Group 12 complexes of 2,6-bis([(2-pyridinylmethyl)thio]methyl)pyridine: Synthesis and characterization by X-ray crystallography and Proton NMR

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Abstract

New complexes $[\text{ZnL}](\text{ClO}_4)_2$ (**1**), $[\text{CdL}(\text{ClO}_4)]\text{ClO}_4$ (**2**) and $[\text{HgL}](\text{ClO}_4)_2$ (**3**) (**L** = 2,6-bis([(2-pyridinylmethyl)thio]methyl)pyridine) were prepared and characterized by X-ray crystallography and variable temperature ^1H NMR. The ligand had an extended planar conformation when crystallized in pure form and a pentadentate corkscrew conformation with the terminal pyridyl nitrogen on either side of the plane formed by the other three donor atoms in the complexes. Nearly symmetric **1** and symmetric **3** had well separated perchlorates. In contrast, **2** had one bidentate perchlorate leading to a $\text{N}_3\text{O}_2\text{S}_2$ metal coordination sphere. Although rapid intermolecular exchange is common for Group 12 metal ion complexes of simple ligands, in dilute CD_3CN solution slow intermolecular exchange conditions on the δ_{HH} , J_{CdH} and J_{HgH} time scales were found for **1**, **2** and **3**, respectively, at 20 °C and intramolecular reorganization of bound **L** approached the slow exchange limit under cryogenic conditions.

1. Introduction

One of the motivations for comparing the coordination behavior of the Group 12 metal ions with a single ligand is to gain insight regarding their fascinating differences in bioactivity. Functionally, zinc(II) has more physiological diversity than any other essential metal ion, yet sufficient reactivity in free form to warrant tight regulation.[1-4] Both Hg(II) [5] and Cd(II) [6] have multifaceted toxicity, however some microorganisms transcribe a gene encoding a cadmium-containing carbonic anhydrase to contend with marine Zn(II)-depletion.[7, 8] Developing a fundamental understanding of the bioactivity differences between divalent Group 12 metal ions has been hindered by rapid exchange processes and limited spectroscopic handles.

Replacement of native metal ions in preorganized protein metal binding sites continues to be an active area of heavy metal toxicity research.[9] Recent studies have also provided evidence for altering overall protein structure through the interactions of Group 12 metal ions with accessible functional groups in nascent and non-native forms.[10] For example, Zn(II) and Ni(II) have comparable affinities for the unstructured histidine- and cysteine-rich sequences of nickel chaperones[11], suggesting a disruptive role for zinc in nickel homeostasis.[12] In addition, Hg(II)-exposure induced a β -turn structure into the natively unstructured Alzheimer's disease tau construct R3 in vitro,[13] possibly revealing a metal-dependent trigger to the aggregation associated with the pathological positive feedback circle of Alzheimer's disease.[14] In contrast, Cd(II) counteracts amyloid β -peptide 1-42 aggregation in solution.[15] Interestingly, the distribution of structural states for a peptide model of zinc finger proteins was metal-dependent when exposed to substoichiometric amounts of Zn(II), Cd(II) or Hg(II).[16] Significantly, histidine and methionine are common amino acids in unstructured metal binding regions of proteins associated with neurodegenerative diseases[12] and the mechanisms underlying cadmium[17] and mercury[18] neurotoxicity remain elusive despite considerable research.

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4 These intriguing studies have prompted comparative studies of Group 12 metal ion
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6 coordination with multidentate ligand systems, with the goal of analyzing how the ensemble of
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8 ligand conformations varied under similar conditions for the three metal ions. Although the d¹⁰
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10 Group 12 metal ions tolerate a wide range of coordination numbers and coordination geometries
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12 with simple ligands, multidentate ligands can be effective at limiting intermolecular ligand
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14 exchange.[19-22] Furthermore, the facile intramolecular isomerization commonly observed for
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16 mononuclear Group 12 complexes,[19, 23] has been suppressed with the pentadentate ligand
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18 L'.[24] This paper describes the first solid- and solution-state investigation of all three divalent
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20 Group 12 metal ions with a single ligand providing an N₃S₂ set of donor atoms. Known acyclic
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22 ligand 2,6-bis([(2-pyridinylmethyl)thio]methyl)pyridine (L) provides a combination of aromatic
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24 nitrogen and thioether donors capable of forming four fused chelate rings.[25] Commercially
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26 available perchlorate salts were used because of their demonstrated abilities to form complexes
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28 with the inter- and intramolecular exchange properties suitable for ¹H NMR studies with related
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30 ligands.[24] Herein, we show that nearly symmetric [ZnL](ClO₄)₂ (**1**) and symmetric
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32 [HgL](ClO₄)₂ (**3**) have very similar conformations of L and well-separated perchlorates. In
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34 contrast, a bidentate perchlorate in [CdL(ClO₄)](ClO₄) (**2**) produced a new complex with
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36 biscapped square pyramidal coordination geometry. Proton NMR spectroscopy is used to
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38 investigate intermolecular ligand exchange and intramolecular ligand reorganization processes.
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50 **2. Experimental**

51 *2.1 Materials and physical measurements.*

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53 Starting materials were of commercially available reagent quality. The perchlorate
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55 complexes included in this work were stable for routine synthesis and purification procedures.
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58 However, caution should be exercised because perchlorate salts of metal complexes with organic
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ligands are potentially explosive.[26, 27] Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, Georgia. X-ray diffraction data were collected on a Bruker SMART Apex II three-circle diffractometer system with graphite monochromator, Cu K α fine-focus sealed tube ($\lambda = 1.54178 \text{ \AA}$) and CCD detector using ϕ and ω scans. Selected crystallographic data are given in Tables 1 and 2. The structures were solved by direct methods or intrinsic phasing using the SHELXTL program package and refined on F^2 by full-matrix least squares using the SHELXL program package.[28, 29] All non-hydrogen atoms were refined anisotropically; the hydrogen atomic positions were fixed as riding to the bonded carbons with fixed isotropic thermal parameters. Proton NMR spectra were collected in 5 mm o.d. NMR tubes on a Varian Mercury 400VX NMR or Agilent 400-MR DD2 NMR spectrometer operating in the pulse Fourier transform mode. Calibrated autopipets were used to prepare nominally 2 mM solutions for variable temperature NMR measurements by dissolution of elementally analyzed complexes. The sample temperature was maintained by blowing chilled nitrogen over the NMR tube in the probe. Proton chemical shifts were measured relative to internal solvent but are reported relative to tetramethylsilane (TMS). All coupling constants are reported in Hz and J_{HH} unless otherwise noted. Line fit analysis was performed using NUTS - NMR Utility Transform Software 1D Version 1.0.0.1 for Windows 95/NT.

2.2. Synthesis of the compounds

2.2.1. Synthesis of 2,6-Bis([(2-pyridylmethyl)thio]methyl)pyridine (**L**).

The ligand was prepared by variation of the procedure described by Newkome and coworkers.[25] Picolyl chloride hydrochloride (1.0 g, 6.2 mmol) was added to a solution of 2,6-pyridinedimethanethiol (514 mg, 3.0 mmol) and NaOH (500 mg, 12.5 mmol) in 70% EtOH (25

mL). The reaction mixture was refluxed under argon with stirring for 2.5 hours, cooled, and the solvent removed in vacuo. The brown residue was extracted with chloroform (3 x 20 mL). The combined organics were dried over Na₂SO₄ and concentrated in vacuo. Alumina chromatography using 1:1 ethyl acetate:hexane as the mobile phase provide **L** as a viscous yellow oil (757 mg, 71%). Overnight suffusion with a few drops of acetonitrile provided an off-white crystalline material. X-ray quality needles were obtained by slow diffusion of pentane into a concentrated toluene solution of **L**. MP 57.8-59.0 °C. ¹H NMR (CDCl₃) δ 8.54 (d, 2H, ³J_{HH} = 5 Hz, H_a), 7.62 (dt, 2H, ³J_{HH} = 8, ⁴J_{HH} = 2, H_c), 7.58 (t, 1H, ³J_{HH} = 8, H_b), 7.39 (d, 2H, ³J_{HH} = 8, H_d), 7.24 (d, 2H, ³J_{HH} = 8, H_g), 7.15 (dd, 2H, ³J_{HH} = 8, 5, H_b), 3.84 (s, 4H, pyCH₂), 3.80 (s, 4H, pyCH₂); (CD₃CN) δ 8.47 (ddd, 2H, ³J_{HH} = 4.9 Hz, ⁴J_{HH} = 0.9, 2.0 Hz H_a), 7.70 (dt, 2H, ³J_{HH} = 7.9, ⁴J_{HH} = 1.9, H_c), 7.63 (t, 1H, ³J_{HH} = 7.7, H_b), 7.39 (d, 2H, ³J_{HH} = 7.9, ⁴J_{HH} = 1.8 Hz, H_d), 7.24 (d, 2H, ³J_{HH} = 7.8, H_g), 7.19 (ddd, 2H, ³J_{HH} = 7.6, 4.9, ⁴J_{HH} = 1.0 Hz, H_b), 3.82 (s, 4H, CH₂), 3.77 (s, 4H, CH₂).

2.2.2. Preparation and characterization of [Zn**L**](ClO₄)₂ (**1**).

An acetonitrile (1.5 mL) solution of vacuum dried Zn(ClO₄)₂·6 H₂O (26 mg, 71 μmol) was mixed with a solution of **L** (25 mg, 71 μmol) in 0.5 mL acetonitrile and *m*-xylene (5 mL) was added rapidly dropwise. Vacuum filtration and drying provided **1** as a white precipitate (39 mg, 63 μmol, 89% yield). Clear, colorless crystals suitable for X-ray diffraction were obtained by slow evaporation from acetonitrile/*m*-xylene. m.p.: >260 °C. ¹H NMR (dry CD₃CN, 2 mM, 20°C) δ 8.681 (d, 2H, ³J_{HH} = 5.5, H_a), 8.126 (ddd, 2H, ³J_{HH} = 7.9, 7.9, ⁴J_{HH} = 1.2 Hz, H_c), 8.032 (t, 1H, ³J_{HH} = 7.8, H_b), 7.698 (d, 2H, ³J_{HH} = 8.0, H_d), 7.639 (dd, 2H, ³J_{HH} = 7.6, 5.6, H_b), 7.572 (d, 2H, ³J_{HH} = 7.8, H_g), 4.494 (bs, 8H, CH₂). Elemental Analysis C₁₉H₁₉Cl₂N₃O₈S₂Zn: calculated 36.95% C, 3.10% H, 6.80% N; found 36.81% C, 3.03% H, 6.76% N.

2.2.3. Preparation and characterization of [Cd**L**(ClO₄)](ClO₄) (**2**).

An acetone (3 mL) solution of vacuum dried $\text{Cd}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (36 mg, 86 μmol) was added to a solution of **L** (31 mg, 88 μmol) in 1 mL acetone. The solution was filtered through celite, partitioned into 1 mL aliquots and layered with ether for slow diffusion. Yellow crystals suitable for X-ray diffraction formed overnight (36 mg, 54 μmol , 62%). m.p.: 189 °C (dec.). ^1H NMR (acetonitrile- d_3 , 2 mM, 20°C) δ 8.603 (bd, 2H, $^3J_{\text{HH}} = 5.1$, H_a), 8.006 (ddd, 2H, $^3J_{\text{HH}} = 7.6$, 7.6, $^4J_{\text{HH}} = 1.4$, H_c), 7.696 (t, 1H, $^3J_{\text{HH}} = 7.8$, H_b), 7.612 (d, 2H, $^3J_{\text{HH}} = 7.8$, H_d), 7.525 (dd, 2H, $^3J_{\text{HH}} = 5.5$, 7.7, H_b), 7.234 (d, 2H, $^3J_{\text{HH}} = 7.7$, H_g), 4.422 (bs, CH_2), 4.127 (bs, CH_2). Elemental Analysis $\text{C}_{19}\text{H}_{19}\text{CdCl}_2\text{N}_3\text{O}_8\text{S}_2$: calculated 34.34% C, 2.88% H, 6.32% N; found 34.42% C, 2.88% H, 6.28% N.

2.2.4. Preparation and characterization of $[\text{HgL}](\text{ClO}_4)_2$ (**3**).

An acetonitrile (1.5 mL) solution of vacuum dried $\text{Hg}(\text{ClO}_4)_2 \cdot 3\text{H}_2\text{O}$ (32 mg, 71 μmol) was mixed with a solution of **L** (25 mg, 71 μmol) in 0.5 mL acetonitrile and *m*-xylene (5 mL) was added rapidly dropwise with stirring. Vacuum filtration and drying provided **3** as a white precipitate (42 mg, 56 μmol , 78%). Clear, colorless crystals were obtained by slow evaporation from acetonitrile/*m*-xylene and slow diffusion of ether into a solution of **3** in acetonitrile. Crystals were all twinned or modest diffractors. An acceptable structure was obtained in orthorhombic space group *Ibca* at room temperature (Table 1). Upon cooling to 200 K, the crystal underwent a reversible phase change from a body centered to primitive orthorhombic cell with doubling of the *b* axis and unit cell volume (*Pbcn*; $a = 29.5816(4)$; $b = 13.6908(2)$ Å; $c = 23.9607(3)$ Å; $\alpha = \beta = \gamma = 90$; $V = 9704.0(2)$ Å³; $Z = 16$; see Table S1, Table S2 and Fig. S5). A further destructive phase change was observed between 200 and 100 K. m.p.: 156 °C (dec.). ^1H NMR (dry CD_3CN , 2 mM, 20 °C) δ 8.714 (bd, 2H, $^3J_{\text{HH}} = 5.4$, H_a), 8.140 (dd, 2H, $^3J_{\text{HH}} = 7.5$, 7.5, H_c), 7.894 (t, 1H, $^3J_{\text{HH}} = 7.8$, H_b), 7.774 (d, 2H, $^3J_{\text{HH}} = 7.7$, H_d), 7.693 (bdd, 2H, $^3J_{\text{HH}} = 8.5$,

4.0, H_b), 7.441 (d, 2H, $^3J_{\text{HH}} = 7.8$, H_g), 4.550 (bs, 4H, CH₂), 4.337 (bs, 4H, CH₂). Elemental Analysis C₁₉H₁₉Cl₂HgN₃O₈S₂: calculated 30.32% C, 2.54% H, 5.58% N; found 30.37% C, 2.45% H, 5.51% N.

3. Results & Discussion

3.1. Syntheses

A viscous oil of 2,6-bis[*[(*2-pyridylmethyl)thio]methyl]pyridine (**L**) was prepared according to the previously described method.[25] Suffusion with acetonitrile provided a crystalline material with identical ¹H NMR. Slow diffusion of pentane into a concentrated toluene solution of **L** provided needles suitable for X-ray crystallography.

The desired metal complexes were obtained by reaction of **L** with equimolar Zn(ClO₄)₂·6 H₂O, Cd(ClO₄)₂·6 H₂O or Hg(ClO₄)₂·3 H₂O. X-ray quality crystals of [Zn**L**](ClO₄)₂ (**1**) were prepared by slow evaporation from a solution of acetonitrile and *m*-xylene. Slow diffusion of ether into an equimolar acetone solution of Cd(ClO₄)₂·6 H₂O and **L** provided X-ray quality crystals of Cd**L**(ClO₄)]ClO₄ (**2**). Weakly diffracting crystals of [Hg**L**](ClO₄)₂ (**3**) were produced by both slow diffusion and slow evaporation methods with a variety of solvents. The three new complexes had satisfactory elemental analysis.

3.2. Solid State Characterization

The crystalline form of **L** had an extended puckered conformation (Fig. 1). The three pyridyl rings were roughly parallel to each other with the five heteroatoms aligned on one side of the molecule in the solid state. Herringbone crystal packing led to 2D supramolecular sheets with a variety of intermolecular σ–π and offset π–π interactions (Figure S1).

Crystallographic characterization of **1**, **2** and **3** provided the mononuclear cations shown in Figures 2 through 4, respectively. Selected bond distances and angles for these complexes are

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4 shown in Table 2. A disordered perchlorate in complex **1** was satisfactorily modeled using two
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6 positions of roughly equal occupancy. One of the perchlorates in **3** was seriously disordered in
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8 the room temperature structure motivating data collection at a lower temperature. The crystal
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10 underwent a reversible phase change on cooling to 200 K producing two crystallographically
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12 independent but nearly structurally identical molecules of **3** (Table S2).
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17 In complex **1**, the Zn(II) atom is five-coordinated in a distorted trigonal bipyramidal
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19 geometry ($\tau = 0.64$).^[30] The three nitrogens of **L** form the equatorial plane and the ligand
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21 sulfurs occupy apical positions (Fig. 2). The two perchlorates are well-separated from the metal
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23 ion. While the complex does not have true C_2 symmetry, the Zn-N bonds involving the terminal
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25 pyridyl nitrogens are comparable in length and approximately 0.07 Å shorter than the one
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27 involving the central pyridyl. The two Zn-S bonds are also comparable. The $[\text{ZnL}]^{2+}$ complexes
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29 are connected by intermolecular edge-to-face $\sigma-\pi$ interactions between the N2 and N3 pyridyl
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31 rings with 4.95 Å between centroids, generating a 1D supramolecular chain extending along the
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33 b direction (Figure S2). The 1D chains are arranged into 2D sheets through offset parallel face-
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35 to-face $\pi-\pi$ interactions between pairs of N2 pyridyl rings with 4.71 Å between centroids.
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42 In contrast, complex **2** has a seven coordinate Cd(II) atom (Fig. 3). Pentadentate **L**
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44 provides a distorted square pyramidal coordination environment ($\tau = 0.32$). A bidentate
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46 perchlorate caps the basal plan for an overall pentagonal bipyramidal coordination geometry with
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48 the terminal pyridyl nitrogens in apical positions. The second perchlorate is ordered and well-
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50 separated from the metal ion. For comparison, $\tau = 0.13$ for the five **L** donors in the chloride
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52 capped cations of previously reported $[\text{CoLCl}]_2[\text{CoCl}_4] \cdot 2 \text{H}_2\text{O} \cdot 2 \text{MeOH}$ (**4**).^[25] While longer
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54 M-S bond lengths in **2** than **1** could largely be accounted for by the larger van der Waals radius
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56 of cadmium (2.01 Å for Zn, 2.18 Å for Cd),^[31] additional factors such as the higher
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4 coordination number are required to explain the longer M-N bonds in **2**. The central pyridyl was
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6 notably canted from alignment with the Cd-N bond (Cd1-N2-C10 angle 134.7°) in the solid
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8 state. As a result, the metal was 0.515 Å from the S1N2S2 plane and the Cd-N2 bond was
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10 unusually long, permitting formation of 1D chains through intra- and intermolecular offset
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12 parallel face-to-face π - π interactions to N1 pyridyl rings with 3.58 Å and 4.35 Å distances
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14 between centroids, respectively (Fig. S3). Two dimensional sheets are formed from these chains
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16 through offset parallel face-to-face π - π interactions between pairs of N3 pyridyl rings with 3.89
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18 Å centroid separations. Strong intraligand π - π interactions were reported previously in
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21 [Ag₃L₂](NO₃)₃. [32]
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27 Complex **3** has an N₃S₂ metal coordination sphere with well-separated perchlorate ions,
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29 similar to complex **1** (Figure 3), but with a C₂ symmetric distorted square pyramidal geometry (τ
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31 = 0.27). The Hg-N2 bond length is 0.128 Å longer than the Hg-N1 bond lengths in complex **3**.
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33 Intermolecular offset parallel face-to-face π - π interactions between pairs of N1 pyridyl rings
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35 with 4.34 Å centroid separation were observed (Fig. S4). Upon cooling to 200 K, this centroid
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37 separation shortened to 3.61 Å, likely contributing to the phase change observed (Fig. S5). In the
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39 room temperature structure, the N2 pyridyl rings are sandwiched between a pair of N1 pyridyl
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41 rings from adjacent molecules forming stabilizing intermolecular edge-to-face σ - π interactions
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43 with a 4.97 Å centroid separation, generating a 2D sheet in the bc plane (Fig. S4).
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50 Although the five M-L bonds provide metal coordination geometries in mononuclear
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52 cations with τ ranging from 0.13[25] to 0.64, the ligand has a similar corkscrew conformation in
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54 the mononuclear cations of **1-4**. The two terminal pyridyl nitrogen are involved in the largest N-
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56 M-N bond angle amongst all four complexes, and this is the largest bond angle in complexes **2**
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58 and **4** where a capping ligand is located between the terminal pyridyl rings. The S-M-S bond
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angle is largest in complexes **1** and **3** and second largest in complex **2** and **4**. An alternative ligand conformation with only one terminal pyridyl nitrogen displaced from the plane formed by the other four donor atoms has been observed for some metal ion complexes of **L'**. In the latter conformation, the largest N-M-N bond involved the central pyridyl nitrogen and one terminal pyridyl nitrogen.[24] The rigidity of the central portion of **L** and bulkiness of the terminal groups make other conformations unlikely for these types of ligands.[24]

3.3. Solution State Characterization

Solution ^1H NMR spectroscopy was used to investigate intermolecular exchange and intramolecular ligand reorganization processes for **L** with Group 12 perchlorate salts under similar conditions. Preliminary spectra were recorded for dilute solutions of **1**, **2** and **3** in CD_3CN (Fig. S6) and acetone- d_6 (data not shown) over the solvent accessible temperature ranges. Similarity of the ^1H NMR for the three complexes in the two solvents suggests solvent does not have a role in the dynamic behavior observed. Ligand protons were shifted downfield by the presence of each metal salt. The deshielding effects of Zn(II) and Hg(II) were comparable to each other and greater than those of Cd(II), as also observed for complexes of **L'**.

To investigate whether ligand dissociation contributed to differences in ^1H NMR peak width for **1**, **2** and **3** (Fig. S6), titration of **L** with each metal salt was monitored by ^1H NMR spectroscopy.[33, 34] As shown in Figure 5, separate resonances are observed for each symmetry related pyridyl proton of **1** and free **L** at 20 °C in CD_3CN when $[\text{Zn}(\text{ClO}_4)_2]/[\text{L}] < 1$, with no further change in proton chemical shift at modestly higher metal to ligand ratios. These observations are consistent with slow intermolecular exchange between **1** and excesses of either ligand or $\text{Zn}(\text{ClO}_4)_2$. Note that the two singlets for the methylene protons of **L** are replaced by

one sharp singlet and one resonance broadened to obscurity as **1** is formed under these conditions, indicating an intramolecular reorganization process occurring on an intermediate rate relative to the chemical shift time scale. In contrast, solutions with $[\text{Cd}(\text{ClO}_4)_2]/[\text{L}] < 1$ and $[\text{Hg}(\text{ClO}_4)_2]/[\text{L}] < 1$ had a single resonance for each symmetry-related ligand proton with a chemical shift corresponding to a mole fraction weighted average of **L** with **2** and **3**, respectively (Fig. 6). The rapid intermolecular ligand exchange observed for the larger Group 12 congeners is considerably more common for complexes of d^{10} metal ions, especially with low coordination number ligands. Significantly, the proton chemical shifts for **2** and **3** became invariant at $[\text{M}(\text{ClO}_4)_2]/[\text{L}] > 1$. Furthermore, excess M(II) permitted collection of ^1H NMR with sufficiently narrow peaks widths for detection of extensive heteronuclear coupling interactions between protons of **L** and the high natural abundance spin $I = 1/2$ metal nuclei $^{111/113}\text{Cd}$ (Fig. 7c, d) and ^{199}Hg (Fig. 7e, f), providing definitive evidence for slow intermolecular exchange of **L**. The J_{MH} observed for **3** were larger than those observed for **2**, and extended over a greater number of intervening bonds, as observed previously for Hg(II) and Cd(II) complexes of related ligands.[19-22, 24, 35, 36] The ^{199}Hg couplings to H_c and H_h provide rare examples of five-bond coupling between these two nuclei in a coordination compound.[20, 22, 24]

The ^1H NMR spectra of **1**, **2** and **3** under slow intermolecular ligand exchange conditions were investigated as a function of temperature to gain insight regarding intramolecular ligand reorganization (Fig. 7). The pyridyl protons of the three complexes were observed as sets of six resonances for symmetry related protons with modest temperature dependence (<1 ppb/ $^\circ\text{C}$). The methylene protons had varying degrees of broadening consistent with conformational reorganization of metal-bound ligand on an intermediate rate relative to the chemical shift time scale.

Dramatic differences in the appearance of the methylene proton resonances for the three complexes as a function of temperature indicated differences in intramolecular ligand reorganization rates. The downfield exchange averaged singlet methylene resonances for the complexes were consistently more narrow than the upfield singlet methylene resonance at 20 °C. The upfield methylene resonance ranged from slightly broadened to broadened to obscurity in the order **2** < **3** < **1**. Significantly, four geminally coupled doublets ($^2J_{\text{HH}} = 16 - 18$ Hz) were observed for the methylene protons of **1** under cryogenic conditions (Fig. 7b), consistent with the approximate C_2 symmetry of the solid-state structure (Fig. 2). Residual broadening of the methylene resonances was still evident at -40 °C in CD_3CN (Fig. 7b) and at -80 °C in acetone- d_6 (data not shown), precluding detailed quantitative analysis of exchange rates. In contrast, under similar conditions slow exchange on the δ_{H} and $^2J_{\text{HH}}$ time scales between asymmetric and two-fold symmetric ligand environments was observed for $[\text{ZnL}'](\text{ClO}_4)_2$. Geminal coupling between the methylene protons of **3** at -40 °C in CD_3CN was also indicated by broad spectral features between 3.8-4.7 ppm (Fig. 7f). The downfield and upfield spectral features integrated to six protons and two protons, respectively. Using line fitting analysis, the very broad upfield feature was fit to a doublet with chemical shift 4.03 ppm and a 15 Hz coupling constant. The downfield feature was fit to pairs of methylene protons with chemical shifts of 4.55 and 4.50 ppm and an 11 Hz geminal coupling constant, along with a much broader upfield shoulder with approximate chemical shift 4.46 and 15 Hz geminal coupling constant. In contrast, the methylene proton resonances for **2** in CD_3CN were broader at -40 °C (Fig. 7d) than at 20 °C (Fig. 7c), however neither set of protons had reach the coalescence point. Assuming **1** and **3** would have comparable peak widths under conditions of no exchange, differences in peak width at -40 °C suggest **L** undergoes slower reorganization when bound to Zn(II) than when bound to Hg(II). Since the

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4 coalescence points for the methylene proton resonances of **2** were not experimentally accessible,
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6 we have no way of assessing $\Delta\delta_{\text{H}}$, $^2J_{\text{HH}}$ or peak widths as the slow exchange limit is approached
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8 and the relative rate of reorganization of **L** when bound to Cd(II) remains unclear. The potential
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10 influence of differential metal-perchlorate interactions on reorganization of metal bound **L** was
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12 not investigated directly, other than to note that variable temperature ^1H NMR behavior remained
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14 constant for **1** - **3** with 5-25% excess $\text{M}(\text{ClO}_4)_2$ (data not shown).
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19 3.3. Correlation of Solid State and Solution State Characterizations 20 21

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23 One of the major challenges associated with investigating divalent Group 12 metal ions is
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25 controlling the donor atoms in the primary coordination sphere. All three metal ions tolerate
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27 coordination numbers up to eight and have a robust affinity for a variety of donor groups. The
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29 crystallographic forms of **1** and **3** have N_3S_2 primary coordination spheres provided exclusively
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31 by one molecule of **L** while **2** had an additional bidentate perchlorate bound to Cd(II). The four
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33 published structurally characterized complexes of Cd(II) bound to a single ligand providing an
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35 N_3S_2 donor set have coordination numbers ranging from six to eight.[37] The comparably sized
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37 Hg(II) ion has commonly had other atoms, including perchlorate oxygen,[38] bound to the metal
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39 with pentadentate N_3S_2 ligands. However, the N_3S_3 crown thioether variant of **L** formed a Hg(II)
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41 five coordinate complex ($\tau = 0.48$) with pendant sulfur.[39] Zinc(II) has a smaller ionic radius
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43 and there are eight structurally characterized complexes where a single N_3S_2 donor ligand
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45 exclusively occupies the primary coordination sphere. However, complexes with other groups,
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47 including perchlorate,[40] bound to the metal ion are more common. In that context, it cannot be
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49 assumed that **1** and **3** remain exclusively five coordinate in solution. However, these complexes
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51 consistently had lower solubility in organic solvents and ligand chemical shifts that were shifted
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53 further downfield with respect to free ligand than **2**, suggesting the relative concentrations of
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[ML]²⁺ and [ML(ClO₄)]⁺ were shifted towards the later with Cd(II) and the former with Zn(II) and Hg(II) under metal saturated conditions.

Based on the corkscrew conformation of **L**, the three new complexes had geometries intermediate between trigonal bipyramidal and square pyramidal in the solid state as indicated by the τ parameter. For d¹⁰ metal ion complexes involving simple ligands, ligand relocation with interconversion of coordination geometries involves numerous simple angular distortions with very modest energy demands. In contrast, the short tethers between donor atoms in unbranched pentadentate **L** and other steric constraints impose an abridged mechanism requiring thioether inversion[41] to isomerize two pairs of symmetric (**5a**, **5b**) and asymmetric (**6a**, **6b**) enantiomers (Figure 8).[24] The three new complexes are capped (**2**), uncapped (**3**) and uncapped with the terminal pyridyl N displaced significantly from the basal plane towards the open position (**1**) variants of **5**. In contrast, structurally characterized Cd(II) and Hg(II) complexes of **L'** were square pyramidal with an apical terminal pyridyl N (**6**) and two perchlorate caps[24] while the Zn(ClO₄) complex was an uncapped distorted trigonal bipyramid (**5**).[42] The methylene protons of **L** and **L'** can act as reporters of solution state conformation producing up to four geminally coupled doublets in conformation **5**, up to eight geminally coupled doublets in conformation **6** and a pair of singlets when conformational exchange is rapid on the chemical shift time scale.

The conformational behavior of structurally related ligands **L** and **L'** were different in the Group 12 perchlorate coordination complexes. Solution studies suggested the N₅ ligand (**L'**) preferentially adopted an asymmetric conformation with all three metal ions in solution at ambient temperature as represented by **6**. [24] No evidence for the symmetric **L** conformation associated with **5** was found for [Hg**L'**]²⁺, but a temperature-dependent equilibrium between the ligand conformations of **5** and **6** was suggested by the proton NMR behavior for the other Group

12 metal ions. In contrast, no more than four methylene proton environments were observed for **1-3** suggesting solution and solid state conformation are comparable and the conformation of metal bound **L** associated with **6** is transient under accessible solution conditions. Intriguingly, the smaller, harder Zn(II) ion was most effective at imposing conformational stability on **L** and the softer Hg(II) ion was most effective at imposing conformational stability on **L'**. Additional studies will be needed to rationalize those differences.

4. Conclusions

Mixed donor ligand 2,6-bis([(2-pyridinylmethyl)thio]methyl)pyridine) was used to provide the first series of structurally characterized Group 12 metal ion complexes involving a common N₃S₂ set of donor atoms. A similar approximately C₂ symmetric coiled conformation was adopted by **L** in [Zn**L**](ClO₄)₂ (**1**), [Cd**L**(ClO₄)]ClO₄ (**2**) and [Hg**L**](ClO₄)₂ (**3**) despite differences in overall coordination number. In acetonitrile solution, the three Group 12 pentadentate ligand complexes were stable to intermolecular exchange with excess metal on the chemical shift time scale, and the Zn(II) complex was additionally stable to intermolecular exchange with excess ligand. All three complexes underwent rapid intramolecular reorganization at elevated temperatures. Under cryogenic conditions, slow intramolecular exchange conditions consistent with a predominantly symmetric ligand conformation were approached for **1** and **3**. A ligand of modest complexity bound to Group 12 metal ions provided a rare example of metal-dependent differences in the ensemble of conformations.

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Table 1. Crystallographic Data for **L**, [Zn**L**](ClO₄)₂ (**1**), [Cd**L**(ClO₄)]ClO₄ (**2**) and [Hg**L**](ClO₄)₂ (**3**)

	L	1	2	3
Empirical Formula	C ₁₉ H ₁₉ N ₃ S ₂	C ₁₉ H ₁₉ Cl ₂ N ₃ O ₈ S ₂ Zn	C ₁₉ H ₁₉ CdCl ₂ N ₃ O ₈ S ₂	C ₁₉ H ₁₉ Cl ₂ HgN ₃ O ₈ S ₂
Formula mass [g mol ⁻¹]	353.49	617.76	664.79	752.98
Crystal Size [mm ³]	0.39 × 0.16 × 0.06	0.24 × 0.24 × 0.21	0.57 × 0.30 × 0.29	0.21 × 0.11 × 0.09
Crystal System	Orthorhombic	Monoclinic	Monoclinic	Orthorhombic
Space Group	<i>Pna</i> 2 ₁	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>c</i>	<i>I</i> bca
<i>a</i> [Å]	12.9828(4)	16.6514(2)	7.3214(5)	13.78080(10)
<i>b</i> [Å]	6.4338(2)	8.49690(10)	33.811(2)	14.8695(2)
<i>c</i> [Å]	21.0820(5)	16.8825(2)	9.8343(7)	24.2789(3)
β [°]	90	98.9630(10)	107.102(3)	90
<i>V</i> [Å ³]	1760.95(9)	2359.46(15)	2326.8(3)	4975.08(10)
<i>Z</i>	4	4	4	8
Radiation (monochromatic)	Cu Kα	Cu Kα	Cu Kα	Cu Kα
<i>T</i> [K]	100(2)	296(2)	100(2)	296(2)
ρ _{calcd} [g cm ⁻³]	1.333	1.739	1.898	2.011
λ [Å]	1.54178	1.54178	1.54178	1.54178
μ [mm ⁻¹]	2.767	5.659	11.792	15.098
Measured reflections	13265	25814	22464	26860
Independent reflections [<i>R</i> _(int)]	2992 [0.0419]	4157 [0.0474]	4075 [0.0524]	2219 [0.1547]
Completeness of data (θ = 67.000°)	99.8%	98.8%	98.1%	100%
Data / restraints / parameters	2992 / 1 / 218	4157 / 0 / 326	4075 / 0 / 316	2219 / 145 / 181
<i>R</i> 1 ^{<i>a</i>} , <i>wR</i> 2 ^{<i>b</i>} [<i>I</i> > 2σ(<i>I</i>)]	0.0571, 0.1545	0.0486, 0.1382	0.0525, 0.1291	0.0637, 0.1921
<i>R</i> 1 ^{<i>a</i>} , <i>wR</i> 2 ^{<i>b</i>} (all data)	0.586, 0.1566	0.0519, 0.1408	0.0528, 0.1292	0.0822, 0.2113
GOOF	1.087	1.046	1.369	1.027

$$^a R1 = \sum ||F_o| - |F_c|| / \sum |F_o|, \text{ and } S = [\sum [w(F_o^2 - F_c^2)^2] / (n - p)]^{1/2}$$

$$^b wR2 = [\sum [w(F_o^2 - F_c^2)]^2 / \sum [w(F_o^2)^2]]^{1/2}$$

Table 2. Selected bond lengths (Å) and bond angles (°) for [ZnL](ClO₄)₂ (**1**), [CdL(ClO₄)](ClO₄) (**2**), and [HgL](ClO₄)₂ (**3**).

	1	2	3^a
M1-N1	2.024(3)	2.310(5)	2.258(11)
M1-N2	2.095(3)	2.464(5)	2.387(14)
M1-N3	2.019(3)	2.256(5)	
M1-S1	2.5108(10)	2.6489(17)	2.632(3)
M1-S2	2.4706(9)	2.7225(17)	
M1-O1		2.585(5)	
M1-O2		2.591(5)	
N1-M1-N2	122.72(12)	78.66(19)	113.8(2)
N1-M1-N3	127.19(12)	165.7(2)	132.4(5)
N1-M1-S1	81.35(9)	77.81(14)	78.9(3)
N1-M1-S2	99.80(9)	111.64(14)	114.4(3)
N1-M1-O1		81.39(17)	
N1-M1-O2		78.39(17)	
N2-M1-N3	110.08(11)	115.56(19)	
N2-M1-S1	82.28(8)	77.81(14)	74.24(8)
N2-M1-S2	84.87(8)	72.85(14)	
N2-M1-O1		140.86(17)	
N2-M1-O2		149.16(17)	
N3-M1-S1	105.97(8)	103.05(14)	
N3-M1-S2	85.14(8)	75.73(15)	
N3-M1-O1		87.46(18)	
N3-M1-O2		87.84(18)	
S1-M1-S2	165.30(4)	146.24(5)	148.48(15)
S1-M1-O1		129.82(11)	
S1-M1-O2		77.43(11)	
S2-M1-O1		83.93(11)	
S2-M1-O2		135.44(11)	
O1-M1-O2		53.75(15)	

^a Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1/2,z+0; #2 -x+3/2,y+0,-z+0; #3 x+0,-y+1,-z+1/2

List of Captions

Figure 1. Ortep structure of **L**, showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 50% probability.

Figure 2. Ortep structure of $[\text{ZnL}]^{2+}$ (cation of **1**), showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 50% probability.

Figure 3. Ortep structure of $[\text{CdL}(\text{ClO}_4)]^+$ (cation of **2**), showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 50% probability.

Figure 4. Ortep structure of $[\text{HgL}]^{2+}$ (cation of **3**), showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 30% probability.

Figure 5. ^1H NMR (400 MHz, CD_3CN , 20 °C) of nominally 2 mM **L** with added $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ with approximate $[\text{Zn(II)}]/[\text{L}]$ of (a) 0.25, (b) 0.50, (c) 0.75, (d) 1.00, and (e) 1.25. Proton resonance associated with free **L** and **1** are labeled above and below the spectra, respectively.

Figure 6. Observed chemical shifts for H_c of **L** as a function of nominal $[\text{Cd}(\text{ClO}_4)_2]/[\text{L}]$ (■) and $[\text{Hg}(\text{ClO}_4)_2]/[\text{L}]$ (●) ratios in CD_3CN at 20 °C. Linear trendlines are shown for $[\text{M}(\text{ClO}_4)_2]/[\text{L}] < 1$. The open square and circle correspond to the chemical shift observed for H_c of **2** and **3**, respectively, under comparable conditions. Chemical shift trends for the other protons of **L** as a function of $[\text{Cd}(\text{ClO}_4)_2]$ and $[\text{Hg}(\text{ClO}_4)_2]$ are shown in Figures S7 and S8, respectively.

Figure 7. Selected ^1H NMR (400 MHz, CD_3CN , nominally 2 mM) of complexes: **1** at (a) 60 °C and (b) −40 °C; **2** with ~10% excess $\text{Cd}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ at (c) 20 °C and (d) −40 °C; **3** with ~10%

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4 excess $\text{Hg}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ at (e) 20 °C and (f) –40 °C. Aromatic proton labels are provided below
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6 their resonances in the lower temperature spectrum for each complex and shifted downfield at
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8 higher temperature. Heteronuclear $^3J(^{111/113}\text{Cd}^1\text{H})$ and $^3J(^{199}\text{Hg}^1\text{H})$ couplings are highlighted in
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10 (c) and (d), respectively, with comparable couplings observed at –40 °C unless obscured by peak
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12 broadening. Unlabeled peaks in the region δ 3.8–4.8 ppm are associated with H_e and H_f .
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17 **Figure 8.** Octahedral edge configuration schematic of proposed conformational isomerization for
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19 divalent Group 12 perchlorate complexes of **L**. The sixth coordinate position may be empty or
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21 occupied by perchlorate or solvent; possible capping of triangular faces not shown for clarity.
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23 Letters a and b are used to denote enantiomers. Blue circles = N1 & N3; Red diamonds = S1 &
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25 S2; White circle = N2.
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Scheme 1. Pentadentate ligands

Figure 1. Ortep structure of **L**, showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 50% probability.

Figure 2. Ortep structure of [ZnL]²⁺ (cation of **1**), showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 50% probability.

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Figure 4. Ortep structure of $[\text{HgL}]^{2+}$ (cation of **3**), showing the crystallographic numbering scheme. Thermal ellipsoids are shown at 30% probability.

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Figure 6. Observed chemical shifts for H_c of **L** as a function of nominal [Cd(ClO₄)₂]/[**L**] (■) and [Hg(ClO₄)₂]/[**L**] (●) ratios in CD₃CN at 20 °C. Linear trendlines are shown for [M(ClO₄)₂]/[**L**] < 1. The open square and circle correspond to the chemical shift observed for H_c of **2** and **3**, respectively, under comparable conditions. Chemical shift trends for the other protons of **L** as a function of [Cd(ClO₄)₂] and [Hg(ClO₄)₂] are shown in Figures S7 and S8, respectively.

Figure 7. Selected ^1H NMR (400 MHz, CD_3CN , nominally 2 mM) of complexes: **1** at (a) 60 $^\circ\text{C}$ and (b) -40 $^\circ\text{C}$; **2** with $\sim 10\%$ excess $\text{Cd}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ at (c) 20 $^\circ\text{C}$ and (d) -40 $^\circ\text{C}$; **3** with $\sim 10\%$ excess $\text{Hg}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ at (e) 20 $^\circ\text{C}$ and (f) -40 $^\circ\text{C}$. Aromatic proton labels are provided below their resonances in the lower temperature spectrum for each complex and shifted downfield at higher temperature. Heteronuclear $^3J(^{111/113}\text{Cd}^1\text{H})$ and $^3J(^{199}\text{Hg}^1\text{H})$ couplings are highlighted in (c) and (d), respectively, with comparable couplings observed at -40 $^\circ\text{C}$ unless obscured by peak broadening. Unlabeled peaks in the region δ 3.8–4.8 ppm are associated with H_e and H_f .

Figure 8. Octahedral edge configuration schematic of proposed conformational isomerization for divalent Group 12 perchlorate complexes of **L**. The sixth coordinate position may be empty or occupied by perchlorate or solvent; possible capping of triangular faces not shown for clarity. Letters a and b are used to denote enantiomers. Blue circles = N1 & N3; Red diamonds = S1 & S2; White circle = N2.