COMMUNICATION

ChemComm
www.rsc.org/chemcomm

A new bis(imidazolyl)(alkylthiolate) tripodal ligand and the spontaneous formation of a disulfide-linked, hydroxo-bridged dinuclear zinc complex†

Vivek V. Karambelkar,[a] Divya Krishnamurthy,[a] Charlotte L. Stern,[b] Lev N. Zakharov,[c] Arnold L. Rheingold[c] and David P. Goldberg*[a]

[a] *Department of Chemistry, The Johns Hopkins University, 3400 N. Charles Street, Baltimore, Maryland 21218, USA. E-mail: dpg@jhu.edu*

[b] *X-ray Crystallography Facility, Northwestern University, Evanston, Illinois 60208, USA*

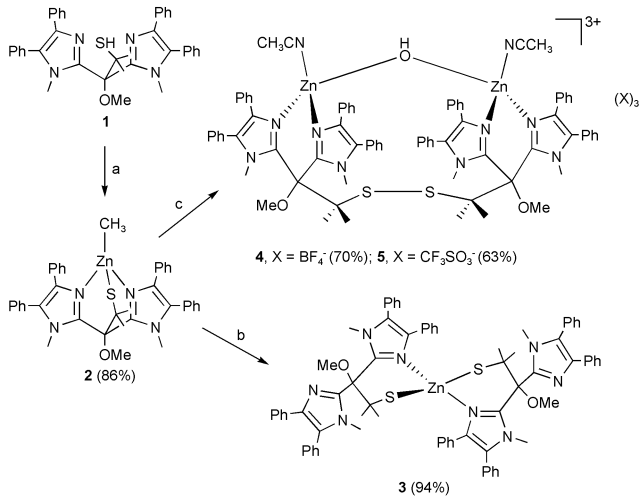
[c] *Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716, USA*

Received (in Cambridge, UK) 8th August 2002, Accepted 8th October 2002
First published as an Advance Article on the web 28th October 2002

The new sterically encumbered, tripodal N_2S(alkylthiolate) ligand, L^{Im_2SH}, has been synthesized and used to prepare $[(L^{Im_2S})ZnCH_3]$, which upon protonolysis under acidic conditions leads to the synthesis of a novel dinucleating ligand and a zinc dimer with an unusual structure.

Tripodal ligands have been employed in the synthesis of a vast number of transition metal complexes. Perhaps the most well-known of these systems are the tris(pyrazolyl)borates, whose remarkable versatility is only hampered by their restriction to an all-nitrogen (N_3) donor set.[1] We have an ongoing interest in the synthesis of *mixed* N,S donor ligands and their divalent metal complexes (N_xS_y–M^{II}) as models for certain metalloenzymes (*e.g.* peptide deformylase).[2–4] Alkylthiolate (RS^-) donors[2–10] are particularly challenging to synthesize and employ because of their tendency to form polymeric coordination compounds. Here we report the synthesis of a new sterically encumbered tripodal N_2S(alkylthiolate) ligand, L^{Im_2SH} (**1**), which contains a rare combination of both biomimetic *imidazole* and *alkylthiolate* donors. With L^{Im_2SH} in hand, a new zinc alkyl complex, $(L^{Im_2S})ZnCH_3$ (**2**), was synthesized. Examination of the reactivity of **2** has led to the formation of a novel disulfide-linked, hydroxo-bridged dinuclear zinc complex. The structure of this complex has some interesting implications for designing models of bimetallic enzymes that cleave DNA/RNA.

The synthesis of **1**, which can be routinely prepared on a 5 gram scale, was accomplished as described in the supplementary information (ESI†). We prepared the zinc(II)–alkyl complex **2** by addition of **1** to 1.4 equivalents of $Zn(CH_3)_2$ in toluene (86% yield, Scheme 1). The ^1H NMR spectrum of **2** shows a characteristic singlet at −1.31 ppm for the Zn–CH_3 group, and reflects the expected C_s symmetry for this complex. Identification of **2** was confirmed by FAB-MS ($[M + Na]^+$ = 685.3). The Zn–CH_3 peak at −1.31 ppm for **2** is shifted further upfield than most of the known four-coordinate Zn–CH_3 complexes.[4,5] Such a large upfield shift can be attributed to a combination of having an electron-donating alkylthiolate ligand attached to zinc and ring current effects caused by the phenyl substituents in close proximity.[11]



Scheme 1 *Reagents and conditions*: (a) 1.4 $Zn(CH_3)_2$, toluene, rt, 3 h, (b) 30 H_2O, toluene, rt, 6 d, (c) 2 HBF_4 (aq.) or 2 CF_3SO_3H, CH_3CN, rt, 24 h.

Reaction of **2** with an excess of H_2O in either toluene for 6 days or in CH_3CN at 50 °C for 3 h resulted in the formation of a new species (**3**) (Scheme 1) which was characterized by ^1H NMR and FAB-mass spectroscopies. The NMR spectrum of this new product lacked the upfield Zn–CH_3 peak, and revealed two new singlets at 2.95 and 3.87 ppm assigned to inequivalent CH_3 substituents on the Ph_2ImMe groups based on a similar pattern for a crystallographically characterized $(L^{Im_2S})_2Zn_2Br_2$ complex.[12] The presence of inequivalent imidazole rings predicts that the *gem*-dimethyl groups should be diastereotopic, which is confirmed by the different singlets at 2.62 and 2.06 ppm. The FAB-mass spectrum reveals a peak at 1231.4, which corresponds to $[M + H]^+$ for the formula $[(L^{Im_2S})_2Zn]$ (**3**). These data indicate that there has been a rearrangement of the ligand to an N,S bonding mode and redistribution to give an $[N_2S_2Zn]$ complex.

Interestingly, protonolysis of **2** under acidic conditions leads to a very different product. When **2** was reacted with aqueous HBF_4 in acetonitrile, the dinuclear complex $[(L^{Im_2S})_2Zn_2(CH_3CN)_2(\mu\text{-}OH)](BF_4)_3$ (**4**) was obtained and crystallographically characterized.‡ The structure revealed a hydroxide-bridged zinc dimer.[13] In addition, a disulfide bond had formed, linking the two ligands into a larger organic framework.[14,15] Moreover, the generality of this transformation was demonstrated by the reaction of **2** with CF_3SO_3H in CH_3CN, which led to the formation of the same disulfide-linked dimer (**5**). An ORTEP diagram of the cation in **5** is shown in Fig. 1.‡

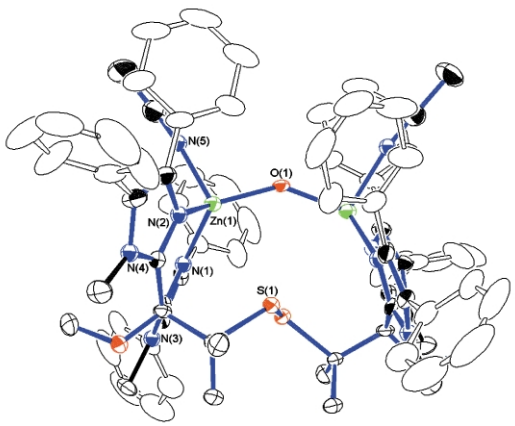


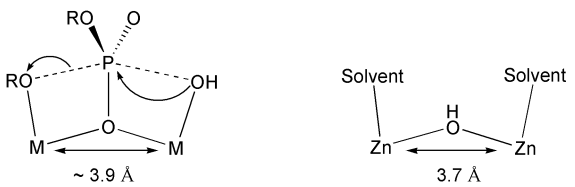
Fig. 1 Thermal ellipsoid plot of the cation in **5** (45% probability). Hydrogen atoms are omitted for clarity.

† Electronic supplementary information (ESI) available: synthesis and characterisation of compounds **1**–**5**. See http://www.rsc.org/suppdata/cc/b2/b207770a/

DOI: 10.1039/b207770a

The sulfur atoms in the disulfide unit for **4** (**5**) are well out of bonding range (Zn(1)–S(1) 3.395(2) (3.359(1) Å), Zn(1)–S(1)′ 3.652(2) (3.621(1) Å)).[16] In addition to the μ-OH ligand, the pseudotetrahedral zinc atoms are each coordinated by two imidazoles from L^{Im_2S} and a labile CH_3CN solvent molecule. The Zn–N(imidazole) bond lengths of 1.983(6) (1.976(5)) and 1.989(6) (1.991(5) Å) and the Zn–N(CCH_3) bond length of 2.025(7) (2.025(5) Å) for **4** (**5**) are unremarkable.[13,17] The Zn–OH bond length of 1.915(2) (1.919(2) Å) for **4** (**5**) closely matches those found for other Zn–O(H)–Zn compounds, such as $[L_3Zn–O(H)–ZnL_3](ClO_4)_3$ (L = 5-*tert*-butylpyrazole), where *d*(Zn–OH) = 1.90, 1.91 Å,[13] and is considerably shorter than the Zn–μ(OH_2) distance of 2.27–2.32 Å found in a rare aquo-bridged zinc complex.[18] Given that both **4** and **5** are synthesized from the reaction of **2** with HBF_4 or CF_3SO_3H, one might expect a protonated μ-OH_2 bridge instead of an OH^- bridge to be favored. However, the structural evidence unambiguously identifies a hydroxide bridge. In support of these results is the fact that a search of the Cambridge Database[19] reveals only three μ-OH_2 zinc complexes.[18,20,21] Complexes **4** and **5** are freely soluble in acetonitrile and nitromethane, and NMR spectra in either of these solvents are consistent with the dinuclear structure determined from X-ray crystallography. These data indicate the dimers **4** and **5** are stable in solution. A plausible mechanism for the synthesis of the dimer involves the initial formation of an (L^{Im_2S})ZnOH complex, followed by dimerization through the OH bridge, which in turn brings the sulfur atoms near each other and poised for oxidation by exogenous O_2 to a disulfide.

It is fortuitous that the reaction of **2** with strong acid leads to the synthesis of the disulfide-linked, dinucleating ligand of complex **4** (**5**), since there is interest in the design of polydentate ligands that can form bimetallic structures for various biomimetic and catalytic applications.[22–24] The polydentate ligand in **4** (**5**) accommodates a structural motif that may be of potential utility in modelling certain enzymes that cleave DNA/RNA, such as alkaline phosphatase, the 3′,5′-exonuclease domain of DNA polymerase I, and certain ribozymes.[25–27] For these enzymes a bimetallic mechanism has been proposed which requires 1) two metal ions spaced ~ 3.9 Å apart in order to bind the phosphate diester substrate in the appropriate geometry and 2) an exchangeable site on each metal that lies in the plane of the M–O–M unit to simultaneously bind the attacking nucleophile and leaving group. The second requirement has been difficult to fulfill with small-molecule model systems.[22–24] Complex **4** (**5**) has some relevant structural features in this regard; the metal ions are separated by 3.697 (3.645 Å), and the two labile CH_3CN solvent molecules occupy exchangeable sites that lie in the plane of the M–O(H)–M unit. Thus the disulfide ligand may be useful in preparing other dimetallic complexes that bind and cleave phosphate diesters.



We thank the National Institutes of Health (GM 62309) for generous support of this work.

Notes and references

‡ *Crystal data*: for **4**·H_2O: $C_{78}H_{79}B_3F_{12}N_{10}O_4S_2Zn_2$, M = 1672.83, T = 153(2) K, monoclinic, *C*2/*c*, a = 28.526(10), b = 14.601(5), c = 25.161(9) Å, β = 121.576(5)°, V = 8928(5) Å^3, Z = 4, D_c = 1.308 g cm^{-3}, μ = 0.668 mm^{-1}; 10690 reflections collected of which 5598 independent (R_{int} = 0.1065). Final R indices [$I > 2\sigma(I)$]: R_1 = 12.48, wR_2 = 35.47. CCDC 191657.

For **5**·CF_3SO_3H·$(CH_3CN)_2$: $C_{86}H_{84}F_{12}N_{12}O_{15}S_6Zn_2$, M = 2076.75, T = 173(2) K, monoclinic, *C*2/*c*, a = 28.5067(16), b = 14.7799(8), c = 26.0837(15) Å, β = 122.981(10)°, V = 9218.8(9) Å^3, Z = 4, D_c = 1.496 g cm^{-3}, μ = 0.750 mm^{-1}. X-Ray diffraction intensities were collected on a Bruker SMART APEX CCD diffractometer (T = 173(2) K, Mo-Kα radiation, 28570 reflections collected of which 10778 independent (R_{int} = 0.049)).

SADABS absorption corrections were applied. The structure was solved using direct methods and completed by subsequent difference Fourier syntheses and refined by full matrix least-squares procedures on reflection intensities (F^2). In the crystal structure of **5** there is a CH_3CN disordered solvate molecule. The solvent content was verified by the SQUEEZE program (A. L. Spek *Acta Crystallogr., Sect. A*, 1990, **46**, C-34); correction of the X-ray data for **5** (177 electron/cell) was very close to the required value (176 electron/cell). All non-H atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were placed in the structure factor calculations at idealized positions. One triflate ion is disordered and was refined with isotropic thermal parameters and restrictions on its geometry. Based on charge balance considerations, this site is a composite of $CF_3SO_3^-$ and CF_3SO_3H (the presence of CF_3SO_3H as a solvate is well-precedented, see for example: W. Schuh, H. Wachtler, G. Laschober, H. Kopacka, K. Wurst and P. Peringer, *Chem. Commun.*, 2000, 1181–1182). Final R indices [$I > 2\sigma(I)$]: R_1 = 11.41, wR_2 = 28.52. All software and sources of scattering factors are contained in the SHELXTL (5.10) program package (G.Sheldrick, Bruker XRD, Madison, WI). CCDC 191658.

See http://www.rsc.org/suppdata/cc/b2/b207770a/ for crystallographic data in CIF or other electronic format.

1 S. Trofimenko, *Scorpionates-The Coordination Chemistry of Polypyrazolylborate Ligands*, Imperial College Press, River Edge, NJ, 1999.
2 S. Chang, V. V. Karambelkar, R. D. Sommer, A. L. Rheingold and D. P. Goldberg, *Inorg. Chem.*, 2002, **41**, 239–248.
3 S. Chang, V. V. Karambelkar, R. C. diTargiani and D. P. Goldberg, *Inorg. Chem.*, 2001, **40**, 194–195.
4 S. Chang, R. D. Sommer, A. L. Rheingold and D. P. Goldberg, *Chem. Commun.*, 2001, 2396–2397.
5 B. S. Hammes and C. J. Carrano, *J. Chem. Soc., Dalton Trans.*, 2000, 3304–3309.
6 S. C. Shoner, A. M. Nienstedt, J. J. Ellison, I. Y. Kung, D. Barnhart and J. A. Kovacs, *Inorg. Chem.*, 1998, **37**, 5721–5726.
7 C. A. Grapperhaus, J. A. Bellefeuille, J. H. Reibenspies and M. Y. Darensbourg, *Inorg. Chem.*, 1999, **38**, 3698–3703.
8 L. A. Tyler, J. C. Noveron, M. M. Olmstead and P. K. Mascharak, *Inorg. Chem.*, 2000, **39**, 357–362.
9 U. Brand and H. Vahrenkamp, *Inorg. Chim. Acta*, 2000, **308**, 97–102.
10 C. A. Grapperhaus, A. K. Patra and M. S. Mashuta, *Inorg. Chem.*, 2002, **41**, 1039–1041.
11 S. Klod and E. Kleinpeter, *J. Chem. Soc. Perkin Trans. 2*, 2001, 1893–1898.
12 V. V. Karambelkar, C. Stern and D. P. Goldberg, unpublished results.
13 For an example of the formation of a Zn_2–μ-OH complex from a zinc alkyl complex see: R. Alsfasser and H. Vahrenkamp, *Chem. Ber.*, 1993, **126**, 695–701.
14 M. Handa, M. Mikuriya and H. Ōkawa, *Chem. Lett.*, 1989, 1663–1666.
15 C. Lai, J. Reibenspies and M. Y. Darensbourg, *Chem. Commun.*, 1999, 2473–2474.
16 J. Bremer, R. Wegner and B. Krebs, *Z. Anorg. Allg. Chem.*, 1995, **621**, 1123–1132.
17 V. K. Bel′sky, N. R. Streltsova, B. M. Bulychev, P. A. Storozhenko, L. V. Ivankina and A. I. Gorbunov, *Inorg. Chim. Acta*, 1989, **164**, 211–220.
18 W. Wolodkiewicz and T. Glowiak, *Pol. J. Chem.*, 2001, **75**, 299–306.
19 F. H. Allen and O. Kennard, *Chem. Des. Autom. News*, 1993, **8**, 1 and 31–37.
20 E. Dubler, G. Hanggi and H. Schmalle, *Inorg. Chem.*, 1990, **29**, 2518–2523.
21 G. Smith, E. J. O′Reilly and C. H. L. Kennard, *Aust. J. Chem.*, 1983, **36**, 2175–2183.
22 U. Kuhn, S. Warzeska, H. Pritzkow and R. Krämer, *J. Am. Chem. Soc.*, 2001, **123**, 8125–8126.
23 C. He, V. Gomez, B. Spingler and S. J. Lippard, *Inorg. Chem.*, 2000, **39**, 4188–4189.
24 N. H. Williams, A. Lebuis and J. Chin, *J. Am. Chem. Soc.*, 1999, **121**, 3341–3348.
25 L. S. Beese and T. A. Steitz, *EMBO J.*, 1991, **10**, 25–33.
26 E. E. Kim and H. W. Wyckoff, *J. Mol. Biol.*, 1991, **218**, 449–464.
27 T. A. Steitz and J. A. Steitz, *Proc. Natl. Acad. Sci. USA*, 1993, **90**, 6498–6502.