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Structure and physical properties of several pseudotetrahedral zinc complexes containing a new alkyl thiolate heteroscorpionate ligand

Brian S. Hammes and Carl J. Carrano *

The Department of Chemistry, Southwest Texas State University, San Marcos, TX 78666, USA

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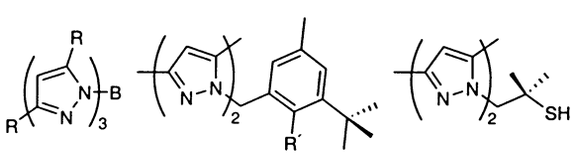
A series of pseudotetrahedral and octahedral zinc(II) complexes of the heteroscorpionate ligand bis(3,5-dimethylpyrazolyl)(1-methyl-1-sulfanylethyl)methane (L3SH) have been synthesized and most characterized by X-ray crystallography. Pseudotetrahedral complexes isolated include [Zn(L3S)(CH_3)], [Zn(L3S)(Cl)], [Zn(L3S)(OAc)], [Zn(L3S)(SPh^{F5})], [Zn(L3S)(SBz)] (Bz = CH_2Ph), [Zn(L3S)($OPh^{p\text{-}NO_2}$)], and [$Zn(L3S)_2$]. In addition, the octahedral complex [$Zn_2\{(L3S)_2Zn\}\{O_2P(OPh)_2\}_4$] was also synthesized. Comparisons between these complexes and those of the corresponding tris(pyrazolyl)borate, Tp^-, or aromatic phenol or benzenethiolate ligands $(L1O)^-$ and $(L2S)^-$ reveal significant differences. Among these is a change in binding of acetate from pure unidentate to anisobidentate as the ligand donor is changed from S to N to O. Trends such as these may aid in understanding how the donor set affects the structure and reactivity at pseudotetrahedral zinc centers in metalloproteins.

Introduction

Zinc is the active metal in the largest group of metalloproteins found in nature. While the biological functions of zinc in these proteins varies considerably, their active sites exhibit a common structural motif.[1] Thus, most active sites are comprised of a pseudotetrahedral zinc center containing a combination of nitrogen, oxygen, and/or sulfur donors, originating from solvent water, and/or histidine, tyrosine, aspartic or glutamic acids, and cysteine residues of the protein itself. It is therefore particularly important to understand how the [$N_xO_yS_z$] donor array modulates the chemistry around a pseudotetrahedral zinc center.

One way to approach this question is to synthesize, structurally characterize, and perform reactivity studies on small synthetic analogs to these zinc metalloproteins. Thus far, the most successful metalloprotein models have utilized tris(pyrazolyl)borate ligands, Tp^R, as a template, which provides a facial array of three nitrogen donors from which a number of pseudotetrahedral zinc complexes of the form LZnX have been prepared.[2–16] However, the tris(pyrazolyl)borate ligand is restricted to providing an all nitrogen (N_3) donor set around the zinc ion, inappropriate for many zinc-containing biomolecules. Recently efforts to synthesize unsymmetrical ligands with mixed N, O, S donor atoms has been undertaken with some success. Vahrenkamp and co-workers have reported a number of tripodal N_3O or N_3S ligands that incorporate carboxylate, phenolate, or thiolate moieties,[17–20] while Parkin and co-workers have synthesized several facially coordinating N_2O or N_2S heteroscorpionate ligands containing thioethers, thioimidazolyl, or carboxylate moieties attached to the B–H group.[21–23] In addition, Riordan and Fenton and co-workers have also explored other tripodal ligands in an effort to achieve the same goal.[24,25] Nevertheless, so far, no single family of easily synthesized complexes containing all the biologically relevant donor atoms have been reported. The synthesis of zinc(II) complexes with thiolate ligands has been especially difficult due to the propensity of the sulfur atoms to bridge and produce oligomeric complexes.[26,27]

We have recently described the synthesis and characterization of two new heteroscorpionate ligands (L1OH and L2SH) which, along with the tris(pyrazolyl)borates, form a family of ligands with the same coordination geometry, charge, *etc.* varying only in the donor set, *i.e.* N_3, N_2O, N_2S.[28–30] Now we continue our investigation of novel heteroscorpionate ligands by introducing a new alkyl thiol heteroscorpionate ligand bis(3,5-dimethylpyrazolyl)(1-methyl-1-sulfanylethyl)methane (L3SH). Reported herein are the synthesis and structural and physical properties for several pseudotetrahedral zinc(II) complexes containing the alkyl thiolate heteroscorpionate ligand $(L3S)^-$ along with comparisons to previous members of this family.



Tp^R | R´ | Name | L3SH
OH | L1OH
SH | L2SH

Experimental

All syntheses were carried out in air and the reagents and solvents purchased from commercial sources and used as received unless otherwise noted. Toluene was distilled under argon over Na–benzophenone. The ligand precursor, bis(3,5-dimethylpyrazolyl) ketone, was prepared using previously reported procedures.[31]

Syntheses

L3SH 1. 2-(Methyldisulfanyl)isobutyraldehyde (5.8 g, 39 mmol) was combined with bis(3,5-dimethylpyrazolyl) ketone (8.43 g, 39 mmol) and $CoCl_2 \cdot 6H_2O$ (0.13 g, 0.46 mmol) in a 100 cm^3 round-bottom flask. The mixture was warmed to 80 °C and stirred for 3 h or until CO_2 evolution had ceased. It was then cooled to room temperature, dissolved in dichloromethane and washed two times with water and once with a saturated solution of NaCl. The organic layer was collected and dried over anhydrous $MgSO_4$. Volatiles were removed under vacuum and the residue was taken up in pentane. Cooling to −20 °C overnight gave 7.1 g (56%) of pure disulfide (L3SSMe). The disulfide intermediate was dissolved in THF and added drop-

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wise to a solution of $LiAlH_4$ (23 ml, 23 mmol) in THF. After addition was complete the mixture was refluxed for 1 h, after which the excess of $LiAlH_4$ was destroyed by careful dropwise addition of water (**CAUTION**: foaming due to H_2 evolution!!). The reaction mixture was then filtered through Celite, and washed with THF and water. Most of the THF was removed under reduced pressure and the resulting oil acidified, extracted with dichloromethane and dried over anhydrous $MgSO_4$. The volatiles were removed under reduced pressure to yield 4.6 g (41% based on 2-(methyldisulfanyl)isobutyraldehyde) of pure L3SH as a colorless oil. Calc. (found) for $C_{14}H_{22}N_4S\cdot0.25\ H_2O$: C, 59.80 (59.43); H, 7.72 (8.03); N, 19.51 (19.80)%. ^{1}H NMR ($CDCl_3$): δ 6.15 (s, 1 H, CH), 5.79 (s, 2 H, Pz H), 2.85 (s, 1 H, S*H*), 2.23 (s, 6 H, Pz CH_3), 2.12 (s, 6 H, Pz CH_3) and 1.69 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 147.71, 140.51, 106.22, 77.92, 49.14, 29.84, 13.77 and 11.53. FTIR (NaCl, cm^{-1}): ν_{SH} 2549.

[Zn(L3S)(CH_3)] 2. A solution of L3SH (0.60 g, 2.2 mmol) in 25 mL of toluene was treated with 1.3 mL of a toluene solution of $Zn(CH_3)_2$ (0.24 g, 2.6 mmol) under argon. The reaction mixture containing the precipitated product was stirred for 1 h and subsequent work-up was performed in air. The white product was filtered off and washed with ether to yield 0.64 g (83%) of [Zn(L3S)(CH_3)]. Calc. (found) for [Zn(L3S)(CH_3)]·$0.28C_6H_5CH_3\cdot0.25H_2O$, $C_{17}H_{26.7}N_4O_{0.25}SZn$: C, 52.54 (52.16); H, 6.94 (6.55); N, 14.42 (14.12)%. ^{1}H NMR ($CDCl_3$): δ 5.95 (s, 1 H, CH), 5.90 (s, 2 H, Pz H), 2.37 (s, 6 H, Pz CH_3), 2.30 (s, 6 H, Pz CH_3), 1.35 (s, 6 H, $C(CH_3)_2$) and −0.55 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 148.85, 140.00, 105.84, 72.81, 47.05, 33.88, 13.06, 11.22 and −15.69.

[Zn(L3S)Cl] 3. A solution of complex **2** (0.31 g, 0.86 mmol) in 30 mL of CH_2Cl_2 was treated dropwise with 1 equivalent of conc. HCl (0.031 g, 0.86 mmol as a solution in CH_2Cl_2). The resulting reaction mixture was stirred for 1 h and concentrated under reduced pressure to yield 0.264 g (81%) of the zinc complex [Zn(L3S)Cl]. Recrystallization was accomplished by slow evaporation of a 1.5:1 CH_2Cl_2–hexane solution. Calc. (found) for [Zn(L3S)Cl]·$0.75H_2O$, $C_{14}H_{22.5}ClN_4O_{0.75}SZn$: C, 42.92 (43.08); H, 5.80 (5.48); N, 14.30 (14.08)%. ^{1}H NMR ($CDCl_3$): δ 5.99 (s, 1 H, CH), 5.98 (s, 2 H, Pz H), 2.44 (s, 6 H, Pz CH_3), 2.40 (s, 6 H, Pz CH_3) and 1.37 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 149.95, 141.05, 106.31, 72.65, 48.21, 33.66, 12.95 and 11.35.

[Zn(L3S)(OAc)] 4. A solution of complex **2** (0.41 g, 1.1 mmol) in 30 mL of CH_2Cl_2 was treated with HOAc (0.068 g, 1.1 mmol) as a solution in CH_2Cl_2. The resulting solution was stirred for 1 h, concentrated under reduced pressure, and layered with hexane. Over a 2 day period [Zn(L3S)(OAc)] crystallized as colorless blocks, which were filtered off and dried under reduced pressure to yield 0.31 g, 69%. Calc. (found) for [Zn(L3S)(OAc)], $C_{16}H_{24}N_4O_2SZn$: C, 47.82 (47.75); H, 6.03 (6.03); N, 13.94 (13.78)%. FTIR (KBr, cm^{-1}): ν_{CO}(OAc^-) 1623, 1375. ^{1}H NMR ($CDCl_3$): δ 5.95 (s, 1 H, CH), 5.94 (s, 2 H, Pz H), 2.38 (s, 6 H, Pz CH_3), 2.36 (s, 6 H, Pz CH_3), 2.14 (s, 3 H, $OC(O)CH_3$) and 1.36 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 179.08, 149.71, 140.70, 106.27, 72.68, 47.90, 33.82, 12.87 and 11.39.

[Zn(L3S)(SPh^{F5})] 5. A solution of complex **2** (0.17 g, 0.48 mmol) in 30 mL of CH_2Cl_2 was treated 1 equivalent of $HSPh^{F5}$ (0.095 g, 0.48 mmol). The resulting solution was stirred for 1 h, concentrated under reduced pressure and crystallized by layering the concentrated CH_2Cl_2 solution with hexane to give [Zn(L3S)(SPh^{F5})] as colorless crystals (0.20 g, 79%). Calc. (found) for [Zn(L3S)(SPh^{F5})]·$0.33C_6H_{12}\cdot H_2O$, $C_{22}H_{27}F_5N_4OS_2Zn$: C, 44.94 (45.09); H, 4.64 (4.35); N, 9.52 (9.37)%. ^{1}H NMR (CD_2Cl_2): δ 5.98 (s, 2 H, Pz H), 5.97 (s, 1 H, CH), 2.42 (s, 6 H, Pz CH_3), 2.39 (s, 6 H, Pz CH_3) and 1.34 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 149.96, 140.93, 106.48, 72.90, 47.98, 31.55, 22.62, 14.08, 13.16 and 11.35.

[Zn(L3S)(SBz)] 6. A solution of complex **2** (0.22 g, 0.60 mmol) in 20 mL of CH_2Cl_2 was treated with a CH_2Cl_2 solution of $PhCH_2SH$ (0.075 g, 0.60 mmol). The resulting solution was stirred for 6 h, dried under reduced pressure and crystallized by layering a CH_2Cl_2 solution of the [Zn(L3S)(SBz)] with hexane to yield 0.19 g (67%). Calc. (found) for [Zn(L3S)(SBz)]·$0.25H_2O$, $C_{21}H_{28.5}N_4O_{0.25}S_2Zn$: C, 53.61 (53.38); H, 6.12 (5.85); N, 11.91 (11.92)%. ^{1}H NMR ($CDCl_3$): δ 7.42 (d, 2 H, *J* 7, $SCH_2C_6H_5$), 7.24 (t, 2 H, *J* 7, $SCH_2C_6H_5$), 7.12 (t, 1 H, *J* 7 Hz, $SCH_2C_6H_5$), 5.95 (s, 1 H, CH), 5.93 (s, 2 H, Pz H), 3.88 (s, 2 H, SCH_2Ph), 2.38 (s, 6 H, Pz CH_3), 2.36 (s, 6 H, Pz CH_3) and 1.38 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 149.92, 145.50, 140.52, 128.35, 128.17, 125.60, 106.21, 72.84, 47.96, 33.84, 30.57, 13.11 and 11.32.

[Zn(L3S)($OPh^{p\text{-}NO_2}$)] 7. A solution of complex **2** (0.18 g, 0.46 mmol) in 20 mL of CH_2Cl_2 was treated with a CH_2Cl_2 solution of *p*-nitrophenol (0.069 g, 0.46 mmol). The resulting solution was stirred for 24 h and dried under reduced pressure to give [Zn(L3S)($OPh^{p\text{-}NO_2}$)] as a light yellow solid. The product was crystallized by layering a concentrated CH_2Cl_2 solution of the complex with hexane to yield 0.19 g (87%). Calc. (found) for [Zn(L3S)($OPh^{p\text{-}NO_2}$)], $C_{20}H_{25}N_5O_3SZn$: C, 49.95 (49.73); H, 5.25 (5.12); N, 14.56 (14.40)%. ^{1}H NMR ($CDCl_3$): δ 8.03 (d, 2 H, *J* 7, $OC_6H_4NO_2$), 6.75 (d, 2 H, *J* 7 Hz, $OC_6H_4NO_2$), 6.03 (s, 1 H, CH), 6.01 (s, 2 H, Pz H), 2.42 (s, 6 H, Pz CH_3), 2.29 (s, 6 H, Pz CH_3) and 1.40 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 149.64, 140.66, 126.54, 118.15, 106.35, 72.62, 48.77, 33.57, 12.98 and 11.31.

[$Zn(L3S)_2$] 8. A solution of complex **4** (0.22 g, 0.54 mmol) in 20 mL of CH_2Cl_2 was treated with a 0.1 M aqueous NaOH solution (4 mL). The resulting solution was stirred for 20 min before separation. The organic layer was dried over anhydrous $MgSO_4$, filtered, dried under reduced pressure and recrystallized from a hexane–CH_2Cl_2 solution to give 0.14 g, 82% of [$Zn(L3S)_2$]. (Calc. (found) for [$Zn(L3S)_2$]·$0.25\ H_2O$, $C_{28}H_{42.5}N_8O_{0.25}S_2Zn$: C, 53.44 (53.69); H, 6.82 (6.75); N, 17.81 (17.64)%. ^{1}H NMR ($CDCl_3$): δ 6.05 (s, 1 H, CH), 5.82 (s, 2 H, Pz H), 2.40 (s, 6 H, Pz CH_3), 2.31 (s, 6 H, Pz CH_3) and 1.59 (s, 6 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 148.75, 140.17, 105.58, 74.06, 49.29, 33.51, 13.73 and 11.87.

[Zn_2{$(L3S)_2Zn$}{$O_2P(OPh)_2$}$_4$] 9. A solution of complex **2** (0.20 g, 0.55 mmol) in 20 mL of CH_2Cl_2 was treated with a CH_2Cl_2 solution of diphenyl phosphate (0.14 g, 0.55 mmol). The resulting solution was stirred for 1 h and dried under reduced pressure to give a sticky white solid. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a 1.3:1 CH_2Cl_2–hexane solution to yield 0.13 g (27%) of the zinc(II) complex. Calc. (found) for [Zn_2{$(L3S)_2Zn$}{$O_2P(OPh)$}$_4$], $C_{76}H_{82}N_8O_{16}P_4S_2Zn_3$: C, 52.22 (52.19); H, 4.74 (4.86); N, 6.41 (6.48)%. ^{1}H NMR ($CDCl_3$): δ 7.21 (br, 32 H, Ar H), 7.03 (br, 8 H, Ar H), 5.94 (s, 2 H, CH), 5.91 (s, 4 H, Pz H), 2.36 (s, 12 H, Pz CH_3), 2.33 (s, 12 H, Pz CH_3) and 1.59 (s, 12 H, $C(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 152.20, 150.29, 141.34, 129.18, 123.55, 120.29, 120.23, 106.42, 72.62, 48.49, 33.56, 12.90 and 11.37.

Physical methods

Elemental analyses were obtained from Quantitative Technologies, Inc., Whitehouse, NJ. All samples were dried *in vacuo* prior to analysis. The presence of solvates was corroborated by FTIR, ^{1}H NMR, or X-ray crystallography. ^{1}H and ^{13}C NMR spectra were collected on a Varian UNITY INOVA 400 MHz NMR spectrometer. Chemical shifts are reported in ppm relative to an internal standard of TMS. The ^{13}C quaternary carbon

peaks that are not observed are a result of either poor solubility and/or overlapping signals. IR spectra were recorded as KBr disks on a Perkin-Elmer 1600 Series FTIR spectrometer and are reported in wavenumbers.

Crystallographic structure determination

Crystal, data collection, and refinement parameters for complexes **3**, **4**, **5**, **8** and **9** are given in Table 1. Crystals of all complexes, except **8**, were sealed in thin-walled quartz capillaries, mounted on a Siemens P4 diffractometer with a sealed-tube molybdenum X-ray source (λ 0.71073 Å) controlled *via* PC computer running Siemens XSCANS 2.1. Crystals of **8** were mounted on a Nonius Kappa CCD diffractometer. The structures were solved using direct methods or *via* the Patterson function, completed by subsequent Fourier difference syntheses, and refined by full-matrix least-squares procedures on F^2. Complex **3** crystallized with two crystallographically independent, but virtually identical, molecules per unit cell. The metrical parameters quoted in the text refer to only one of the molecules but structural parameters of both crystallographically independent molecules are available in the Supporting Information. The asymmetric unit of **9** contains 2 half molecules of CH_2Cl_2, while **5** contains a full molecule of H_2O. All non-hydrogen atoms were refined with anisotropic displacement coefficients, and treated as idealized contributions using a riding model except where noted. All software and sources of the scattering factors are contained in the SHELXTL 5.0 program library.[32]

CCDC reference number 186/2130.

See http://www.rsc.org/suppdata/dt/b0/b004037l/ for crystallographic files in .cif format.

Results

Synthesis and reactivity

The synthesis of L3SH begins with the corresponding heterodisulfide, obtained in reasonable yield *via* the route previously used to prepare other members of this series.[28] Thus bis(3,5-dimethylpyrazolyl) ketone reacted readily with 2-methyldisulfanylisobutyraldehyde as a melt at 80 °C in the presence of $CoCl_2$ as a catalyst. The thio-protected intermediate, L3SSMe, was cleanly reduced with $LiAlH_4$ to yield the desired product. Although the Li^+ salt precipitated from the THF reaction mixture following the reduction, it was contaminated with Al containing solids and difficult to purify. The protonated ligand, L3SH, was therefore isolated by removal of the THF, acidification, and extraction with dichloromethane. Both the lithium salt and the free thiol ligand are sensitive to oxygen and were stored in a dry box.

The complex [Zn(L3S)(CH_3)] proved to be easily prepared and a versatile synthon for the formation of a variety of other pseudotetrahedral [Zn(L3S)X] complexes since it is precipitated in nearly pure form and in >80% yield when dimethylzinc (*ca.* 2 M, in toluene, 10% excess) is added dropwise to a solution of L3SH in toluene. The methyl derivative reacts cleanly with exogenous protic reagents, HX, to liberate methane and form the corresponding [Zn(L3S)X] complex. However, success of the reaction depends on the pK_a of the protic ligand used. Hence, while reactions with HCl, HOAc, *p*-nitrophenol ($HOPh^{NO_2}$) or pentafluorobenzenethiol ($HSPh^{F5}$) proceeded smoothly to produce the desired [Zn(L3S)X] product, water or phenol itself did not. Previously, work done in our laboratory has determined that protic reagents with pK_a <9 (as determined in water) proceeded smoothly to product regardless of donor atom.[28] However for ligands with pK_a at or above 9 the success of the reaction depends upon the thiophilicity of the zinc ion. Thus while $PhCH_2CSH$, pK_a *ca.* 10–11, reacts cleanly to produce the desired products within hours, reactions with phenol or water produced no reaction over 3 d.

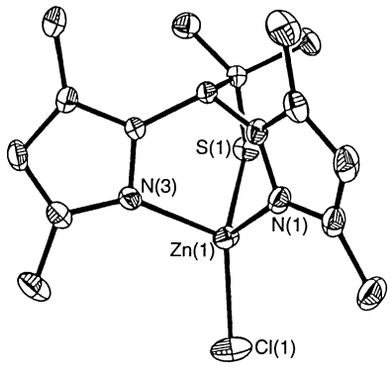

Fig. 1 An ORTEP[33] diagram with 30% thermal ellipsoids for [Zn(L3S)Cl] showing atomic labeling for the coordination sphere only.

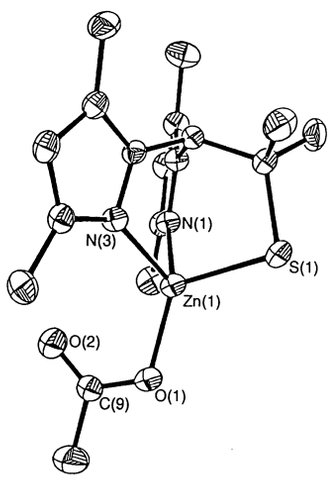

Fig. 2 An ORTEP diagram for [Zn(L3S)(OAc)]. Details as in Fig. 1.

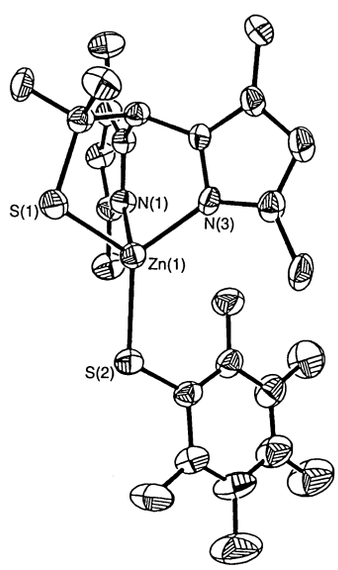

Fig. 3 An ORTEP diagram for [Zn(L3S)(SPh^{F5})]. Details as in Fig. 1.

Molecular structures

Single-crystal X-ray diffraction studies on [Zn(L3S)Cl] **3**, [Zn(L3S)(OAc)] **4**, [Zn(L3S)(SPh^{F5})] **5**, [Zn(L3S)$_2$] **8** and [Zn_2{(L3S)$_2$Zn}{$O_2P(OPh)_2$}$_4$] **9** confirm that $(L3S)^-$, formed by deprotonation of the thiolate sulfur in L3SH, binds to the zinc ion in a tridentate fashion. Selected bond distances and angles for the zinc complexes are shown in Table 2 and Figs. 1–5 show the thermal ellipsoid plots. Additional structural parameters are available in the Supporting Information.

The molecular structures of complexes **3**–**5** confirm the pseudo-tetrahedral coordination geometry. The two pyrazolyl

Table 1 Summary of crystallographic data and parameters for [Zn(L3S)Cl] **3**, [Zn(L3S)(OAc)] **4**, [Zn(L3S)(SPh^{F5})]·H_2O **5**·H_2O, [Zn(L3S)$_2$] **8**, and [Zn{(L3S)$_2$Zn$_2$}{$O_2P(OPh)_2$}$_4$]·CH_2Cl_2 **9**·CH_2Cl_2

	3	**4**	**5**·H_2O	**8**	**9**·CH_2Cl_2
Molecular formula	$C_{14}H_{21}ClN_4SZn$	$C_{16}H_{24}N_4O_2SZn$	$C_{20}H_{23}F_5N_4OS_2Zn$	$C_{28}H_{42}N_8S_2Zn$	$C_{82}H_{76}N_8O_{16}S_2P_4Zn_3$
M	378.23	401.82	559.98	620.19	1838.9
T/K	293(2)	293(2)	293(2)	153(2)	293(2)
Crystal system	Triclinic	Orthorhombic	Monoclinic	Monoclinic	Triclinic
Space group	$P\bar{1}$	$Cmc2_1$	$P2_1/n$	$P2_1/c$	$P\bar{1}$
a/Å	9.905(2)	11.889(2)	8.563(2)	8.7338(2)	10.996(2)
b/Å	13.758(2)	11.694(2)	33.701(5)	14.6710(5)	14.959(2)
c/Å	14.787(3)	13.953(3)	9.454(3)	24.6109(6)	26.801(3)
α/°	67.815(12)				83.64(4)
β/°	87.213(14)		93.58(2)	96.225(2)	84.41(4)
γ/°	71.473(14)				71.78(2)
Z	4	4	4	4	4
V/Å^3	1763.4(5)	1939.9(6)	2722.8(11)	3134.9(2)	4476(3)
μ_{calc}/mm^{-1}	1.661	1.389	1.127	0.948	1.039
No. reflections collected	4499	832	3561	17232	11259
No. unique reflections	4198	828	3297	4884	10983
$R(F)$	0.0371	0.0303	0.0717	0.0418	0.1215
$R_w(F^2)$	0.0940	0.0811	0.2177	0.1077	0.3089

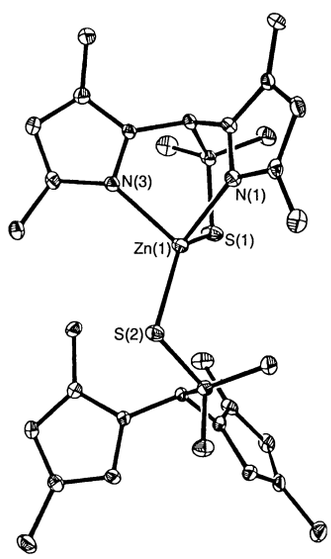

Fig. 4 An ORTEP diagram for [Zn(L3S)$_2$]. Details as in Fig. 1.

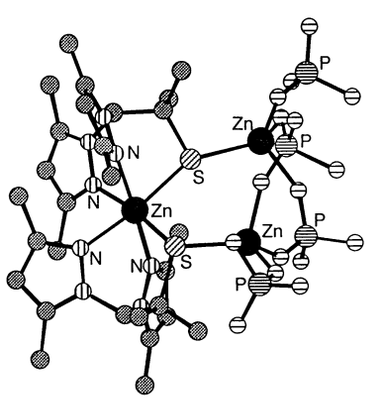

Fig. 5 Structural diagram for [Zn_2{(L3S)$_2$Zn}{$O_2P(OPh)_2$}$_4$] at its present state of refinement. Phenyl rings from the diphenyl phosphates have been removed for clarity.

nitrogens and one thiolate sulfur donor of $(L3S)^-$ constitute the trigonal face of the tetrahedron. The N_{pz}–Zn(1)–N_{pz} bond angles range from 86.65(13)° for [Zn(L3S)Cl] to 90.8(2)° for [Zn(L3S)(OAc)], while the average N_{pz}–Zn(1)–S(1) bond angles range from 96.8(1)° for [Zn(L3S)(SPh^{F5})] to 97.77(7)° for [Zn(L3S)Cl]. All angles are less than the 109.5° expected for idealized tetrahedral geometry due to the "bite" of the tridentate ligand and in all cases the thiolate sulfur supports the largest internal angle. The Zn(1)–S(1) bond distances for **3** and **4** are statistically indistinguishable, 2.249(1) and 2.242(2) Å, respectively; that for **5** was slightly longer at 2.252(3) Å. The Zn(1)–N_{pz} and Zn(1)–S(1) bond distances in **3**–**5** are not unusual and are similar to those reported for other Zn^{II}–N_{pz} and Zn^{II}–$S_{thiolate}$ complexes.[28] The "axial" ligands are positioned perpendicular to the trigonal plane formed by the two pyrazolyl nitrogens and the thiolate sulfur of $(L3S)^-$, resulting in Zn(1)–Cl(1) for **3** and Zn(1)–S(2) for **5** of 2.1907(14) and 2.276(3) Å, respectively. In **5** the S(1)–Zn(1)–S(2) and average N_{pz}–Zn(1)–S(2) bond angles are 114.04(11) and 126.7(1)°, respectively. In complex **4** the acetate is bound in a nearly complete unidentate mode to the zinc ion with a Zn(1)–O(1) bond distance of 1.928(5) Å and a Zn(1)–O(1)–C(9) bond angle of 115.3(5)°. The second acetate oxygen, O(2), is essentially uncoordinated at 2.875 Å away from the zinc.

Table 2 Selected bond distances (Å) and angles (°) for complexes **3**–**5** and **8**[a]

	3	**4**	**5**	**8**
Zn(1)–N(1)	2.079(3)	2.054(3)	2.080(8)	2.069(2)
Zn(1)–N(1)#1		2.054(2)		
Zn(1)–N(3)	2.078(3)		2.034(8)	2.087(3)
Zn(1)–S(1)	2.2488(13)	2.242(2)	2.252(3)	2.2744(11)
Zn(1)–O(1)		1.928(5)		
Zn(1)–S(2)			2.276(3)	2.2306(8)
Zn(1)–Cl(1)	2.1907(14)			
N(1)–Zn(1)–N(3)	86.65(13)		88.4(3)	86.31(10)
N(1)–Zn(1)–N(1)#2		90.8(2)		
N(1)–Zn(1)–S(1)	98.13(10)	97.4(2)	95.4(2)	95.42(9)
N(1)#2–Zn(1)–S(1)		97.4(2)		
N(3)–Zn(1)–S(1)	97.41(10)		98.2(2)	97.48(9)
N(1)–Zn(1)–S(2)			127.8(2)	125.11(8)
N(3)–Zn(1)–S(2)			125.6(2)	114.44(8)
N(1)–Zn(1)–O(1)		121.2(2)		
N(1)#2–Zn(1)–O(1)		121.2(2)		
N(1)–Zn(1)–Cl(1)	117.16(11)			
N(3)–Zn(1)–Cl(1)	118.11(11)			
S(1)–Zn(1)–Cl(1)	129.67(6)			
S(1)–Zn(1)–O(1)		121.8(2)		
S(1)–Zn(1)–S(2)			114.04(11)	127.99(3)
Zn(1)–O(1)–C(9)		115.3(5)		

[a] Numbers in parentheses are estimated standard deviations.

The X-ray structural analyses of [Zn(L3S)$_2$] **8** and [Zn_2{(L-3S)$_2$Zn}{$O_2P(OPh)$}$_4$] **9** show two different coordination modes for complexes of basic chemical formula [Zn(L)$_2$]. For [Zn-(L3S)$_2$] the molecular structure shows an unexpected pseudo-tetrahedral coordination around the zinc(II) ion rather than the

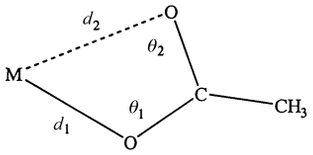

Fig. 6 Parameters used in assigning the coordination mode in acetate complexes.

octahedral geometry implied by the formula. Two pyrazolyl nitrogens and the thiolate sulfur donor from one molecule of $(L3S)^-$ constitute the trigonal face of the tetrahedron. The N(1)–Zn(1)–N(3) bond angle is 86.31(10)° while the average N_{pz}–Zn(1)–S(1) bond angle is 96.45(6)°. The Zn(1)–S(1) and average Zn(1)–N_{pz} bond distances for **8** are 2.2744(11) and 2.078(2) Å, respectively. The second $(L3S)^-$ ligand, which occupies the fourth site in the tetrahedral geometry, is coordinated to the zinc ion only through the thiolate sulfur with a Zn(1)–S(2) bond distance of 2.2306(8) Å and S(1)–Zn(1)–S(2) and average N_{pz}–Zn(1)–S(2) bond angles of 127.99(3) and 119.78(6)°, respectively. Surprisingly the two pyrazole rings from the second $(L3S)^-$ molecule remain uncoordinated and are rotated away from the metal.

For $[Zn_2\{(L3S)_2Zn\}\{O_2P(OPh)_2\}_4]$ **9** the asymmetric unit of the crystal structure contains one zinc ion octahedrally encapsulated by two tridentate L3S moieties with the sulfur donors in a *cis* arrangement. This *cis* arrangement of sulfur donors allows them to bridge to a $(PhO)_2PO_2Zn(\mu\text{-}(PhO)_2PO_2)_2\text{-}Zn(PhO)_2PO_2$ unit to form a trinuclear complex. Unfortunately the only available crystals of **9** diffracted extremely weakly giving a final structure with weighted *R* values well outside the acceptable limits. Thus we choose not to report the structure in detail with full bond lengths and angles, which are in any event unexceptional. Nevertheless the core structure refined nicely and the atom connectivity is unambiguous.

Discussion

With the introduction of $(L3S)^-$ we now a have family of isostructural, isosteric and isoelectronic tripodal ligands providing N_3 $(Tp)^-$, $N_2O_{phenol}(L1O)^-$ and $N_2S_{alkyl/aryl}(L3S)^-$ or $(L2S)^-$ donor spheres to zinc. One of the goals of our research is to see how changing the donor atom, keeping all other variables constant, affects the structure/reactivity at a pseudotetrahedral zinc center. We have now accumulated enough data to begin to describe some potential trends.

In carbonic anhydrase (CA), an enzyme involved in the reversible hydration of CO_2, substitution of the native Zn^{II} by other divalent metals leads to enzymes with decreasing or no activity following the approximate order Zn > Co ≫ Cu,Ni,Cd or Hg.[34,35] The mode of binding (monodentate *vs.* bidentate) of the product, bicarbonate ion, to the metal center has been proposed to be important to this changing reactivity. The structure of human CA I with bicarbonate has shown that the anion binds in a pure unidentate mode while the binding in the cobalt(II) analog is better described as anisobidentate.[34,35] Thus Parkin and co-workers suggested that the varying activity of metal substituted CA can be attributed to a change in bonding of bicarbonate from anisobidentate in the active zinc(II) and cobalt(II) substituted enzymes to a symmetric bidentate mode in the inactive analogs of Cu^{II}, Ni^{II}, Cd^{II} and Hg^{II}. This proposal is based on the structures found for a series of TpM complexes where M = Zn, Co, Ni or Cu, with the nitrate ion (which is isoelectronic with bicarbonate).[34,35] A scheme to describe the denticity of potentially mono- or bi-dentate ligands such as nitrate, bicarbonate or by analogy acetate has been devised based on a combination of M–O distances $d_2 - d_1$/Å and the M–O–X angles $\theta_1 - \theta_2$/° (Fig. 6).[36] Using these criteria, the binding of nitrate to complexes of Zn and Co of sterically bulky tris(pyrazolyl)borate or tris(imidazolyl)phosphine ligands can be described as being anisobidentate while that of the copper and nickel analogs as symmetrical bidentate.[34,35] With the recent discovery of CAs with donor spheres around the zinc that are not N_3O,[37] it becomes of interest to determine if the donor set could also affect the reactivity of the enzyme *via* a changing coordination mode of the bicarbonate ion. Our results with a series of LZn(OAc) complexes show a clear trend. As the donor sphere is changed from N_2SO to N_3O to N_2O_2 (L = L3S, $Tp^{t\text{-}butyl,H}$ and L1O) Δd/Å varies from 0.95 to 0.53 and $\Delta\theta$/° from 44.2 to 25.9, that is from pure unidentate to anisobidentate.[36] This would suggest that the addition of sulfur to the donor sphere should lead to an inherently more reactive CA. Interestingly the recently structurally characterized CA from *Porphyridium purpureum* has been found to have an NS_2O environment around the zinc.[37]

In addition to the structural trends noted above, differences in reactivity at N_2X coordinated zinc centers as the donor atom is changed from N to O to S were also evident. Some of these will be reported in a separate publication[30] but noteworthy in this context is our complete inability to isolate stable zinc hydroxo complexes of the $(L1O)^-$, $(L2S)^-$ or $(L3S)^-$ ligands using any of the methods that work for the analogous $(Tp)^-$ complexes.[2,3,11] This despite the fact that such species appear to be the thermodynamic "sink" for the zinc-tris(pyrazolyl)borates in the presence of water or alkali. Thus upon treatment with NaOH, [Zn(L)X], where L = $(L1O)^-$, yields only $Zn(OH)_2$ and "free" ligand, while with $(L2S)^-$ and $(L3S)^-$ rearrangement products of the form $[Zn(L)_2]$ were isolated. It seems likely that hydroxo complexes are in fact initially formed in all cases but that they are much more reactive than those of the corresponding $(Tp)^-$ complex. For $(L1O)^-$ it appears that the weakly bound phenoxide simply cannot compete with OH^- as a ligand for the metal while with $(L2S)^-$ and $(L3S)^-$ the rearrangement is driven by the enormous preference for zinc to adopt an N_2S_2 donor sphere,[38] *i.e.* $2(LS)ZnX + 2OH^- \longrightarrow 2(LS)Zn(OH) \longrightarrow (LS)_2Zn + Zn(OH)_2$. Interestingly the exact nature of the $[Zn(LS)_2]$ complex formed was different for each of the two thio ligands. In the case of $(L2S)^-$ the final product was one where the zinc was tetrahedrally encapsulated by two ligands where each one coordinated in an unexpected NS bidentate mode leaving one pyrazole arm free. For $(L3S)^-$ the tetrahedrally coordinated N_2S_2Zn complex in the solid state is composed of one tripodally coordinated ligand with the other monodentate through the sulfur. In solution, however, NMR shows that all the pyrazoles are equivalent, a situation incompatible with the solid state structure. At least two possibilities to account for this discrepancy exist: (1) the structure in solution is the octahedrally coordinated L_2Zn species where each ligand is tripodally coordinated and the two sulfur donors are *trans* to one another giving a plane of symmetry or (2) The tridentate and monodentate ligands in the tetrahedral complex seen in the solid state exist in solution but are in rapid equilibrium. The latter explanation is supported by the somewhat broad lines seen in the NMR spectra of **8**.

Further differences in reactivity between the two thio ligands were also noted. For example the lack of reactivity of complex **2** with water stands in stark contrast to what was seen for the aromatic analog, $(L2S)^-$, which reacted rapidly with even traces of water in solvents.[28] It is somewhat difficult to attribute this vast difference in reactivity of the zinc methyl derivative of $(L3S)^-$ and $(L2S)^-$ to the nature of the donor (aliphatic *vs.* aromatic thiol). Rather it is more likely that it is the difference in the S-donor chelate ring size, *i.e.* 6-membered for $(L3S)^-$ and 7 for $(L2S)^-$, that destabilizes the latter.

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