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**Chelation and Bridging of Zinc(II) by Tetradentate N₂S₂
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Chelation and Bridging of Zinc(II) by Tetradentate N₂S₂ Donor Ligands:

Similarities and Differences to Copper(I) and Copper(II) Systems

Johannes Schnödt,^[a] Monika Sieger,^[a] Thomas Schleid,^[a] Ingo Hartenbach,^[a] and

Wolfgang Kaim^{*[a]}

Dedicated to Professor Hans-Jörg Deiseroth on the Occasion of his 65. Birthday

Keywords: Benzimidazole; Crystal structure; Thioether ligands; Zinc compounds

Abstract. Reaction of zinc(II) triflate with neutral bis(benzimidazole-thioether) ligands yielded the complexes [Zn(bmbdh)(H₂O)(η^1 -SO₃CF₃)](SO₃CF₃) (**1**) with tetradentate chelating 1,6-bis(N-methylbenzimidazol-2-yl)-2,5-dithiahexane (bmbdh), and dinuclear {[Zn(μ -bmdhp)(H₂O)(η^1 -SO₃CF₃)]₂}(SO₃CF₃)₂ (**2**) with bis-bidentate bridging 1,7-bis(N-methylbenzimidazol-2-yl)-2,6-dithiaheptane (bmdhp). In both cases the oxygen donor ligands aqua and triflate adopt *cis* positions at the approximately octahedrally configured Zn²⁺ ions. The hexacoordination is facilitated by rather long Zn-S(thioether) distances in contrast to the typically shorter Zn-S(thiolate) bonds from classical zinc finger proteins or their models. With the shorter central (CH₂)_n chain (n = 2) the ligand bmbdh exhibits facial coordination of the two NSS donor sets in **1**, similar as in [Cu(bmdhp)]⁺ ions with lower coordinate copper(I) but in contrast to the related [Cu^{II}(bmdhp)(H₂O)](ClO₄)₂ with the longer chain ligand bmdhp. In **2**, the bis-bidentate coordination of bmdhp ligands to each Zn²⁺ ion occurs in an all-*cis* fashion for the pairs of N, S and O donor atoms, in contrast to related [Cu^I(mmb)₂](BF₄), mmb = 1-methyl-2-methylthiomethyl-1*H*-benzimidazole.

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Introduction

In contrast to mainly “hard” or mainly “soft” metal ions the Zn^{2+} ion can be equally well bonded through O, N and S donor ligands in corresponding proteins [1,2]. Although the coordination has to be compatible with the biological function such as enzymatic catalysis, structural stabilization, or transport, there are many cases where mixed donor ligation from histidine, cysteinate, aspartate or glutamate has been found for zinc in its natural biological environment [2,3]. In addition, most hydrolytic enzymes offer at least one “free” coordination site for substrate binding, usually occupied by labile water [1-3].

The N_2S_2 ligation of the zinc ion has received much attention [4-7] since zinc finger proteins were discovered to contain modular motifs (“fingers”) involving two neutral histidine-N and two anionic cysteinato-S donor atoms coordinated to Zn^{2+} [1-3,5]. These zinc fingers (Figure 1) act as structure-maintaining entities for specific protein-nucleic acid recognition in the transcription process [3,5]. In connection with modelling the zinc finger coordination there have been previous synthetic and structural reports on complexes with bis(thiolato)-bis(imidazole) [6] or -bis(benzimidazole) [7] and bis(thioether)-bis(pyridyl) or -bis(amine) coordinated zinc, with and without additional O donor ligation [8]. Bis(thioether)-bis(benzimidazole) ligation has not yet been described.

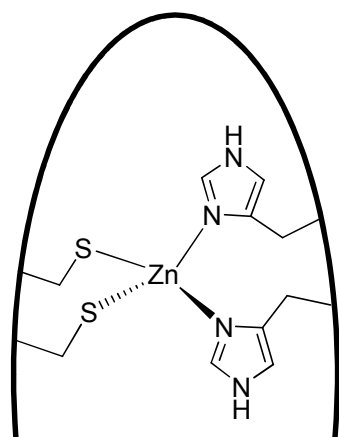
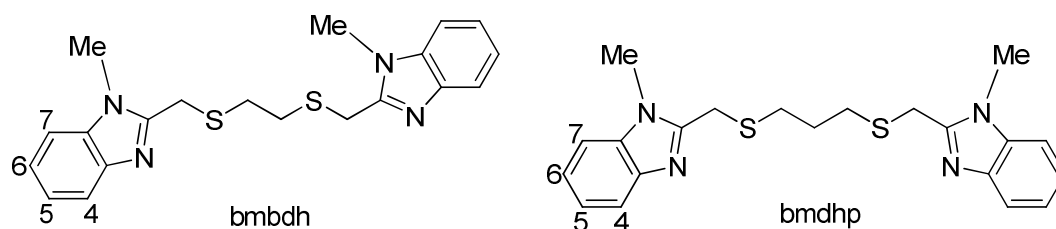


Figure 1. Zinc finger.

Probing the mixed benzimidazole-thioether ligand binding to copper(I) and copper(II) [9] with a view on O_2 utilising monooxygenases such as PHM (α -peptidylglycine hydroxylating monooxygenase) with its $Cu(His)_2(Met)$ arrangement (His = histidine, Met = methionine) [10] we have been interested in the coordination characteristics of mixed N_2S_2 donor ligands involving neutral S(thioether) functions in the absence of special effects such as Jahn-Teller distortion (Cu^{II} [11]) or low coordination number preference (Cu^I) [12]. We therefore report here our results from the reactions of zinc triflate with the tetradentate bis(benzimidazole-thioether) ligands $bmbdh = 1,6$ -bis(*N*-methylbenzimidazol-2-yl)-2,5-dithiahexane and $bmdhp = 1,7$ -bis(*N*-methylbenzimidazol-2-yl)-2,6-dithiaheptane (see Scheme 1) which have already been used to obtain partially structurally characterized complexes such as $[Cu(bmdhp)(H_2O)](ClO_4)_2$ and $[Cu(bmdhp)](X)$, $X = ClO_4, O_3SCF_3$ [11,13].



Scheme 1.

Results and Discussion

Reaction of zinc triflate in acetone with the neutral bis(benzimidazole-thioether) ligands from Scheme 1 yielded two different kinds of compounds. In the absence of electron or charge transfer activity and lacking prominent signature features in IR or NMR spectroscopy the characterization of the two seemingly 1:1 complexes $[\text{Zn}(\text{L})(\text{H}_2\text{O})(\text{OTf})_2]$ obtained from $\text{L} = \text{bmbdh}$ or bmdhp and $\text{Zn}(\text{OTf})_2$ had to rely on the molecular structure analysis of single crystalline material. Crystallographic information and bond parameters are listed in Tables 1 and 2, Figures 2 and 3 show the molecules in their setting.

Tabelle 1. Crystallographic and structure refinement data.

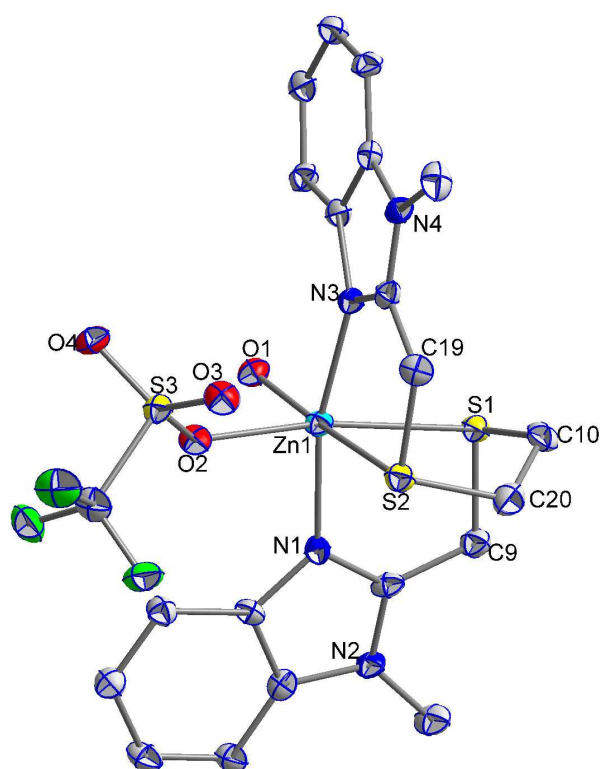
	1*2 OC(CH₃)₂	2*2 OC(CH₃)₂
Formula	C ₂₈ H ₃₆ F ₆ N ₄ O ₉ S ₄ Zn	C ₂₉ H ₃₈ F ₆ N ₄ O ₉ S ₄ Zn
Formula weight /gmol ⁻¹	880.22	894.24
Crystal system	triclinic	triclinic
Space group	P-1	P-1
Cell parameters a /Å	10.902(0)	9.517(0)
b /Å	12.109(1)	13.317(1)
c /Å	15.348(1)	15.554(1)
α /°	71.244(2)	87.543(3)
β /°	88.773(2)	86.136(3)
γ /°	71.129(2)	73.284(3)
V /Å ³	1807.72(13)	1883.10(15)
Z	2	2

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Calc. density /g cm ⁻³	1.617	1.577
Temperature /K	100(1)	100(1)
θ Range /°	0.41- 27.48	0.41- 23.26
F(000)	904	920
Index range	-14<h>12; -15<k>15; -19<l>19	-10<h>10; -14<k>14; -17<l>17
Absorption correction	numerical	numerical
Reflns. collect.	33943	29275
Reflns. unique	8242	5351
Reflns. gt	5214	3884
μ /mm ⁻¹	0.997	0.959
Parameters	511	522
Goodness of fit	1.006	1.108
R ₁ / wR ₂ [all]	0.1135 / 0.1512	0.0988 / 0.1399
R ₁ / wR ₂ [I>2σ(I)]	0.0594 / 0.1273	0.0588 / 0.1184
Δρ /eÅ ⁻³	0.588 / -0.655	0.704 / -0.759

Tabelle 2. Selected bond lengths and bond angles.

	1*2 OC(CH ₃) ₂	2*2 OC(CH ₃) ₂
Zn-O1	2.051(3) Å	2.089(5) Å
Zn-O2	2.134(3) Å	2.151(4) Å
Zn-S1	2.595(1) Å	2.665(2) Å
Zn-S2	2.625(1) Å	2.591(2) Å
Zn-N1	2.097(4) Å	2.048(5) Å
Zn-N3	2.094(4) Å	2.076(5) Å
O1-Zn-S2	175.71(10)°	80.02(14)°
O1-Zn-N3	96.12(14)°	91.1(2)°
O1-Zn-N1	90.39(14)°	162.2(2)°
O1-Zn-O2	89.43(12)°	90.39(18)°
O1-Zn-S1	97.40(9)°	83.66(15)°
N3-Zn-N1	167.28(13)°	105.8(2)°
N3-Zn-O2	96.43(12)°	93.31(18)°
N3-Zn-S2	79.98(10)°	79.74(15)°
N3-Zn-S1	89.09(9)°	172.83(15)°
S1-Zn-O2	170.74(9)°	91.63(12)°
S1-Zn-S2	84.38(4)°	94.48(5)°
S1-Zn-N1	79.21(9)°	78.95(15)°



(acetone molecules are not shown).

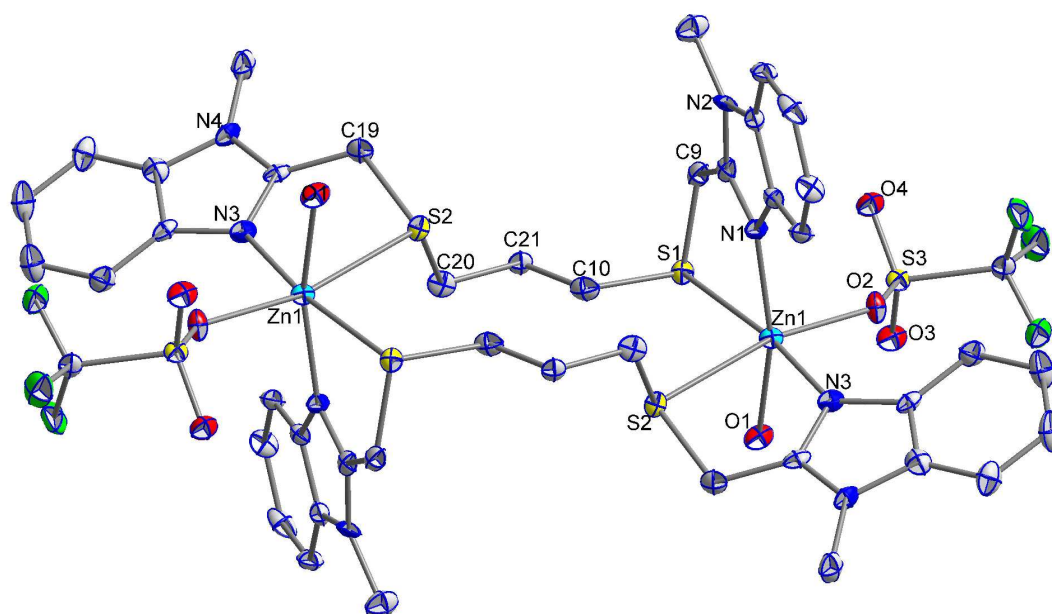


Figure 3. Molecular structure of $\{[Zn(\mu\text{-bmdhp})(H_2O)(\eta^1\text{-SO}_3CF_3)]_2\}(\text{SO}_3CF_3)_2$ (**2**) in the crystal (acetone molecules are not shown).

In both cases **1** and **2** the oxygen donor ligands aqua and triflate adopt *cis* positions at the approximately octahedrally configured Zn^{2+} ions. This coordination number is tolerated because of the presence of four light donor atoms (2 O, 2 N) and two weakly bonded S(thioether) donor centers. Specifically, the rather long Zn-S(thioether) distances at about 2.60 Å stand in contrast to the typically shorter Zn-S(thiolate) bonds (ca. 2.3 Å) from classical zinc finger proteins [3,5] or their models [4,6,7].

Remarkably, the two compounds **1** and **2** showed a different degree of aggregation. Compound **1** obtained with bmbdh turned out to be a mononuclear complex with one aqua and one triflate ligand coordinated in *cis* position of Zn^{2+} in $[Zn(bmbdh)(H_2O)(\eta^1\text{-SO}_3CF_3)](\text{SO}_3CF_3)$ (Figure 2,4). The tetradentate chelating bmbdh ligand adopts an arrangement with *cis* positioned thioether-S donors and *trans* positioned imine-N donor atoms from the benzimidazoles (*fac/fac* combination of NSS and SSN). At $167.3(1)^\circ$ the N-Zn-N angle is fairly close to linearity.

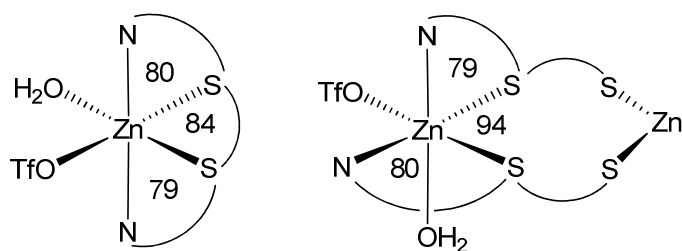
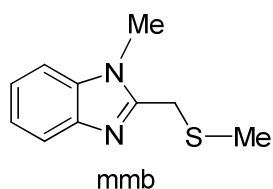


Figure 4. Coordination arrangements for **1** (left) and **2** (right) (bond angles in deg.).

On the other hand, bmdhp in compound **2**, $\{[\text{Zn}(\mu\text{-bmdhp})(\text{H}_2\text{O})(\eta^1\text{-SO}_3\text{CF}_3)]_2\}(\text{SO}_3\text{CF}_3)_2$, acts as a bis(bidentate) bridge between two zinc ions (Figures 3,4). Again, the aqua ligand (probably from less than 100% dry acetone) and one OTf^- anion occupy a *cis* position at the approximately octahedrally configured metal, however, this time the two independent N,S chelates from two bmdhp molecules bond with the two N atoms also in *cis* position (angle N-Zn-N $105.8(2)^\circ$), like the two S donors (all-*cis* situation).

The configuration of mononuclear **1** is somewhat reminiscent of that of $[\text{Cu}(\text{mmb})_2]^+$ [9b], mmb = 1-methyl-2-methylthiomethyl-1*H*-benzimidazole, which involves the $3d^{10}$ configuration Cu^+ (like Zn^{2+}) and exhibits a large N-Cu-N angle of $169.8(1)^\circ$ (Figure 5, bottom left) but leaves a “free” sector where the Zn complex bonds two O donor ligands. The configuration in compound **2** has no such precedent in copper chemistry because the structural preference of Cu^I is for smaller coordination numbers (e.g. 2, 2+2, 4) as evident for $[\text{Cu}(\text{mmb})_2]^+$ [9b] and $[\text{Cu}(\text{bmdhp})]^+$ (angle N-Cu-N of ca. 151° [13], Figure 5, top left). The structures of copper(II) analogues such as $[\text{Cu}(\text{bmdhp})_2(\text{OH}_2)]$ [11] or $[\text{Cu}(\text{mmb})_2(\text{OCIO}_3)]^+$ [14] are dominated by the Jahn-Teller effect which leaves a planar *mer/mer* arrangement for the N,S,S,N donor set at pentacoordinate Cu^{2+} (Figure 5, top and bottom right).



Scheme 2.

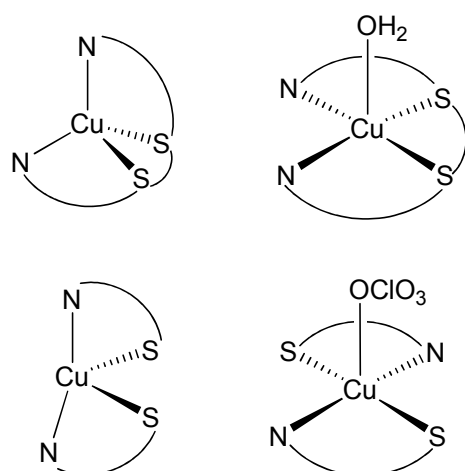


Figure 5. Coordination arrangements in copper(I) (left) and copper(II) complexes (right) of bmdhp (top) and mmb (bottom) (from refs. 9b,11b,13,14).

The absence of special ligand-field or low-coordination-number effects as in copper(II) or copper(I) compounds leaves the Zn^{2+} ion in a seemingly “normal” octahedral configuration which, however, still displays considerable structural variability. The weak bonding of the thioether donors at about 2.6 Å Zn-S distance allows for enough space to adopt additional O donors which is less likely when strongly coordinated thiolate ligands such as in zinc finger configurations and their models are present ($d_{\text{Zn-S}}$ ca. 2.3 Å [4-7]). Then, the tetracoordinate arrangement is the alternative which may also offer a greater degree of structural (angular) flexibility than the hexacoordinate situation.

Using a tetradentate N_2S_2 donor ligand type which has already been established in copper coordination chemistry [9,11] and which offers biomimetic benzimidazole (->

histidine) as well as thioether (-> methionine) coordination functions, we have obtained two different kinds of complexes, depending on the length of the oligomethylene spacer between the two molecular halves of the ligand. In both cases, however, a hexacoordination is observed with two additional O donors (counterion, water) and the weakly bonded S(thioether) donors in the *cis* position. Clearly this coordination arrangement differs from that of zinc fingers and related proteins [5]. Nevertheless, chelate binding of zinc(II) under at least partially physiological conditions is an attractive option which may find uses in the increasingly investigated [15] biochemistry and medicinal chemistry.

Experimental Section

General Information

Commercially available acetone (Merck) was dried by stirring for 10 d with CaSO₄ and subsequent distillation. Zn(SO₃CF₃)₂ from Sigma Aldrich was used without further purification. All reactions involving metal complexes were conducted under argon using standard Schlenk technique.

Instrumentation

¹H-NMR spectra were taken on a Bruker AC 250 spectrometer.

[Zn(bmbdh)(H₂O)(η¹-SO₃CF₃)](SO₃CF₃) (I)

A suspension of bmbdh [11a] (69 mg, 0.181 mmol) in 10 ml acetone was added to hygroscopic Zn(OTf)₂ (66 mg, 0.181 mmol) in 15 ml acetone. The product was precipitated by reducing the solvent after stirring for 4 hours at room temperature. A white powder remained after the solvent was decanted. Yield: 128 mg (0.172 mmol, 95%). Elementary analysis: C₂₂H₂₄F₆N₄O₇S₄Zn (764.11 g mol⁻¹). C 34.69 (cal. 34.58); H 3.13 (calc. 3.17); N 7.33 (7.33)%. ¹H-NMR (250 MHz, acetone-*D*₆, 25 °C): 8.33 (d, J³_{H,H} = 7.5 Hz, 2H, H^{4,4'}), 7.68 (d,

$J_{\text{H,H}}^3 = 7.3 \text{ Hz}$, 2H, $\text{H}^{7, 7'}$), 7.43 (q, $J_{\text{H,H}}^3 = 7.2 \text{ Hz}$, 4H, $\text{H}^{5, 5', 6, 6'}$), 4.56 (s, 4H, S- $\text{CH}_2(\text{benzimidazole})$), 3.98 (s, 6H, CH_3), 3.13 (s, 4H, S- CH_2).



A solution of bmdhp [11b] (91 mg, 0.230 mmol) in acetone (3 ml) was added to $\text{Zn}(\text{OTf})_2$ (84 mg, 0.230 mmol) dissolved in 15 ml degassed acetone. The product precipitated out of the solution as mono-solvate by reducing the solvent after stirring for 30 minutes at room temperature. Yield: 148 mg (0.191 mmol, 83%). Elementary analysis: $\text{C}_{49}\text{H}_{58}\text{F}_{12}\text{N}_8\text{O}_{15}\text{S}_8\text{Zn}_2$ (1614.35 g mol^{-1}). C 37.49 (cal. 36.46); H 3.24 (cal. 3.62); N 7.48 (6.94)%. $^1\text{H-NMR}$ (250 MHz, acetone- D_6 , 25 °C): 7.85 (m, 4H, $\text{H}^{4,4', 7, 7'}$), 7.50 (t, $J_{\text{H,H}}^3 = 7.8 \text{ Hz}$, 2H, $\text{H}^{5, 5'}$), 7.35 (t, $J_{\text{H,H}}^3 = 7.7 \text{ Hz}$, 2H, $\text{H}^{6, 6'}$), 4.66 (s, 4H, S- CH_2 (benzimidazole)), 4.11 (s, 6H, CH_3), 3.06 (m, 4H, S- CH_2), 1.99 (m, 2H, CH_2).

Crystallography

Single crystals of **1** and **2** were grown as colourless needles from acetone solutions at -10°C . The X-ray data were collected on a Bruker-Nonius κ -CCD diffractometer, using graphite monochromated Mo- $\text{K}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$). The structures were solved by the Patterson method using the SHELXTL package [15] while refining was carried out with SHELXL97 employing full matrix least-squares methods on F^2 with $\text{F}\sigma^2 \geq -2\sigma(\text{F}\sigma^2)$. All non-hydrogen atoms were refined anisotropically, hydrogen atoms were placed in the calculated positions and were refined using the riding model.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC-743048 - CCDC-743049. Copies of the information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-

033; e-mail: deposit@ccdc.cam.ac.uk; www: <http://www.ccdc.cam.ac.uk>).

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