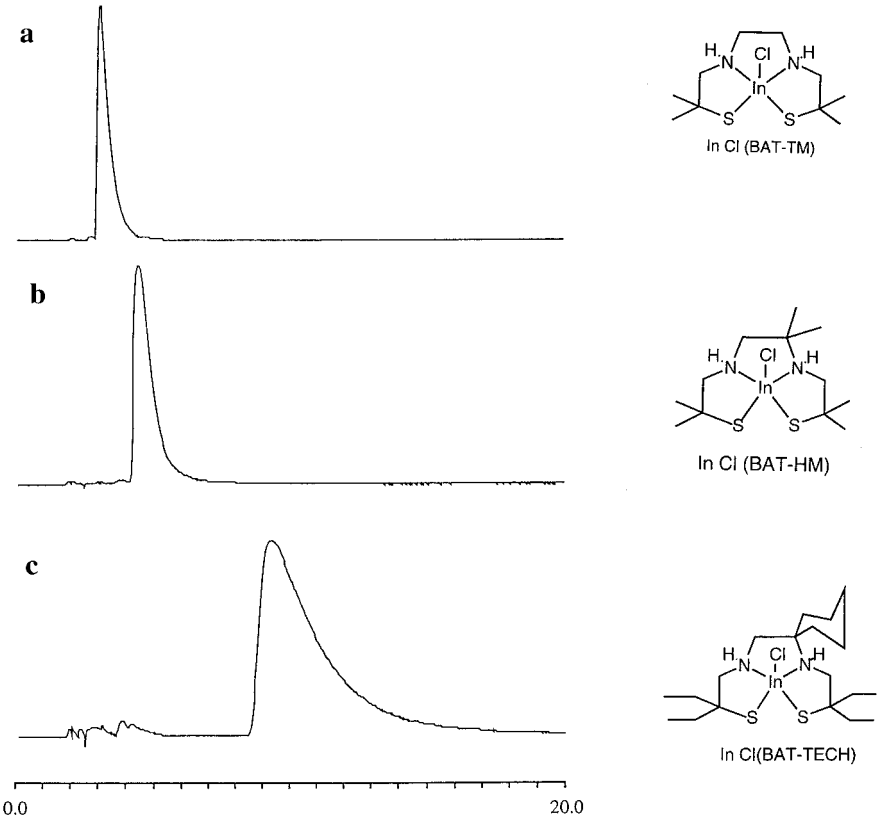


Figure 8. HPLC data for InCl(BAT) complexes. The stationary phase was a Hamilton PRP-1 column; the mobile phase was 90% CH_3CN/10% buffer (50 mM NH_4CH_3COO, pH = 4.6); flow rate = 1.00 mL/min; UV detection at 250 nm. Key: (a) InCl(BAT-TM); (b)InCl(BAT-HM); (c) InCl(BAT-TECH).

the N_2S_2 ligand describes a square pyramidal coordination environment with a very small deviation of the nitrogen and sulfur atoms from the least-squares plane. The BAT-TM ligand in molecule **3**, InSCN(BAT-TM), provides a more distorted square pyramidal coordination environment to the indium(III). Complex **4**, In($O_2CC_6H_5$-*O*,O′)(BAT-TM), shows that the ligand is far distorted from a square pyramid. The metal ion is, in fact, in a distorted octahedral coordination environment, with the N_2S_2 BAT-TM ligand adjusting to accommodate the bidentate binding of the benzoate ligand. In the gallium(III) complex of BAT-TECH, GaCl(BAT-TECH),[27] the analog of compound **9**, the coordination geometry about the gallium is a distorted square pyramid; in this case, the base plane consists of the two nitrogen atoms, one of the sulfur atoms, and the chlorine atom. The axial ligand, the other sulfur atom, is bent by about 10° toward one of the nitrogen atoms. The N_2S_2 ligand adjusts its geometry about the metal ion to accommodate the steric requirements of the ligand(s).

Conclusion

We have prepared novel gallium and indium complexes of bis(amino thiol) (N_2S_2) ligands, where the ancillary ligand can be varied using one of three synthetic methods. A unique feature of the synthetic methods (Scheme 1) developed in this study is the preparation of neutral, organic soluble indium and gallium complexes from completely aqueous precursors. These molecules may serve as starting reagents for exploration of the reactivities of the (N_2S_2)M−R (M = Ga(III), In(III); R = ancillary ligand) species in organic solution.

The solid state coordination geometry about the metal ion and the structures of the gallium(III) and indium(III) N_2S_2 compounds are solely dependent on the steric requirement of the ligand(s). The solution chemistry, probed by proton NMR studies, shows that addition of water to the solvent system, results in formation in 10−50% of a new species, where the N_2S_2 ligand is complexed to the metal ion. The HPLC data consistently indicate that the retention time of the compounds is solely determined by the lipophilicity of the N_2S_2 ligand and not by the ancillary ligand. These observations are consistent with the recently measured stability constants for Ga and In (N_2S_2) complexes.[23]

Using the BAT (N_2S_2) ligand system as a framework upon which to incorporate appropriate moieties which will impart a desired shape and topology to the final molecule, may be useful in designing new ligands for complexation of gallium and indium. Suitable groups when appended to the periphery of the basic N_2S_2 ligand should result in stable, neutral, six- (or seven-) coordinate gallium or indium complexes for evaluation as radiodiagnostic imaging agents.

Acknowledgment. We are grateful to Professor Hank F. Kung for a gift of the BAT-TECH ligand. We acknowledge the following sources of support for this research: Faculty Research Award Program of the City University of New York, Eugene Lang Faculty Development Award, and NIH-Research Centers in Minority Institutions Grant RR03037-08S2. The FAB mass spectrum of compound **5** was generously provided by Columbia University.

Supporting Information Available: Tables S1−S4, giving bond lengths and bond angles for molecules for molecules **1**−**4**, Table S5, giving anisotropic displacement coefficients for molecules **1**−**4**, Table S6, giving H-atom coordinates and isotropic displacement coefficients for molecules **1**−**4**, Table S7, giving NMR data for molecules **1**−**9**, Figure S1, an ORTEP diagram for molecule **2**, Figure S2, showing COSY NMR data for GaCl(BAT-HM), **7**, measured in CD_3CN, Figure S3, showing COSY NMR data for Ga(NCS)(BAT-TM), **5**, measured in CD_3CN, and Figure S4, showing COSY NMR data for Ga(NCS)-(BAT-TM), **5**, measured in 80% CD_3CN/20% D_2O (pD = 4.6) (22 pages). Ordering information is given on any current masthead page.

IC951535+