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Accommodation of the Irregular Coordination Geometry of Lead(II) by a Square Planar N_2S_2 Ligand and Its Preference for Zinc(II)

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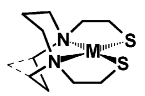
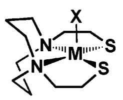
The N_2S_2 ligand, bis-mercaptoethanediazacyclooctane, coordinates to Pb(II) largely through sulfur donors, enlisting a second unit to fulfill an irregular, hemispherical N_2S_3 coordination environment in which a void suggests the location of a stereochemically active lone pair on Pb(II). That the highly exposed lead is vulnerable to metal ion displacement is demonstrated on reaction with zinc which results in a regular square pyramidal coordination about zinc within a $[N_2S_2Zn]_2$ dimer. Analysis of the two dimeric structures finds different connectivities of the monomeric subunits account for the stability of the zinc structure over that of the lead.

The lack of predictability associated with the coordination chemistry of Pb^{2+} has been ascribed to the interplay of electrostatic factors and ligand constraints that might permit the stereochemical activity of lead(II)'s lone pair to be expressed.[1] As articulated by Glusker et al., in an impressive analysis of over 300 structures from the Cambridge Structural Database, a better understanding of the donor arrangements and binding abilities of L in PbL_x and $PbL_xL'_y$ formulations might promote the design of complexing agents specific to the toxic and ubiquitous lead.[2] While patterns of geometrical behavior were not rigorously defined, factors were codified according to those favorable to the "holo-directed" geometries, i.e., those with more or less symmetrical radial distributions of the ligand donor sites, versus the "hemi-directed" geometries which have a void within the coordination sphere, assumed to be occupied by the Pb^{2+} lone pair.

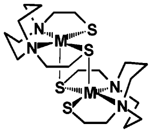
The unique role of tetradentate N_2S_2 ligands in coordination chemistry has been recognized for decades[3] and was recently discovered as a structural motif even in nature.[4,5] Our interest in the bismercaptoethane derivative of diazacyclooctane, the bme-daco ligand, stems from the remarkable array of reactivity exhibited by its nickel complex, **Ni-1**, as well as its scope as a metal-binding agent.[6] Monometallic derivatives include square planar Ni^{II}, Pd^{II}, and Cu^{II} complexes. Other monomeric complexes use the N_2S_2 donor set as a base for a square pyramid in which the apical position is occupied by an oxygen, halide, or nitrosyl ligand.[7] Octahedral derivatives of nickel result from a templated expansion of the donor set while maintaining square planarity in the N_2S_2 set.[8] Binuclear derivatives of Zn, Fe, and Co exist as distorted square pyramidal complexes in which the apical donor atom is a μ-S-thiolate engaged in M_2S_2 cores.[9]



M^{II}: Ni, Pd, (Cu)



M-X: V=O, Ga-Cl, Fe-NO



M: Zn, Fe, Co

The consistency of these structural forms appears to imply a definite ligand constraint or conformation preference for square planar geometry. They furnish small molecule precedents for the carboxamido nitrogen and cysteine sulfur N_2S_2 binding sites found in the Cys-X-Cys amino acid sequences in the active sites of acetyl-coA synthase (which binds nickel(II))[4] and nitrile hydratase (which has an Fe(NO) bound into N_2S_2 in the NO-inhibited form).[5] It is widely held that lead(II) competes with zinc for protein residues such as cysteinyl sulfurs and histidine nitrogen binding sites.[10]

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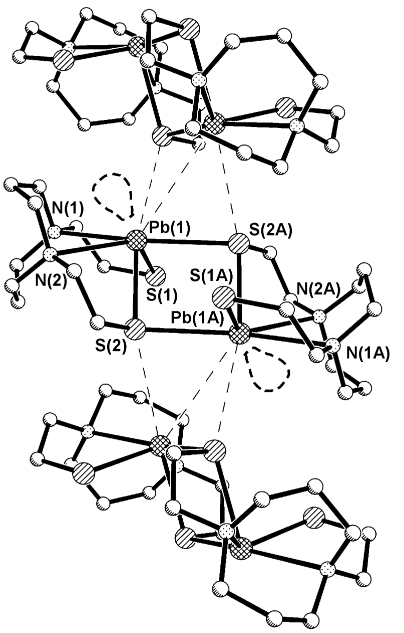

Figure 1. Ball and stick representation of the extended chain of the **Pb-1** dimers. Selected angles (deg): S(1)−Pb−S(2), 89.5(1)°: N(1)−Pb−N(2), 64.0(1)°; N(1)−Pb−S(1), 77.0(3)°, N(1)−Pb−S(2), 106.1(3), N(1)−Pb−S(2A), 158.5°; N(2)−Pb−S(2A), 137.4°; S(2)−Pb−S(2A), 85.47(14)°; Pb(1)−S(2)−Pb(1A), 94.5°. Selected distances (Å): Pb−N(1), 2.787(15); Pb−N(2), 2.814(15); Pb−S(1), 2.619(5); Pb−S(2), 2.732(5); Pb−S(2A), 2.920(4); Pb(1)−Pb(1A), 4.135.

Whether lead might bind into a Cys-X-Cys N_2S_2 binding pocket is not known. As lead is a sulfophile, and with few homoleptic amine complexes fully (structurally) characterized, the study of an N_2S_2Pb complex, the possibility of polarization toward sulfur, and the role of the Pb^{2+} lone pair in determining the coordination geometry about lead were of interest.

Under an inert atmosphere, a methanol solution of $Pb(acac)_2$ was mixed with H_2-bme-daco in toluene to yield a yellow, air-sensitive product that crystallized from a hexane-layered methanol solution. The elemental analysis was consistent with the $[(\text{bme-daco})Pb]_x$, or (**Pb-1**)$_x$, formulation, and *m*/*z* signals in the ESI mass spectrum indicated the presence of both monomeric and dimeric forms. The (**Pb-1**)$_x$ is soluble in polar organic solvents, is poorly soluble in water, and is insoluble in hydrocarbon solvents. The vis−UV spectrum in methanol exhibited an intense band at 320 nm ($\epsilon = 3160\ M^{-1}\ cm^{-1}$), similarly to those assigned to charge-transfer bands of lead thiolates.[11]

The molecular structure was determined by X-ray diffraction studies and is presented in ball-and-stick representations in Figure 1. The fundamental unit of the **Pb-1** structure appears in a dimeric form; nevertheless, the disposition of the bridging thiolate S-donor ligand is entirely different from that found in the Zn, Fe, and Co complexes presented above. The mononuclear **Pb-1** subunit consists of a lead atom bound to two nitrogens, one terminal thiolate sulfur, and one terminal μ-S-thiolate that bridges two of the units. An inversion center relates the two N_2S_2Pb units.

The diazacyclooctane ring produces two fused metallodiazacyclohexane rings in the common chair/boat conformation. The N to S linkers are eclipsed, and the Pb atom is elevated 1.393(1) Å above the best N_2S_2 plane (the mean deviation of N and S from this plane is 0.195 Å). The lead atom is severely displaced from the centroid of this plane toward the sulfurs, resting almost directly over the two sulfur atoms. This polarization results in long Pb−N distances of 2.787(15) and 2.814(15) Å for N(1) and N(2), respectively, some 0.3 Å longer than the Pb−N bond of the 8-mercaptoquinolate N_2S_2 complex.[12] The Pb−S distances show a minor 0.1 Å difference between the lead to terminal sulfur, Pb(1)−S(1) (2.62 Å), and the lead to bridging sulfur, Pb(1)−S(2) (2.73 Å), distances. The Pb(1)−S(2A) and Pb(1A)−S(2) distances in the Pb_2S_2 core of the dimer are, however, longer, 2.92 Å.

The crystal packing diagram shows the dimeric units of (bme-daco)Pb stack along the *b*-axis with Pb and μ-S atoms creating Pb_2S_2 planes that zigzag along a polymeric chain. Interestingly, the Pb···Pb distance between dimers, 4.078 Å, is shorter than the Pb···Pb distance within the dimer, 4.135 Å. The Pb−S connections to adjacent dimers are quite long, 3.5 Å, and not in a position that would indicate “holodirected” coordination. Rather, there is a definite void consistent with stereochemical activity of the lone pair of Pb(II) as indicated in Figure 1. This extremely distorted and hemispherical complex is similar to a recently reported PbO_5 moiety which also aggregates as proximal pairs with intermolecular contacts linking the dimer units.[13] There is no evidence for a long-range interaction at the putative lone pair void in **Pb-1** as was observed in a cationic lead complex recently reported by Hancock et al.[14]

That the exposed lead is vulnerable to displacement was illustrated by reaction with $Zn(acac)_2$. Reaction of the clear yellow methanol solution of (**Pb-1**)$_2$ with $Zn(acac)_2$ hydrate both in stoicheometric and in a 10× excess amounts resulted almost immediately in the precipitation of white $[(\text{bme-daco})Zn]_2$, or (**Zn-1**)$_2$. Interestingly, removal of Pb^{2+} with EDTA was not as rapid. Nevertheless, after 24 h the reaction of EDTA with (**Pb-1**)$_2$ in MeOH also produced a colorless solution with a white precipitate.

The metal ion replacement reactivity is consistent with the relative affinity established for Pb^{2+} versus Zn^{2+} in a series of tetraaza and diazadioxo ligands which also employed daco and related diazacycles as the central rigid framework from which pendant arms contained two additional hard donor sites.[15] Binding constant determinations typically found zinc binding to be several orders of magnitude greater than that of lead. This result was attributed to the selectivity of the diaza cycle for the smaller zinc ion.

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Notably, in some cases, no binding to Pb^{2+} was observed for the ligands with sterically restrictive “doubly connecting bridges”.[15]

While the selectivity for Zn^{2+} versus Pb^{2+} in our study is most likely governed by size preferences imposed by the diazacycle within our ligand and its better match to the smaller Zn^{2+}, it is to be noted that the bme-daco ligand may adopt a configuration in which all binding is through the thiolate sulfurs.[7a] Hence, we were interested in analysis of the ligand conformers that are present in the square planar **Ni-1** complex and the square pyramidal (**Zn-1**)$_2$, as contrasted to that in the (**Pb-1**)$_2$ structure. Deconstruction of the metalated N_2S_2 units required (virtual) removal of the metals and positioning a dummy atom at the centroid of the best N_2S_2 plane. The two nitrogen atoms of the diazacycle and the dummy atom were used as the overlaying points. The nitrogen to sulfur ethylene arms of **Ni-1** are staggered across the N_2S_2 plane, creating a tetrahedral twist of 13.3°. In contrast, the eclipsed arms of (**Pb-1**)$_2$ create a more rigorously planar N_2S_2 donor set. The final overlay of the ligands shows remarkable correspondence despite the fact that the lead atom is 1.39 Å above the best N_2S_2 plane while the nickel atom of **Ni-1** sits within the best N_2S_2 plane.

An even greater similarity of ligand atom positions is seen in the overlay of the “freed” N_2S_2 ligands derived from the lead and zinc derivatives. In both cases, the N to S ethylene links are eclipsed. Comparison of the N_2S_2M units as monomers shows an obvious polarization of the Pb(II) toward sulfurs and a much greater displacement of Pb(II) from the N_2S_2 plane as compared to Zn(II) (1.393 vs 0.216 Å, respectively). The striking structural difference between the zinc and lead dimeric structures is apparent on consideration of the orientation of the monomeric units. Using the diazacyclooctane rings as a point of reference, the inversely related N_2S_2Zn units are stacked face-to-face, vertically, in the (**Zn-1**)$_2$ dimer. In the case of the (**Pb-1**)$_2$ dimer, the severe displacement of lead from the best N_2S_2 plane is accommodated by an end-to-end, horizontal connection of the inversely related N_2S_2Pb units. This arrangement maintains the bme-daco ligand in the configuration most typically seen in its complexes with first- and second-row transition metals, while maximizing sulfur interactions. Although the N_2S_2 ligand used in this study is a model for a Cys-X-Cys N_2S_2 binding site, the qualitative conclusion of specificity for Zn^{2+} is surprisingly consistent with the relative affinity of N_2S_2 donor sets from Cys_2His_2 binding sites.[10,11]

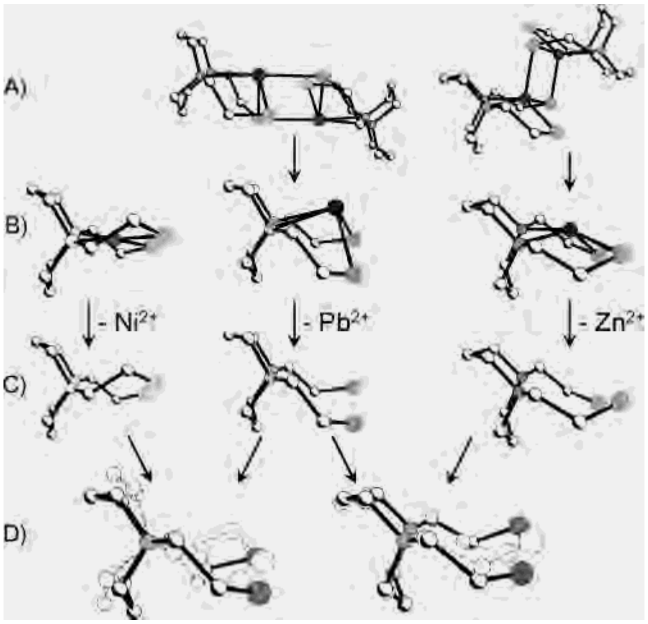

Figure 2. Deconstruction, overlay, and structural comparison of **Ni-1**, (**Pb-1**)$_2$ (shown as solid lines in overlays), and (**Zn-1**)$_2$: (A) dimers, (B) metalated N_2S_2 units, (C) demetalated ligands, (D) ligand overlays.

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Supporting Information Available: Crystallographic data, synthetic procedures, and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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