Assembly of Zinc Ions by the New ON_2S_2 Ligand BMIBIP

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Dedicated to Professor Dieter Sellmann on the occasion of his 60th birthday

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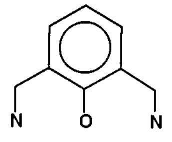
The new ON_2S_2 ligand bis(iminomethyl)-2-6-bis(mercaptoisobutyl)-4-methylphenol (H_3BMIBIP) has been synthesized from 2,6-diformyl-4-methylphenol and 2-mercaptoisobutylamine. Its reaction with diethylzinc in the presence of alcohols yields complexes of composition [(BMIBIP)Zn_2(OR)] (R = CH_3, C_2H_5 and $CH_2C_6H_4CF_3$). A structure determination of the trifluoromethylbenzylate compound has shown it to be a tetranuclear complex consisting of two (BMIBIP)Zn_2 units linked by triply bridging alkoxide ligands to form a double norcubane with a $Zn_4O_4S_2$ framework.

Introduction

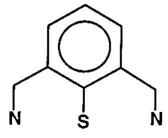
The phenomenon of cooperativity in conventional catalysis and the fact that many metalloenzymes have binuclear reaction centers[1] have spurred the investigations of binuclear coordination compounds in recent years. Out of this has emerged a new class of polydentate ligands, the so-called binucleating ligands.[2] A simple construction principle for these consists in the use of a central bridging unit (phenolate, thiophenolate, bipyridine, pyrazole, etc.) to which two polydentate side groups are attached. The functionalization of the binuclear reaction centers that can be achieved with such ligands has been impressively demonstrated recently by modelling iron[3] and copper[4] containing enzymes.

The most common type of binucleating ligand is derived from the basic framework **A** which itself is a variation of the classical salicylic aldimine type. Its thiophenolate analogue **B** is much less developed in coordination chemistry. This is repeated when the hapticity of the ligands is increased: while the Cambridge Crystallographic Database yields more than 130 entries for complexes derived from type **C**, there are just 9 for type **D**, including two zinc complexes.[5] Finally the sulfur-rich type **E** is represented by only four copper complexes containing the sulfur as a thioether donor,[6] while N_2S_3 ligands of type **F**, or complexes thereof, seem to be unknown so far.

As was shown by the pioneering work of Sellmann and co-workers,[7] sulfur-rich polydentate ligands have a high versatility for bioinorganic and catalytic model complex chemistry. We have tried to apply this in the field of zinc chemistry by the design and use of N_2S,[8,9] NS_2,[10] and N_3S_2 [11] ligands which contain sulfur as thiolate. Like others, we soon found that it is difficult to control oligothiolates because the bridging tendency of the thiolate sulfur causes a rich, but unpredictable, chemistry of oligonuclear complexes. However, we were also able to show that the application of multiply chelating ligands reduces the aggregation tendency and allows the formation of mononuclear zinc-bis(thiolate) complexes.[11]



A



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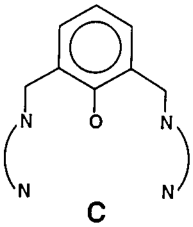
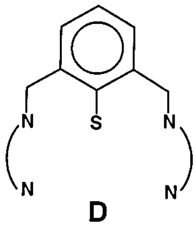


C



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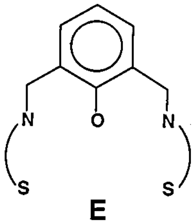

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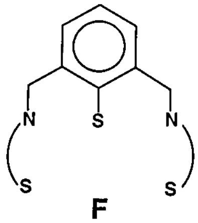
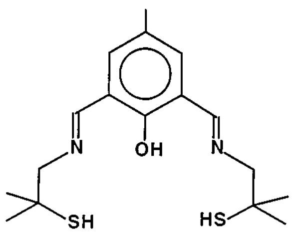


F

Along these lines we started working on binucleating ligands of type **E**. This paper describes the new ligand H_3BMIBIP and some zinc complexes thereof.



H_3BMIBIP

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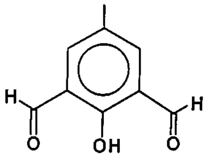
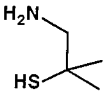
Results and Discussion

Ligand H_3BMIBIP

The ligand synthesis was easy, as both its components 2,6-diformyl-4-methylphenol (**1**) and 2-mercaptoisobutylamine (**2**) are commercially available. Compound **2** was chosen in order to introduce a moderate amount of steric hindrance in the vicinity of sulfur in order to reduce the bridging tendency of the thiolate functions. Schiff base condensation of the two components was straightforward and yielded H_3BMIBIP in moderate yields. The ligand exists as a pale yellow crystalline solid which is easily identified by its simple ^{1}H NMR spectrum (see Experimental Section).



1



2

Zinc Complexes

In its deprotonated state the ligand BMIBIP is trianionic. Its combination with two divalent metal ions therefore calls for the binding of one additional monoanionic ligand. Ideally, this ligand should have the tendency for bridging, thereby completing the square configuration of both metal ions. In simple cases this might be a halide or thiolate ligand, whereas for bioinorganic model studies it might be, for example, an organophosphate. In the case of zinc binding one would envisage the attachment of additional monodentate ligands to complete a square pyramidal or octahedral coordination.

We tried to verify this for zinc complexes by treating the ligand with base and subsequently with zinc salts. The resulting, probably oligomeric or polymeric, complexes could not be obtained in a pure state. However, using diethylzinc both as the base and as the source of zinc yielded crystalline products in good yields. When alcohols were present, either as a solvent or as a co-reagent, these products had the composition L·Zn(OR). Thus, reaction with methanol, ethanol, or 4-trifluoromethylbenzyl alcohol gave the complexes **3a**, **3b**, and **3c**, respectively. Complexes **3** are soluble in polar aprotic organic solvents and crystallize as yellow solvates from chloroform or dichloromethane. Their ^{1}H NMR spectroscopic data (see Experimental Section) are in accordance with the composition [(BMIBIP)Zn_2(OR)] (**3a**: R = Me, **3b**: R = Et, **3c**: R = 4-$CF_3C_6H_4CH_2$).

Structure of 3c

Triclinic crystals of **3c** were obtained from chloroform. They contain four formula units and four solvent molecules per unit cell, the latter disordered over six positions. The four formula units of **3c** make up two crystallographically independent tetranuclear molecular units. These are quite similar and can both be represented by the simplified drawing of Figure 1. Table 1 lists the relevant bond lengths in the tetranuclear dimers.

Table 1. Zinc-ligand bond lengths (Å) in **3c**

	Molecule 1	Molecule 2
Zn1−O1	2.076(4)	2.088(4)
Zn1−N1	2.001(5)	1.999(5)
Zn1−S1	2.389(2)	2.382(2)
Zn1−O2	2.019(4)	2.014(4)
Zn1−O2′[a]	2.094(4)	2.096(4)
Zn2−O1	2.160(4)	2.156(4)
Zn2−N2	2.079(5)	2.084(5)
Zn2−S2	2.295(2)	2.291(2)
Zn2−O2	2.151(4)	2.172(4)
Zn2−S1′[a]	2.377(2)	2.383(2)

[a] Bonds linking the two dinuclear units.

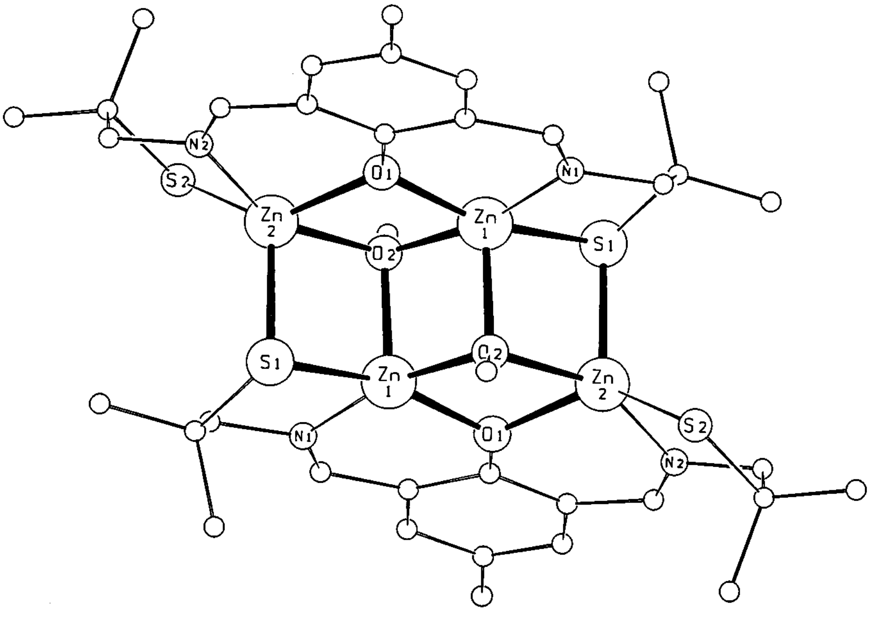


Figure 1. Molecular structure of **3c** (*p*-trifluorobenzylate units at O2 omitted for clarity)

The molecular constitution found for **3c** represents a new type of tetranuclear aggregate which is assembled from two pentadentate ligands. In each of the two dinuclear units, the BMIBIP ligand exerts its expected ligation pattern by giving both zinc ions a square environment. The dimerization of the two dinuclear units is brought about by placing them face to face across a center of symmetry and linking them through the unshared electron pairs of O2 and S1. Thereby the linkage is represented by four rungs of a ladder, and the resulting Zn$_4$O$_4$S$_2$ core has the shape of two open cubes sharing a common face.

The coordination of all four zinc ions is square-pyramidal. Both Zn1 and Zn2 have a basal ZnO$_2$NS coordination, but the apical donor is oxygen for Zn1 and sulfur for Zn2. Accordingly, the BMIBIP ligand uses one of its thiolate functions as a terminal and the other as a bridging ligand. Thus, although the whole tetranuclear complex has inversion symmetry it contains no other symmetry elements.

The observed bond lengths (Table 1) are in their normal ranges (cf. the chemistry of zinc alkoxides or zinc thiolates). The Zn−N bonds are the shortest, corresponding to the fact that N is only terminal. The Zn−S bonds underline this by the clear distinction of the Zn−S2 and Zn−S1 distances. Among the Zn−O bonds it is noticeable that those from Zn1 are significantly shorter than those from Zn2; this may reflect the presence of the very good donor S2 as a terminal ligand on Zn2.

Conclusions

This work has shown that H$_3$BMIBIP is a good candidate for the assembly of metal ions. It is easy to synthesize, it provides a biorelevant ON$_2$S$_2$ donor set able to surround two metal ions in a square-planar fashion, and it can position the two metal ions such that both can coordinate to one and the same additional ligand, i.e. a substrate for a catalytic process. When zinc is present as the divalent metal ion, its tendency to be five-coordinate in the given donor set can easily be met by dimerization of the LZn$_2$X complexes. It should be worthwhile to find out how other divalent metals, for example with preference for square-planar or octahedral coordination, make use of the donor capacity of BMIBIP.

Experimental Section

General: For general working and measuring procedures, see ref.[12] All reactions were performed under an inert atmosphere. Starting materials were obtained commercially.

H$_3$BMIBIP: A solution of 2,6-diformyl-4-methylphenol (1.01 g, 6.18 mmol) in methanol (25 mL) was added to a solution of 2-mercaptoisobutylamine hydrochloride (1.75 g, 12.35 mmol) also in methanol (25 mL). Upon stirring and addition of anhydrous sodium acetate (1.02 g, 12.35 mmol) a cloudy precipitate started forming. After refluxing for 30 min. and cooling to room temp. the solvent was removed in vacuo. The residue was redissolved in 20 mL of dichloromethane, filtered and evaporated to dryness again. Crystallization of the residue from 10 mL of methanol at 4 °C yielded H$_3$BMIBIP (0.84 g, 40%) as a yellow powder, m.p. 99 °C. − C$_{17}$H$_{26}$N$_2$OS$_2$ (338.5): calcd. C 60.31, H 7.74, N 8.27; found C 60.27, H 7.67, N 8.13. − ^{1}H NMR (CD$_3$COOD): δ = 1.55 (s, 12 H, CH$_3$), 2.19 (s, 3 H, CH$_3$), 3.43 (s, 4 H, CH$_2$), 6.22 (d, *J* = 6.8 Hz, 2 H, CH=N), 7.28 (d, *J* = 6.4 Hz, 2 H, Ph).

3a: A 1 M solution of diethylzinc in *n*-hexane (5.00 mL, 5.00 mmol) was slowly dropped with stirring into a solution of H$_3$BMIBIP (0.84 g, 2.49 mmol) in a mixture of absolute methanol (10 mL) and absolute dichloromethane (30 mL). After stirring for 1 h the volume was reduced in vacuo to 20 mL upon which the product precipitated. After filtration, washing with a small amount of diethyl ether and drying in vacuo **3a** (0.68 g, 51%) was obtained as a pale yellow microcrystalline solid. M.p. 165 °C. − C$_{18}$H$_{26}$N$_2$O$_2$S$_2$Zn$_2$·0.5CH$_2$Cl$_2$ (457.3 + 42.5): calcd. C 41.16, H 5.04, N 5.19, Zn 24.23; found C 41.33, H 4.93, N 5.52, Zn 24.25. − ^{1}H NMR (CDCl$_3$): δ = 1.12 (s, 12 H, CH$_3$), 1.76 (s, 3 H, CH$_3$), 2.20 (s, 3 H, CH$_3$), 3.41 (s, 4 H, CH$_2$), 5.32 (s, 1 H, CH$_2$Cl$_2$), 7.09 (s, 2 H, CH=N), 8.15 (s, 2 H, Ph).

3b: A 1 M solution of diethylzinc in *n*-hexane (2.66 mL, 2.66 mmol) was slowly dropped with stirring into a solution of H$_3$BMIBIP (0.45 g, 1.33 mmol) in a mixture of absolute ethanol (2 mL) and absolute chloroform (15 mL). After stirring for 30 min. the solvent was removed in vacuo. The residue was redissolved in a few milliliters of chloroform and layered with diethyl ether. After 4 days at 4 °C the resulting precipitate was filtered off, washed with a few milliliters of diethyl ether and dried in vacuo to give **3b** (0.39 g, 47%) as a pale yellow powder. M.p. 195 °C. − C$_{19}$H$_{28}$N$_2$O$_2$S$_2$Zn$_2$·CHCl$_3$ (511.4 + 119.4): calcd. C 38.09, H 4.63, N 4.44, Zn 20.73; found C 38.09, H 4.70, N 4.70, Zn 21.25. − ^{1}H NMR ([D$_6$]DMSO): δ = 1.07 (t, *J* = 7.0 Hz, 3 H, CH$_3$), 1.45 (s, 12 H, CH$_3$), 2.13 (s, 3 H, CH$_3$), 3.30 (s, 4 H, CH$_2$), 3.58 (q, *J* = 7.0 Hz, 2 H, OCH$_2$), 7.10 (s, 2 H, CH=N), 7.26 (s, 1 H, CHCl$_3$), 8.10 (s, 2 H, Ph).

3c: A 1 M solution of diethylzinc in *n*-hexane (4.03 mL. 4.03 mmol) was dropped slowly with stirring into a solution of H$_3$BMIBIP (0.68 g, 2.02 mmol) and 4-trifluoromethylbenzyl alcohol (0.53 g, 3.00 mmol) in absolute chloroform (25 mL). After stirring for 1 h the solution was filtered, the filtrate reduced to half its volume in vacuo and layered with diethyl ether. After 1 day at 4 °C the precipitate was filtered off and washed with a few milliliters of hexane to give **3c** (0.56 g, 40%) as a colorless powder. M.p. 188 °C. − C$_{25}$H$_{29}$F$_3$N$_2$O$_2$S$_2$Zn$_2$·0.5CHCl$_3$ (641.4 + 59.7): calcd. C 43.69, H 4.24, N 4.00; found C 43.80, H 4.75, N 4.15. − ^{1}H NMR (CDCl$_3$): δ = 1.47 (s, 12 H, CH$_3$), 1.66 (s, 2 H, OCH$_2$), 2.20 (s, 3 H, CH$_3$), 3.57 (s, 4 H, CH$_2$), 7.19 (m, 6 H, Ph), 7.24 (s, 0.5 H, CHCl$_3$), 8.08 (s, 2 H, CH=N).

Structure Determination:[13] From a chloroform solution of **3c** layered with diethyl ether crystals of composition (**3c**)$_2$·2CHCl$_3$ were obtained. Diffraction data were recorded at room temp. with the ω/2θ technique on a Nonius CAD4 diffractometer fitted with a molybdenum tube (K_α, $\lambda = 0.7107$ Å) and a graphite monochromator. No absorption corrections were applied. The structures were solved by direct methods and refined anisotropically with the SHELX program suite.[14] Hydrogen atoms were included with fixed distances and isotropic temperature factors 1.5 times those of their attached atoms. Parameters were refined against F^2. The R values are defined as $R_1 = \Sigma|F_o - F_c|/\Sigma F_o$ and $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]\Sigma[w(F_o^2)^2]\}^{1/2}$. Drawings were produced with SCHAKAL.[15] Table 2 lists the crystallographic data.

Table 2. Crystallographic data for **3c**

Empirical formula	$C_{52}H_{60}Cl_6F_6N_4O_4S_4Zn_4$
Molecular mass	1521.4
Crystal size [mm]	0.6 × 0.3 × 0.3
Space group	$P\bar{1}$
Z	2
a [Å]	13.097(3)
b [Å]	14.477(3)
c [Å]	20.547(4)
α [°]	69.53(3)
β [°]	71.92(3)
γ [°]	85.96(3)
V [Å^3]	3466(1)
d(calcd.) [gcm^{-3}]	1.46
μ(Mo-K_α) [mm^{-1}]	1.78
hkl range	h: −16 to 16 k: 0 to 17 l: −23 to 25
Measured reflections	14190
Independent reflections	13622
Observed refl. [$I > 2\sigma(I)$]	10462
Parameters	709
Refined reflections	13622
R_1(obs.refl.)	0.065
wR_2(all refl.)	0.226
Residual electron density [e/Å^3]	+1.0/-1.0

Acknowledgments

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[13] The crystallographic data of the structures described in this paper were deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-149311 Copies of these data are available free of charge from the following address: The Director, CCDC, 12 Union Road, Cambridge UK, CB2 1EZ [Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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