

Sterically Demanding Multidentate Ligand Tris[(2-(6-methylpyridyl))methyl]amine Slows Exchange and Enhances Solution State Ligand Proton NMR Coupling to $^{199}\text{Hg}(\text{II})$

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The solution state coordination chemistry of $\text{Hg}(\text{ClO}_4)_2$ with tris[(2-(6-methylpyridyl))methyl]amine (TLA) was investigated in acetonitrile- d_3 by proton NMR. Although Hg(II) is a d^{10} metal ion commonly associated with notoriously rapid exchange between coordination environments, as many as six ligand environments were observed to be in slow exchange on the chemical shift time scale at select metal-to-ligand ratios. One of these ligand environments was associated with extensive heteronuclear coupling between protons and ^{199}Hg and was assigned to the complex $[\text{Hg}(\text{TLA})]^{2+}$. The $^5J(\text{H}^{199}\text{Hg}) = 8$ Hz associated with this complex is the first example of five-bond coupling in a nitrogen coordination compound of Hg(II). The spectral complexity of related studies conducted in acetone- d_6 precluded analysis of coordination equilibria. Crystallographic characterization of the T-shaped complex $[\text{Hg}(\text{TLAH})(\text{CH}_2\text{COCH}_3)](\text{ClO}_4)_2$ (**1**) in which two pyridyl rings are pendant suggested that the acidity of acetone combined with the poor coordinating abilities of the neutral solvent adds additional complexity to solution equilibria. The complex crystallizes in the triclinic space group $P\bar{1}$ with $a = 9.352(2)$ Å, $b = 12.956(2)$ Å, $c = 14.199(2)$ Å, $\alpha = 115.458(10)^\circ$, $\beta = 90.286(11)^\circ$, $\gamma = 108.445(11)^\circ$, and $Z = 2$. The Hg–N_{amine}, Hg–N_{pyridyl}, and Hg–C bond lengths in the complex are 2.614(4), 2.159(4), and 2.080(6) Å, respectively. Relevance to development of ^{199}Hg NMR as a metallobioprobe is discussed.

Introduction

Analysis of the solution structure of coordination compounds is complicated by the opportunity for numerous equilibria. Metal ions with d^{10} outer shell electron configuration are especially prone to complex speciation since they do not have strong coordination preferences. On the other hand, the conformational flexibility of d^{10} metal ions makes them ideal candidates for certain protein metal substitution studies. Frequently the goal of metal substitution studies is to introduce a new spectroscopic probe. For example, Cd(II) has proven to be a particularly versatile probe of Ca(II) and Zn(II) coordination sites in metalloproteins by ^{113}Cd NMR. Although ^{199}Hg also has promising NMR characteristics, utilization of ^{199}Hg NMR as a metallobioprobe is restricted to a rather small number of recent studies of iron,¹

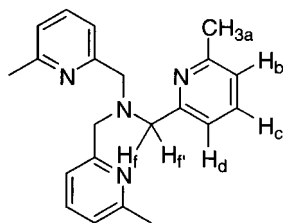
copper,^{2,3} and zinc² metalloproteins. We undertook these studies to further characterize the NMR properties of Hg(II) in biologically relevant coordination environments.

Multidentate ligands geometrically and entropically restrict the number of structures accessible to coordination compounds. Tripodal ligands have been applied extensively to the synthesis of metal complexes because of their ease of preparation, wealth of spectroscopic and X-ray crystallographic data available for their metal complexes, and the predictable changes in the physical properties of the metal

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complex with variation in the ligand. The potentially tetradentate tripodal ligand tris[(2-(6-methylpyridyl)methyl)amine (TLA) was chosen for this study. Stability constants

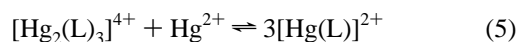
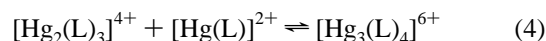
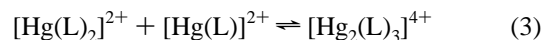
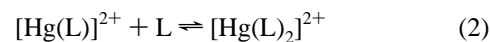
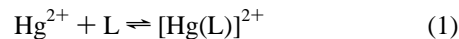


TLA

and thermodynamic data have been reported for 1:1 metal:TLA complexes with 10 metal nitrates.⁴ Complexes of TLA with Ag(I),⁵ Cd(II),⁶ Fe(II),⁷ Fe(III),⁸ Hg(II),⁹ Mn(II),¹⁰ Ni(II)/Ni(III),¹¹ Pb(II),¹² including functional models of copper-containing NO₂⁻ reductases,¹³ and non-heme iron-containing lipooxygenases,¹⁴ catechol dioxygenases,¹⁵ and α -keto acid-dependent enzymes¹⁶ have been structurally characterized. Additional complexes of Ni(II)¹⁷ and Cu(II)¹⁸ have been characterized spectroscopically.

The complexation of Hg(II) by tripodal ligands containing phosphorus and sulfur donor atoms has been examined extensively, and in select cases slow exchange in solution was observed. However, structurally characterized complexes of Hg(II) with tripodal ligands containing exclusively nitrogen donor atoms have only recently been reported.^{9,19} Investigation of the coordination chemistry of Hg(II) is complicated by the tolerance for many different coordination numbers and coordination geometries. Numerous studies have demonstrated that, despite the high thermodynamic stability of Hg(II) complexes, Hg(II) is prone to rapid

exchange in solution among the multitude of ligating groups that it encounters. We recently reported proton nuclear magnetic resonance evidence for the following series of linked equilibria between Hg(ClO₄)₂ and the ligand tris[(2-pyridyl)methyl]amine (TMPA) in acetonitrile:¹⁹



The complexes [Hg(TMPA)₂]²⁺ and [Hg(TMPA)]²⁺ were associated with strong heteronuclear coupling between the protons and carbons of the ligand and ¹⁹⁹Hg(II). Trends in chemical shifts implicated [Hg₂(TMPA)₃]⁴⁺ and [Hg₃(TMPA)₄]⁶⁺ in the exchange of ligand between the 1:1 and 1:2 metal-to-ligand complexes, but the characterization of these complexes was hampered by the low equilibrium constants associated with reactions 3 and 4.

In this study, solution state proton NMR is used to implicate a slight variation on the series of linked equilibria 1–5 in the coordination chemistry of Hg(ClO₄)₂ with tris[(2-(6-methylpyridyl)methyl)] (TLA) in CD₃CN. Depending on the metal-to-ligand ratio and temperature of the sample, as many as six ligand environments were present in slow exchange on the chemical shift time scale, which to our knowledge is unprecedented in mercury coordination chemistry with nitrogenous ligands. Significantly, this ligand system has permitted the first report of ⁵J(¹H¹⁹⁹Hg) in a nitrogen coordinated Hg(II) complex. The spectral complexity of additional studies conducted in acetone-*d*₆ precluded detailed analysis of coordination equilibria. Critical aspects of solvent selection for these studies are discussed in the context of the crystallographically characterized T-shaped complex [Hg(TLAH)(CH₂COCH₃)](ClO₄)₂ (**1**).

Experimental Section

Methods and Materials. Starting materials were of commercially available reagent quality unless otherwise stated. FT-IR spectra were recorded in KBr pellets on a Perkin-Elmer 1600. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, Georgia.

All of the perchlorate salts of mercury(II) complexes included in this work were stable for routine synthesis and purification procedures. However, caution should be exercised because perchlorate salts of metal complexes with organic ligands are potentially explosive.²⁰

Synthesis of Tris[(2-(6-methylpyridyl)methyl)amine (TLA). TLA was prepared by variation of the procedure described by da Mota and co-workers.¹⁷ Freshly prepared 2-chloromethyl-6-methylpyridine²¹ (16.5 g, 117 mmol) was added dropwise with stirring to a solution of sodium bicarbonate (9.8 g, 117 mmol) and 2-(6-

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Table 1. ¹H Chemical Shift Assignments for Complexes of Hg(II) and TLA

complex ^a	chemical shift ^b (ppm)			
	H _a	H _b and H _d	H _c	H _e
▲, 1st precursor to [Hg(TLA) ₂] ²⁺	2.58	7.24, 7.19	7.84	4.11
■, 2nd precursor to [Hg(TLA) ₂] ²⁺	c	7.36, 7.32	7.85	4.12
◆, [Hg(TLA) ₂] ²⁺	2.34	7.08, 7.02	7.57	4.17
△, [Hg ₂ (TLA) ₃] ⁴⁺	2.62	7.24, 7.19	7.72	4.31
□, [Hg ₃ (TLA) ₄] ⁶⁺	2.52	7.17, 7.14	7.65	4.14
○, [Hg(TLA)] ²⁺	2.77	7.46, 7.39	7.91	3.98
◇, [Hg _x (TLA) _y] ²⁺ , x > y	2.44	7.83, 7.74	8.36	4.11

^a Symbols shown are used in Figures 1 and 2 for the corresponding complexes. ^b Nominal [Hg(ClO₄)₂] = 2 mM in CD₃CN at -40 °C. ^c A resonance for these methyl protons could not be identified, possibly because they were indistinguishable from the closely related protons of the first precursor to [Hg(TLA)₂]²⁺.

Table 2. Selected Crystallographic Data for [Hg(TLAH)(CH₂COCH₂)](ClO₄)₂ (1)

empirical formula	C ₂₄ H ₃₀ N ₄ O ₉ Cl ₂ Hg
fw	790.01
space group	triclinic, P $\bar{1}$ (no. 2)
a, Å	9.3525(16)
b, Å	12.956(2)
c, Å	14.199(2)
α, deg	115.458(10)
β, deg	90.286(11)
γ, deg	108.445(11)
V, Å ³	1453.5(4)
Z	2
d _{calc} , mg/m ³	1.805
μ, cm ⁻¹	55.34
radiation (monochromatic)	Mo Kα (λ = 0.710 73 Å)
T, °C	20
R1 ^a	0.0363
R2 ^b	0.0845

$$^a R1 = \sum ||F_o| - |F_c|| / \sum |F_o|. \quad ^b R2 = [\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)]^{1/2}.$$

methylpyridyl)methylamine²² (7.1 g, 58 mmol) in 25 mL of absolute ethanol. The reaction mixture was refluxed for 20 h. The precipitated sodium chloride was removed by vacuum filtration, and the filtrate was evaporated to dryness. The residue was repeatedly recrystallized from hexanes to provide colorless needles with melting point 106–107 °C. Yield 6.6 g (17%). ¹H NMR (CD₃CN): δ 7.58 (t, 3 H, J = 8 Hz, H_c), 7.40 (d, 3 H, J = 7.5 Hz, H_d), 7.04 (d, 3 H, J = 7.5 Hz, H_b), 3.74 (s, 6 H, H_i), 2.44 (s, 9 H, H_g). ¹³C NMR (CD₃CN): δ 160.90 (C_f), 159.25 (C_b), 138.17 (C_d), 122.79 (C_e), 121.52 (C_c), 62.02 (C_g), 25.22 (C_a).

NMR Measurements. All solutions for NMR analysis were prepared by adding stock solutions of mercuric perchlorate in deuterated solvent to a solution of TLA in deuterated solvent using calibrated autopipets. NMR spectra were recorded in 5-mm-o.d. NMR tubes on a General Electric QE-300 operating in the pulse Fourier transform mode. The sample temperature was maintained by blowing chilled nitrogen over the NMR tube in the probe. Chemical shifts were measured relative to internal solvent but are reported relative to tetramethylsilane.

X-ray Crystallography. Selected crystallographic data are given in Table 2, and complete data are given in the CIF file. Data were collected at room temperature on a Siemens P4 four-circle diffractometer using a graphite monochromated Mo Kα X-radiation (λ = 0.710 73 Å) and the θ–2θ technique over a 2θ range of 3°–55°. During data collection three standard reflections were measured after every 97 reflections. The structure was solved by direct methods and Fourier difference maps using the SHELXTL-PLUS²³

Table 3. Selected Bond Distances (Å) and Angles (deg) in [Hg(TLAH)(CH₂COCH₂)](ClO₄)₂ (1)

Hg–N	2.615(4)	N–Hg–C(2)	113.50(17)
Hg–N(1)	2.160(4)	N–Hg–N(1)	73.33(12)
Hg–C(2)	2.082(5)	N(1)–Hg–C(2)	173.17(17)
Hg–O(11)	2.856(4)		
Hg–O(22)	3.160(4)		

package of software programs. Final refinements were done using SHELXL-93.²⁴ All non-hydrogen atoms were refined as anisotropic, the hydrogen atomic positions were fixed relative to the bonded carbons, and the isotropic thermal parameters were fixed.

Preparation and X-ray Diffraction of [Hg(TLAH)(CH₂COCH₃)](ClO₄)₂ (1). Hg(ClO₄)₂ (360 mg, 0.8 mmol) was dissolved in 1.5 mL of acetone and added to a solution of TLA (270 mg, 0.8 mmol) in 3.5 mL of acetone. The solution was slowly diluted with 2 mL of *m*-xylene and set aside for slow evaporation. Colorless X-ray quality crystals formed upon standing for 3 days. Yield 213 mg (34%). mp: 166–168 °C. ¹H NMR (2 mM, DMSO-*d*₆, 20 °C): δ 7.69 (d, J = 7 Hz, 3H), 7.34 (t, J = 6 Hz, 3H), 7.22 (d, J = 6 Hz, 3H), 4.33 (s, 6H), 2.98 (s, 2H), 2.70 (s, 9H), 2.06 (s, 3H). IR (KBr, cm⁻¹): 3084 w, 1673 s, 1603 s, 1573 s, 1460 m, 2930 w, 2853 w, 1358 m, 1223 s, 1094 w, 804 s, 759 m, 642 s. Anal. Calcd for C₂₄H₃₀Cl₂HgN₄O₉: C, 36.49; H, 3.83; N, 7.09. Found: C, 36.60; H, 3.82; N, 7.09.

A crystal measuring 0.20 × 0.58 × 0.27 mm was glued on the end of glass fiber. The data were collected using the θ–2θ technique over a 2θ range of 3°–55°. The crystal turned black in the beam; however, the 4% decay in the intensity of the standards was less than random error so no decay correction was performed on the data. The final data-to-parameter ratio was 19:1.

Results

To investigate the solution state behavior of the TLA complexes of Hg(ClO₄)₂, solutions containing nominally 2 mM metal with discrete molar ratios of TLA in CD₃CN or acetone-*d*₆ were examined by ¹H NMR. Proton NMR spectra highlighting triplet H_c resonances at -40 °C in CD₃CN are shown in Figure 1, and more extensive proton NMR spectra are provided in the Supporting Information (Figure S1). Since integration was impractical for closely spaced peaks, the normalized heights of the center spike of the H_c resonances were used to generate the speciation curves shown in Figure 2. The heights of peaks associated with ¹⁹⁹Hg coupling were corrected for satellite intensity. The heights of incompletely resolved peaks were measured with respect to extrapolations of the sides of adjacent peaks. Although some peaks appeared slightly broadened, corrections were not necessary for the qualitative analysis described.

Analysis of TLA Speciation with Hg(II) in CD₃CN Solution. The proton NMR of TLA consists of singlets for H_a and H_e, doublets for H_b and H_d, and a triplet for H_c. Over the Hg(II)-to-ligand range examined in CD₃CN, H_a resonances were typically small shoulders on the water peak and several H_c resonances were considerably broadened, reflecting environments which were subject to exchange on rates close to the chemical shift time scale (Figure S1). In addition,

(23) SHELXTL-Plus, Version 4.21/V; Siemens Analytical X-ray Instruments, Inc.: Madison, WI, 1990.

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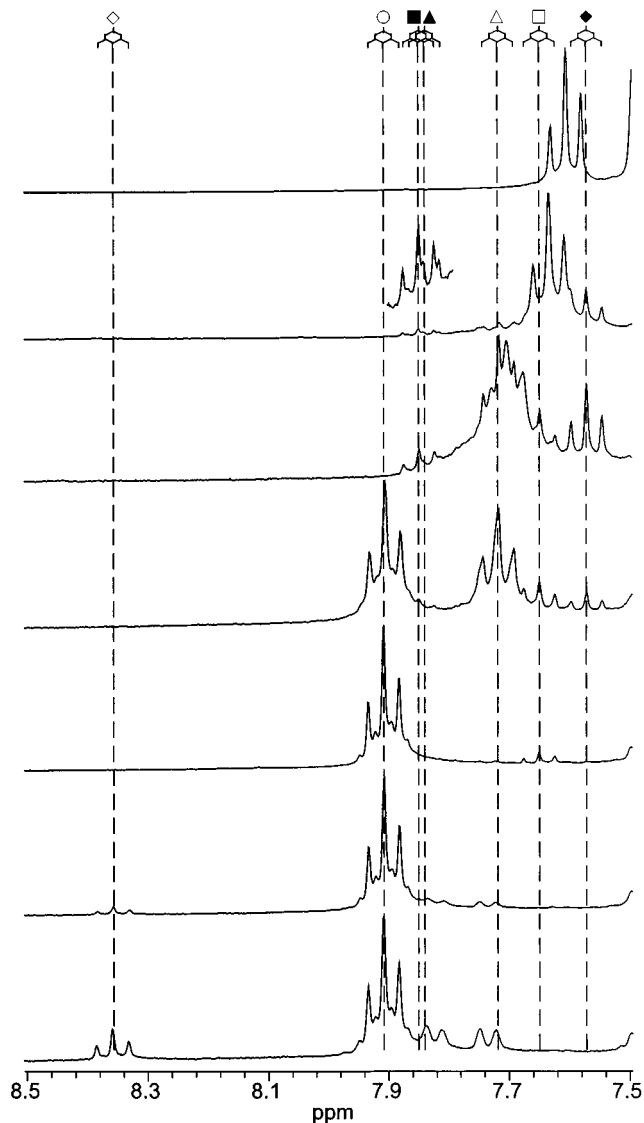


Figure 1. Proton NMR stack plot for H_c at selected ratios of $[\text{Hg}(\text{ClO}_4)_2]/[\text{TLA}]$. Spectra were recorded at -40°C in acetonitrile- d_3 with nominal $[\text{Hg}(\text{II})] = 2\text{ mM}$. From top to bottom $[\text{Hg}]/[\text{TLA}] = 0.00, 0.25, 0.50, 0.75, 1.00, 1.25,$ and 1.50 . Triplets with constant chemical shift are labeled according to species assignments indicated in Figure 2. The doublets in the bottom two spectra are associated with protons H_b and H_d .

the coupling constants for H_c with H_b and H_d are identical and the chemical shift range of their doublets was too narrow to permit definitive resonance assignment (Figure S1). Fortunately, resonances for H_c were observed between 7.5 and 8.5 ppm with very little overlap from other protons (Figure 1).

Eight different resonances were observed for H_c with $\text{Hg}(\text{II})$ -to-ligand ratios up to 1.5 at -40°C . Furthermore, although analysis of the resonances for other protons was not as straightforward, counterparts for these eight H_c resonances were evident and all peaks which appeared reproducibly could be assigned to a chemical species (Table 1). The intensity of the H_c resonances varied independently, suggesting that eight different complexes contributed to the observed spectrum. Six of the eight H_c resonances were observed at 20°C (Figure S2, temperature change in chemical shift $<0.02\text{ ppm}$ for environments with constant

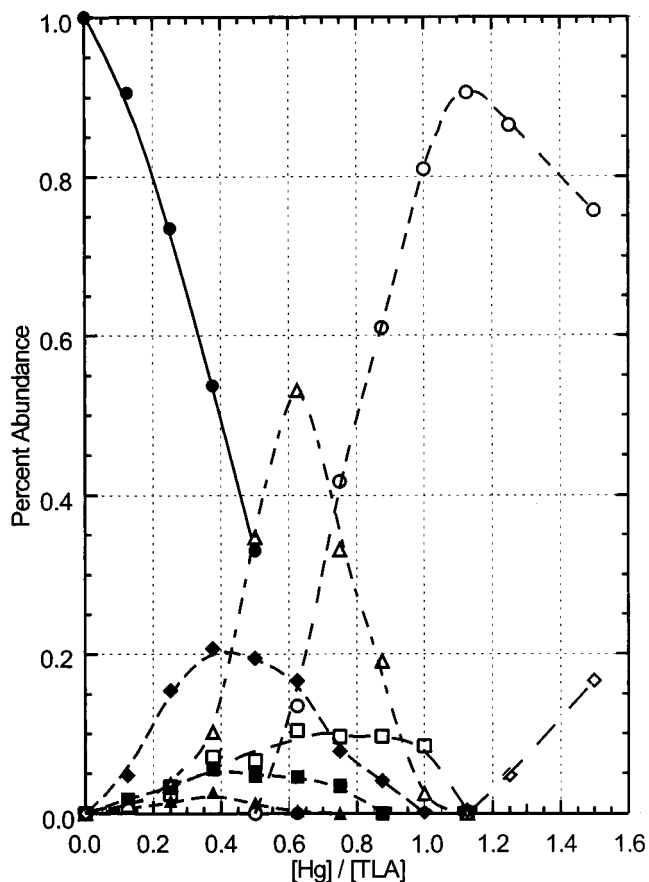


Figure 2. Speciation of acetonitrile solutions of $\text{Hg}(\text{ClO}_4)_2$ and TLA as a function of the metal-to-ligand ratio at -40°C . Percent abundances are based on normalized heights of H_c NMR resonances for each complex. Curves were added to data only to assist visualization. Species assignments (chemical shift (ppm)): ●, TLA in rapid exchange with $[\text{Hg}(\text{TLA})]^{2+}$ (variable); ▲, first precursor to $[\text{Hg}(\text{TLA})_2]^{2+}$ (7.84); ■, second precursor to $[\text{Hg}(\text{TLA})_2]^{2+}$ (7.85); ◆, $[\text{Hg}(\text{TLA})_2]^{2+}$ with eight-coordinate $\text{Hg}(\text{II})$ (7.57); △, $[\text{Hg}_2(\text{TLA})_3]^{2+}$ (7.72); □, $[\text{Hg}_3(\text{TLA})_4]^{2+}$ (7.65); ○, $[\text{Hg}(\text{TLA})]^{2+}$ (7.91); ◇, $[\text{Hg}_x(\text{TLA})_y]^{2+}$ where $x > y$ (8.36).

chemical shift over the $[\text{Hg}]/[\text{TLA}]$ range examined). One of the ligand environments present at both temperatures had a chemical shift which varied approximately linearly with respect to $[\text{Hg}(\text{II})]/[\text{TLA}]$ (Figure S3), while all other environments had constant chemical shifts. The variable chemical shift environment was assigned to free ligand in rapid exchange with a 1:1 $\text{Hg}(\text{II})$ -to-TLA complex according to eq 1. Ideally the change in chemical shift of this environment would be described by eq 6

$$\delta = 7.58\text{ ppm} + (7.90\text{ ppm} - 7.58\text{ ppm})([\text{Hg}(\text{II})]/[\text{TLA}]) \quad (6)$$

where 7.58 and 7.90 ppm are the chemical shifts associated with free TLA and its 1:1 complex with $\text{Hg}(\text{II})$ (vide infra), respectively (Figure S3). As commonly observed in this type of study, the actual chemical shift trend was less steep in slope. Also, this environment was only observed at $\text{Hg}(\text{II})$ -to-ligand ratios up to 0.5, as the free ligand was apparently depleted and the 1:1 $\text{Hg}(\text{II})$ -to-TLA complex was in slow exchange with other complexes at higher metal-to-ligand ratios.

The seven H_c environments with invariant chemical shifts could be grouped according to the $\text{Hg}(\text{II})$ -to-TLA ratio range

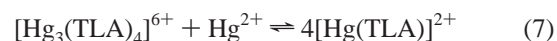
in which they were prevalent. There were three environments that were most prevalent when $[\text{Hg}(\text{II})]/[\text{TLA}] < 0.5$. The mole ratios of these three environments were greatest at $[\text{Hg}(\text{II})]/[\text{TLA}] \cong 0.4$. All three of these environments exhibited a single resonance for H_c (and other protons, see Table 1) requiring rapid exchange among the lutidyl groups of their ligands on the chemical shift time scale. The most abundant of these environments was assigned to an eight-coordinate complex of composition $[\text{Hg}(\text{TLA})_2]^{2+}$. The 7.57 ppm chemical shift of this environment was the only one downfield from free ligand consistent with the previously reported trend for H_c of TMPA and $[\text{Hg}(\text{TMPA})_2]^{2+}$. Furthermore, the concentration of this environment exceeded that of the other two at all $[\text{Hg}(\text{II})]/[\text{TLA}]$ and it was the only one of the three to be observed at 20 °C (Figure S2).

The ligand proton chemical shifts for the other two environments that were most prevalent at low $[\text{Hg}(\text{II})]/[\text{TLA}]$ were similar to each other. Since the relative mole ratios of these two environments vary, they are believed to be associated with different complexes. These environments were not observed for TMPA under similar conditions, suggesting that the 6-methyl groups on the pyridine rings significantly impede the reorganization necessary to achieve an eight-coordinate complex. With the limited information available, it is not possible to make definitive assignments of these two environments. Assignments to complexes with composition $[\text{Hg}(\text{TLA})_2]^{2+}$ and either different geometries or coordination numbers less than eight, as well as to complexes with lower metal-to-ligand ratios, were considered, but all of these suggestions are contestable. Based on analogy to $[\text{Hg}(\text{TMPA})_2](\text{ClO}_4)_2$ in which all Hg–N bond lengths are comparable,¹⁹ relatively small energy differences would be expected between $[\text{Hg}(\text{TLA})_2]^{2+}$ complexes of different geometries.²⁵ Although the 6-methyl groups on the pyridyl rings of TLA might slow geometric isomerism, complexes of identical stoichiometry would be expected to be detectable over the same range of $[\text{Hg}(\text{II})]/[\text{TLA}]$. On the other hand, the substantial energy barriers associated with requisite bond length changes between complexes of type $[\text{Hg}(\text{TLA})_2]^{2+}$ with different coordination numbers provide ample cause for slow exchange. However, the rapid exchange between Hg(II) bound and pendant lutidyl groups necessary for these complexes to exhibit single resonances for each proton necessitates involvement of a species of either lower or higher coordination number. Complexes with lower Hg(II)-to-ligand ratios would be expected to have maximum mole ratios at lower $[\text{Hg}(\text{II})]/[\text{TLA}]$ and to have more difficulty with the structural reorganization necessary to exhibit a single resonance for each type of ligand proton. Furthermore, there is almost no precedent for slow exchange of mono- or bidentate²⁶ nitrogen ligands between Hg(II) complexes in solution. Also, mass balance considerations indicate that detection of the environment representing rapid exchange between free ligand and $[\text{Hg}(\text{TLA})_2]^{2+}$ should cease at the lowest $[\text{Hg}(\text{II})]/[\text{TLA}]$ ratio associated with the

complexes formed. Due to these uncertainties, these environments are referred to simply as the first and second precursors to $[\text{Hg}(\text{TLA})_2]^{2+}$.

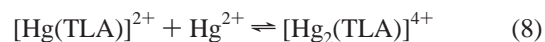
Two additional environments for H_c were present with the three described above, but their maximum mole ratios occurred when $0.5 < [\text{Hg}(\text{II})]/[\text{TLA}] < 1$. One of these environments had a chemical shift of 7.72 ppm for H_c and was present in a higher mole ratio at lower Hg(II)-to-ligand ratios, accounting for as much as 53% of the total TLA. This environment is assigned to $[\text{Hg}_2(\text{TLA})_3]^{4+}$ formed by eq 3 above. The second of these environments had chemical shift 7.65 ppm. Although never accounting for more than 10% of the total TLA, its mole ratio exceeded that of $[\text{Hg}_2(\text{TLA})_3]^{4+}$ at $[\text{Hg}(\text{II})]/[\text{TLA}] = 1$. This environment was assigned to $[\text{Hg}_3(\text{TLA})_4]^{6+}$ formed by eq 4 above. Only one environment for H_c and other TLA protons was associated with each of these complexes, so their structures must allow for rapid intramolecular exchange of all of the lutidyl groups.

The remaining two environments for H_c were prevalent at the higher mole ratios examined and had the most downfield chemical shifts consistent with the commonly observed deshielding influence of greater σ donation to a metal ion. One of these environments had chemical shift 7.90 ppm for H_c . Originally detected at $[\text{Hg}(\text{II})]/[\text{TLA}] = 0.625$, this was the prevalent TLA environment at the higher mole ratios examined. Arguments for assigning this environment to $[\text{Hg}(\text{TLA})]^{2+}$ include its prevalence at the higher Hg(II)-to-ligand ratios and detection of $J(^1\text{H}^{199}\text{Hg})$, which requires that all lutidyl groups must remain bound on the NMR time scale. Le Chatelier's principle suggests that $[\text{Hg}(\text{TLA})]^{2+}$ is formed from $[\text{Hg}_3(\text{TLA})_4]^{6+}$ according to eq 7



as opposed to $[\text{Hg}_2(\text{TLA})_3]^{4+}$ (eq 5) since $[[\text{Hg}_3(\text{TLA})_4]^{6+}]$ exceeds $[[\text{Hg}_2(\text{TLA})_3]^{4+}]$ near $[\text{Hg}]/[\text{TLA}] = 1$.

The environment requiring the highest metal-to-ligand ratio to be observed had H_c chemical shift 8.36 ppm and is assigned to the multinuclear complex $[\text{Hg}_2(\text{TLA})]^{4+}$ formed according to eq 8:



However, alternative assignments for this complex can be envisioned such as $[\text{Hg}_3(\text{TLA})_2]^{6+}$ as long as equilibria giving rise to a single resonance for each type of proton are assumed. Analysis of spectra taken at high metal-to-ligand ratios did not facilitate assignment of this environment, and it was not investigated further.

To supplement these findings, an additional series of spectra were collected with nominal $[\text{Hg}(\text{II})] = 12.5 \text{ mM}$ (data not shown). With the exception of broadening of certain peaks, no notable differences were observed. The peak broadening suggests that there are associative exchange processes for these complexes.

Analysis of $J(^1\text{H}^{199}\text{Hg})$ for complexes of TLA. The $[\text{Hg}(\text{TLA})]^{2+}$ cations had protons coupled to ^{199}Hg when less than 2 mM in acetonitrile. Coupling satellites appeared to be approximately one-fifth the size of the main resonance,

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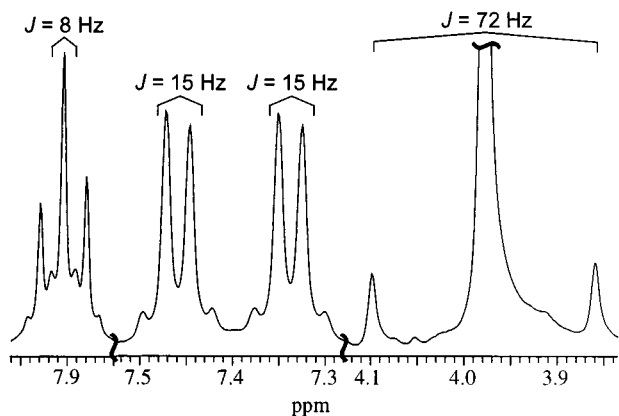


Figure 3. Highlights of the proton NMR of $[\text{Hg}(\text{TLA})]^{2+}$ (2 mM, acetonitrile- d_3 , $-40\text{ }^\circ\text{C}$) indicating the magnitudes of $J(^1\text{H}^{199}\text{Hg})$. A singlet resonance at 2.77 ppm without ^{199}Hg coupling satellites is not shown.

consistent with the 16.8% natural abundance of ^{199}Hg . Coupling was not evident for other complexes. With the exception of $[\text{Hg}(\text{TLA})_2]^{2+}$, the proposed composition of these other complexes requires either pendant or bridging lutidyl groups. Chemical shift averaging due to rapid exchange between the various lutidyl environments in these complexes would preclude detection of coupling. It was somewhat surprising that the methylene protons of $[\text{Hg}(\text{TLA})_2]^{2+}$ were not coupled to ^{199}Hg since a 46 Hz coupling was observed for the related protons of $[\text{Hg}(\text{TMPA})_2]^{2+}$. Exchange between $[\text{Hg}(\text{TLA})_2]^{2+}$ and other thermodynamically stable species may be rapid on the coupling constant time scale even though it is slow on the chemical shift time scale, preventing coupling detection. Alternatively, the Hg– N_{amine} bond through which coupling primarily arises may be elongated in the TLA complex to accommodate the bulk of the added methyl groups, diminishing the magnitude of the coupling constant. The 6-methyl group on the pyridyl rings of TLA replaces the only other proton that was strongly coupled to ^{199}Hg in $[\text{Hg}(\text{TMPA})_2]^{2+}$.

The apparent three-, four-, and five-bond couplings observed between ^{199}Hg and protons of TLA in solutions containing $[\text{Hg}(\text{TLA})]^{2+}$ ($[\text{Hg}(\text{II})]/[\text{TLA}] \geq 0.875$) at room temperature (Figure 3) are notable. The 72 Hz $J(^1\text{H}^{199}\text{Hg})$ to H_e is one of the largest couplings reported for coordination complexes of Hg(II) involving exclusively nitrogen donors and is twice as large as the coupling observed to the methylene protons of $[\text{Hg}(\text{TMPA})]^{2+}$ under similar conditions.¹⁹ Ligand electronics may permit significant, additive coupling contributions from both three- and four-bond paths between the methylene protons and ^{199}Hg when all four nitrogens of TLA are bound. Three-bond coupling constants as large as 30 Hz have been reported for the δ - and ϵ -protons of histidine in mercury-substituted proteins.^{2a} There are 15 Hz $J(^1\text{H}^{199}\text{Hg})$ couplings to both H_b and H_d for which the shortest through bond coupling paths have four bonds. In $[\text{Hg}(\text{TMPA})]^{2+}$, 20 Hz coupling was detected to H_d but coupling to H_b was not resolved. The 8 Hz $^5J(^1\text{H}^{199}\text{Hg})$ to H_c is particularly notable since five-bond scalar coupling has never been reported for small coordination compounds of ^{199}Hg , including the related TMPA complex. Significantly, 20–21 Hz $^5J(^1\text{H}^{199}\text{Hg})$ couplings have been observed to the

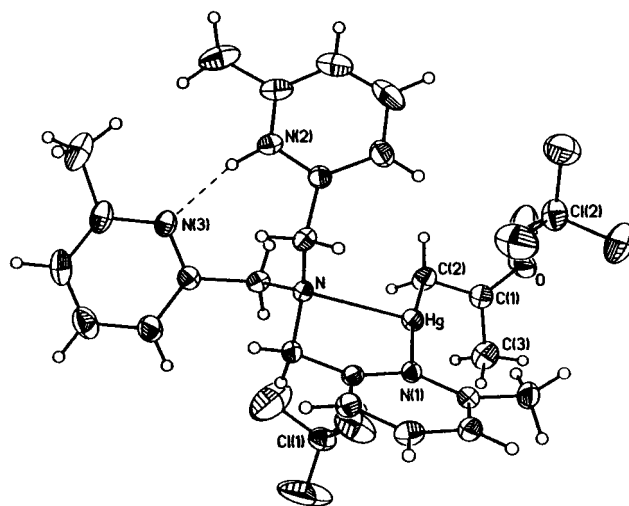


Figure 4. Thermal ellipsoid plot of $[\text{Hg}(\text{TLAH})(\text{CH}_2\text{COCH}_3)](\text{ClO}_4)_2$ (**1**). Ellipsoids are at 50% probability. The pyridinium hydrogen was disordered over pyridine nitrogen atoms N2 and N3 with occupancies of 0.52 and 0.48, respectively. However, in the diagram only the major components of the disordered perchlorate and pyridinium hydrogen are shown.

amide backbone protons of two metal coordinating cysteines in Hg(II)-substituted rubredoxin.¹

Investigation of TLA coordination of Hg(II) in Acetone- d_6 . To complement the studies conducted in CD_3CN , the coordination chemistry of $\text{Hg}(\text{ClO}_4)_2$ with TLA in acetone- d_6 was also investigated briefly. In contrast to the discrete proton environments evident in CD_3CN , in acetone- d_6 under comparable conditions primarily broad, unassignable features were observed in the NMR (data not shown). Similar studies of TMPA revealed comparable behavior with this solvent change.¹⁹ Isolation and crystallographic characterization of the complex $[\text{Hg}(\text{TLAH})(\text{CH}_2\text{COCH}_3)](\text{ClO}_4)_2$ provided some insight into the differences in solution state NMR appearance.

Crystal Structure and Solution State NMR of $[\text{Hg}(\text{TLAH})(\text{CH}_2\text{COCH}_3)](\text{ClO}_4)_2$ (1**).** Although we were keenly interested in correlating the spectroscopic trends observed in acetonitrile- d_3 with complex structure, numerous crystallization attempts failed to produce complexes relevant to the solution state studies in acetonitrile. However, **1** was readily prepared in acetone and suggests additional equilibria complicate analysis of spectra recorded in this solvent. A few 2-oxopropyl mercury derivatives of type $(\text{CH}_3\text{COCH}_2)\text{-HgX}$ ($\text{X} = \text{Cl}, \text{Br}, \text{I}, \text{NO}$) and the diacetonato $(\text{CH}_3\text{COCH}_2)_2\text{-Hg}$ compound have been characterized,²⁷ but few adducts of these derivatives with chelating ligands have been described.^{26,28} The metal coordination sphere in **1** has T-shaped geometry (Figure 4). The metal lies within the

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plane (0.005 Å deviation) of the three donor atoms. The Hg(II) is strongly bound to an oxopropyl carbon atom (Hg–C 2.082(5) Å) and one lutidyl nitrogen (Hg–N(1) 2.160(4) Å) arranged in a nearly linear fashion (C–Hg–N(1) 173.2(2)°). There is a weaker bond to the amine nitrogen of TLA (Hg–N 2.615(4) Å), resulting in a bidentate binding mode for TLA. This is the first structurally characterized metal complex with bidentate TLA coordination. Tetradentate TLA coordination^{7–11,13–16} is most common, although a number of complexes with tridentate TLA coordination^{5,9,13} have been reported previously. In addition, an oxygen atom of each perchlorate is directed at the Hg(II) with distances [Hg–O(11) = 2.856(4), Hg–O(22) = 3.160(4) Å] which are slightly shorter than the sum of the van der Waals radii. Since comparable close contacts have been treated as weak bonds in other Hg(II) complexes,^{26,29} the Hg(II) coordination may also be described as distorted trigonal bipyramidal. This structure is very similar to [Hg(2-(2'-pyridyl)quinoxaline)-(CH₂COCH₃)](ClO₄)₂ in terms of the bond lengths to the organic ligands (within 0.055 Å) and overall geometry.²⁶

The other notable feature of the structure is an apparent hydrogen bond between the nitrogens of the pendant lutidyls. This is apparently the first observation of simultaneous metal chelation and intramolecular hydrogen bond formation by an organic ligand. To preserve charge neutrality, the proton removed from acetone has to remain in the asymmetric unit, and these nitrogens are the strongest bases available for proton binding. The N(2)–N(3) distance of 2.766(7) Å is within the range previously measured for 63 structures with hydrogen bonds between aromatic nitrogens.³⁰ Final refinement of the structure indicated that N(2) is 52% protonated and N(3) is 48% protonated. Distinctions between the lutidyl rings of TLA are lost in dilute DMSO-*d*₆ solution as a single chemical shift averaged set of resonances is observed for the ligand protons of **1**. We expected the NMR spectrum of **1** in DMSO-*d*₆ to possess transient strong ²*J* and ⁴*J* coupling satellites between Hg and the acetonate protons based on spectroscopic characterization of the closely related 2-(2'-pyridyl)quinoxaline compound.²⁶ Since coupling was not detected immediately upon dissolution, we speculate that the proton hydrogen bound to the pendant pyridyl rings may facilitate rapid decomposition of **1** in solution.

Discussion

The excellent chemical shift dispersion for the five unique ligand proton types in TLA presented an opportunity to monitor complex solution coordination equilibria with Hg(ClO₄)₂ in fine detail. Low concentrations and low temperatures enhanced slow exchange on the chemical shift time scale in CD₃CN. The prevalence of rapid exchange in solution state Hg(II) coordination chemistry makes simultaneous observation of as many as six distinct ligand environments with single proton chemical shifts for all

symmetry-related protons very significant. Analysis of differences in relative abundances and ranges of [Hg(ClO₄)₂]/[TLA] over which the resonances were observed led to the conclusion that seven different Hg(II) complexes were associated with the resonances observed in CD₃CN at –40 °C. Although bulkier than the unsubstituted pyridyl rings of TMPA, the 6-methylpyridyl groups of TLA still underwent rapid exchange within individual complexes under the conditions used in this investigation. On the other hand, TLA complexes were less prone to intermolecular exchange than their TMPA counterparts,¹⁹ permitting more extensive characterization of multinuclear complexes.

Coupling between ligand protons and ¹⁹⁹Hg was only detected for [Hg(TLA)]²⁺. The extent of coupling in [Hg(TLA)]²⁺ requires tetradentate binding to TLA. By analogy to [Hg(TMPA)₂]²⁺, detectable heteronuclear coupling was also expected for the methylene protons of [Hg(TLA)₂]²⁺. Significant differences in ligand bonding or small kinetic barriers to exchange with other TLA complexes possibly prevent detection of this coupling. Since structures with 3-fold symmetry are difficult to envision for the other complexes proposed and only one resonance was observed for each proton type, the lutidyl groups of their ligands must be in rapid exchange on the chemical shift time scale.

Based on analysis of NMR data in CD₃CN solution, equilibria 1–4, 7, and 8 are associated with the solution state coordination chemistry of Hg(ClO₄)₂ and TLA. Evidence for additional intermediates early in this series of linked equilibria was also observed, but their compositions and structures were not delineated by these studies. These additional intermediates were not detected in studies of TMPA under similar conditions. Another difference with the TMPA study is the proposed identity of the complex directly preceding formation of [Hg(L)]²⁺ at high metal-to-ligand ratios.¹⁹ Although a species of type [Hg₂(L)₃]⁴⁺ was proposed to form [Hg(TMPA)]²⁺ in the presence of excess Hg²⁺, the mole fractions of both [Hg₂(TMPA)₃]⁴⁺ and [Hg₃(TMPA)₄]⁶⁺ never exceeded 10% and the NMR data did not preclude involvement of the later complex as the intermediate leading directly to formation of [Hg(TMPA)]²⁺.

Although we noted that the discrete TMPA proton environments evident during Hg(ClO₄)₂ coordination studies in CD₃CN became broad, unassignable features when the solvent was changed to acetone-*d*₆,¹⁹ we did not investigate the cause of this changed behavior. Similar spectral changes were observed upon switching the solvent from CD₃CN to acetone-*d*₆ in the TLA studies described herein. The X-ray structure of **1** suggests that introduction of additional equilibria involving acetonate contributes to the differences in spectral behavior. Anderegg and Wenk reported a first *K*_b of 1.5 × 10^{–8} M for TMPA,³¹ and the first *K*_b of TLA is probably comparable. The p*K*_a of acetone (1 × 10^{–20} M) is roughly 5 orders of magnitude greater than that of acetonitrile, so deprotonation of acetonitrile is much less likely in the presence of the organic amine ligands. The difference in coordinating abilities of these two solvents is probably also

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relevant. Acetonitrile is a more coordinating solvent than acetone, and would be better able to complete the coordination sphere of the metal, enhancing the barrier-to-ligand exchange. Complexes of Hg(II) bound to multidentate pyridyl-containing ligands and acetonitrile have been structurally characterized.³²

One of the tremendous advantages of tripodal ligands is the ability to correlate changes in complex structure and properties with changes in the conformation of the ligand. Tetradentate and tridentate binding modes for TLA have been found in complexes previously characterized. In the tridentate TLA complexes, strong metal bonds to at least two other ligands were present. The structure of **1** documents a bidentate binding mode for TLA when protonated. A variety of TLA metal binding modes must be associated with the coordination chemistry of Hg(ClO₄)₂ in CD₃CN to generate the seven discrete proton environments observed. Some of these environments are assigned to multinuclear complexes that must involve bridging ligands. Although slow exchange between bound and pendant pyridyl groups in solution has been demonstrated for tripodal ligands with other metal ions,³³ Hg(II) does not have strong coordination number or geometry preferences to help restrict intramolecular exchange. Intramolecular exchange between the pendant, chelating and/or bridging lutidyl rings of TLA(s) in all seven complexes described was rapid on the chemical shift time scale.

Conclusions

Exchange phenomena frequently complicate interpretation of solution state studies of coordination compounds. While temperature reduction and steric enhancement of ligands are well precedented means of slowing exchange, these measures have rarely been adequate for d¹⁰ metal ions. For Hg(II), the thermodynamic stability of complexes with a particular donor type is typically very high for a range of coordination numbers. Furthermore, the kinetic barriers between Hg(II) complexes tend to be small due to the polarizability of the

outer electron shell of Hg(II). Key elements to slow exchange in the system investigated included use of a coordinating solvent, steric bulk in the vicinity of coordinating groups, and use of a ligand with thermodynamically stable bidentate, tridentate, and tetradentate binding modes.

These studies encourage further development of ¹⁹⁹Hg NMR as a metallobioprobe. The characteristically high thermodynamic stability of Hg(II)–N bonds coupled with the preorganized nature of protein metal binding sites provides conditions strongly favoring formation of slow exchange complexes. In addition, the magnitudes of *J*(¹H¹⁹⁹Hg) in coordination compounds as well as the range of detectable interactions appear to exceed those reported for other transition metal probes. Larger coupling constants enhance the sensitivity of indirect detection NMR experiments, and coupling detectable over a longer range should permit greater structural characterization of protein metal binding sites.

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Supporting Information Available: Figures S1–S4, showing thermal ellipsoid plots and additional NMR data, and an X-ray crystallographic file, in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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