# Zinc complexes of the N,N,S ligand bis(pyrazolyl)(thienyl)methane*

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## Abstract

The recently described ligand bis(pyrazol-1-yl)(thien-2-yl)methane ($L^3$) was reacted with zinc halides with the aim of obtaining complexes with a tetrahedral Zn(N,N,S)Hal coordination. Molecular compounds $L^3ZnHal_2$ (Hal = Cl, Br, I) were obtained. A structure determination of the bromide complex showed it to be tetrahedral with two bromine and two pyrazole N ligand atoms. The thiophene sulfur was found to be non-coordinating.

## Introduction

One of the aims of modern zinc coordination chemistry is the modelling of zinc containing enzymes [1]. The synthetic challenge associated with this is the preparation of tetrahedral zinc complexes containing one labile ligand ($H_2O$, $OH^-$, $Hal^-$) together with three nitrogen or sulfur containing ligands ensuring chemical and coordinative stability [2]. In the specific case of alcohol dehydrogenase the labile ligand models a water molecule (resting enzyme) or the substrate (active enzyme) whereas the three other ligands must model one histidine nitrogen and two cysteine sulfur atoms from the polypeptide chain [3]. Likewise, in acylamino acid amidohydrolase the zinc coordination has been suggested to comprise the substrate, two histidine nitrogen, and one cysteine sulfur atoms [4]. Model compounds for these enzymes thus have to contain ligands providing (N,S,S) or (N,N,S) donor sets.

One way of obtaining functional model compounds of this type is the use of tridentate ligands $L^3$ providing an appropriate set of donor atoms and a favourable stereochemical disposition [1, 2]. We have successfully applied this concept to the modelling of carbonic anhydrase with zinc complexes of substituted pyrazolyl borates, i.e. anionic $L^3$ ligands providing an (N,N,N) donor set [5]. It therefore seemed attractive to us to apply the same approach to $L^3$ ligands with mixed N and S, specifically (N,N,S) donor sets. However, no bis(pyrazolyl)-mono(mercapto) ligand has been reported so far [6]. But the stereochemically equivalent

$L^3$ ligand bis(pyrazol-1-yl)(thien-2-yl)methane (**1**) was recently described [7]. We therefore started our investigations into the (N,N,S) system of $L^3$ ligands with this compound.



**1**
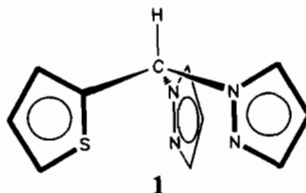
## Experimental

The general experimental techniques and physical measurements were as described before [8]. The title ligand **1** was prepared according to the published procedure [7].

*1·ZnCl₂ (2a).* To a solution of 200 mg (0.87 mmol) **1** in 40 ml of $CH_2Cl_2$ were added 165 mg (1.21 mmol) $ZnCl_2$ (containing some water due to its hygroscopicity) with stirring. The reaction mixture was warmed to 40 °C for 2 h, pumped down to 15 ml, and cooled to $-20$ °C overnight. 219 mg (60%) of colourless **2a**, m.p. 185 °C (dec.) were obtained by filtration and drying *in vacuo*. *Anal.* Calc. for $C_{11}H_{10}Cl_2N_4SZn$ ($M_r$ 366.6): C, 36.04; H, 2.75; N, 15.29. Found: C, 36.19; H, 2.86; N, 14.72%.

*1·ZnBr₂ (2b).* Like **2a** from 110 mg (0.47 mmol) of **1** and 106 mg (0.47 mmol) of $ZnBr_2$ in 10 ml of methanol. Reaction for 1 h at 20 °C. Yield 123 mg (57%) of colourless **2b**, m.p. 170 °C (dec.). *Anal.* Calc. for $C_{11}H_{10}Br_2N_4SZn$ ($M_r$ 455.5): C, 29.01; H, 2.21; N, 12.30. Found: C, 29.26; H, 2.21; N, 12.11%.

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*Dedicated to Professor Pedro Aymonino on the occasion of his 65th birthday.

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$1 \cdot ZnI_2$ *(2c).* Like **2a** from 100 mg (0.43 mmol) of **1** and 137 mg (0.43 mmol) of $ZnI_2$ in 10 ml of methanol. Reaction for 1 h at 20 °C. Yield 128 mg (54%) of colourless **2c**, m.p. 172 °C (dec.). *Anal.* Calc. for $C_{11}H_{10}I_2N_4SZn$ ($M_r$ 549.5): C, 24.04; H, 1.83; N, 10.20. Found: C, 24.29; H, 1.82; N, 10.14%.

## Structure determination

Crystals of **2b** (formula $C_{11}H_{10}Br_2N_4SZn$, mol. wt. 455.5) were obtained by slowly cooling a hot methanol solution to room temperature, and a colourless platelet of size $0.3 \times 0.2 \times 0.1$ mm was chosen for the measurement. Crystals belong to the monoclinic system, space group $P2_1/c$, $a = 9.359(2)$, $b = 15.589(3)$, $c = 11.038(2)$ Å, $\beta = 105.77(3)°$, $V = 1549.8(5)$ Å$^3$, $Z = 4$, $D_{calc} = 1.95$ g cm$^{-3}$, $\mu = 68.5$ cm$^{-1}$. All crystallographic data were obtained with a Siemens R3m/V diffractometer using Mo $K\alpha$ radiation. Of the 2654 reflections obtained with the $\omega/2\Theta$ technique in the range $+h + k \pm l$ for $2\Theta = 2-45°$, 2009 were independent, and 1317 with $F \geqslant 4\sigma(F)$ were used for the calculations after an empirical absorption correction based on $\Psi$ scans. The SHELXTL program system [9] was used to solve the structure with direct methods and for the full matrix least-squares refinement. Anisotropic temperature factors were applied for the zinc, bromine and nitrogen atoms. Hydrogen atoms were included with a C–H bond length of 0.96 Å and a common isotropic temperature factor. The refinement for 102 parameters converged to an unweighted R value of 0.059 and a *GOF* of 3.79. The largest peak in the final difference map corresponds to $+1.2$ e/Å$^3$ near C32. Inspection of the thermal parameters of S31 and C32 points to a certain degree of disorder of the thiophene ring such that these two atoms are exchanged. As the thiophene sulfur atom is not coordinated to the zinc ion this has no significance for the discussion below. Atomic parameters are given in Table 1, the structure drawing was produced with the SCHAKAL program [10]. See also 'Supplementary material".

## Results and discussion

### Reactions and products

The reaction between **1** and the zinc halides in methanol proceeded smoothly and produced the three complexes **2** in good yields as precipitates from the reaction mixture. The compositions of **2a–c** could be deduced from the elemental analyses and from the ¹H NMR spectra (Table 2). The latter, like the IR spectra, are however of little value with respect to the constitution of the compounds. The low solubility in alcohols and acetone pointed to an ionic formulation like $[(L^3)ZnHal]^+Hal^-$. But the structure determination

TABLE 1 Atomic parameters for **2b** (atomic coordinates $\times 10^4$, equivalent isotropic temperature factors pm$^2 \times 10^{-1}$)

| Atom | $x$ | $y$ | $z$ | $U_{eq}$ |
|---|---|---|---|---|
| Zn | 2479(2) | 659(1) | 1291(2) | 40(1) |
| Br(1) | 2394(2) | −573(1) | 2461(2) | 53(1) |
| Br(2) | 2551(2) | 441(1) | −805(2) | 62(1) |
| C(1) | 2644(16) | 2262(9) | 3221(13) | 38(4) |
| N(11) | 3955(13) | 2197(7) | 2756(10) | 38(3) |
| N(12) | 4186(13) | 1481(8) | 2125(11) | 41(5) |
| C(11) | 5572(19) | 1524(11) | 2079(16) | 52(4) |
| C(12) | 6297(22) | 2250(12) | 2677(16) | 64(5) |
| C(13) | 5217(19) | 2652(11) | 3126(15) | 52(4) |
| N(21) | 1316(13) | 2254(7) | 2167(10) | 37(3) |
| N(22) | 958(13) | 1585(7) | 1378(11) | 40(5) |
| C(21) | −426(18) | 1738(10) | 646(16) | 53(4) |
| C(22) | −962(20) | 2519(11) | 974(16) | 58(5) |
| C(23) | 136(18) | 2819(10) | 1964(15) | 51(4) |
| C(31) | 2598(17) | 1581(9) | 4171(14) | 41(4) |
| C(32) | 1132(13) | 1252(7) | 4448(11) | 17(3) |
| C(33) | 1845(21) | 664(12) | 5528(17) | 70(5) |
| C(34) | 3275(22) | 602(13) | 5918(18) | 73(5) |
| S(31) | 4202(8) | 1242(5) | 5139(7) | 107(2) |

(see below) revealed the molecular composition in which two pyrazole N atoms and two halide ligands comprise the tetrahedral environment of zinc while the thiophene part of the $L^3$ ligand remains uncoordinated.
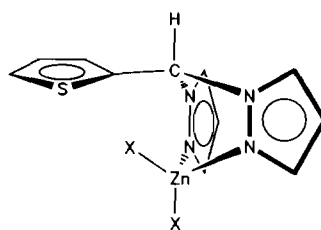


$X = Cl$ **(2a)**, $Br$ **(2b)**, $I$ **(2c)**

This observation is in agreement with the experience that thioether complexes of zinc are rather labile [11]. But thiophene complexes of zinc are known [1], and zinc thiolates are a very stable class of compounds [12]. The bonding situation in **2a–c** resembles that in the $ZnCl_2$ complex of 1,3-bis(5'-methyl-4'-imidazolyl)-2-thiapropane [13], while copper forms complexes of this latter ligand in which the thioether S atom is coordinated [14]. Similarly, in bis(S-methylcysteinato)zinc the metal is only N- and O-coordinated [15]. It must be stated that the preference of Zn–Hal bonding rather than Zn–S(thioether) bonding in **2** overcompensates the stereochemical favourability of the ligand **1**, whereas in the related tris(pyrazolyl)borate complexes all three N donor atoms are always bonded to zinc. Most probably the negative charge of the pyrazolylborates which is not present in **1** is the decisive factor in the stability and geometry of their complexes.
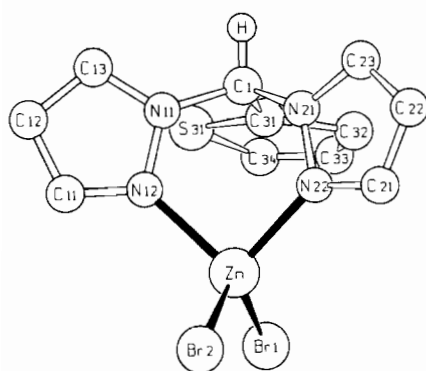
TABLE 2. $^1$H NMR data of complexes 2 ($\delta$ (ppm)/$J$ (Hz), acetone-$d_6$, int. TMS)

| | C–H | Pyrazole ring | | | Thiophene ring | | |
|---|---|---|---|---|---|---|---|
| | | H3 | H5 | H4 | H3 | H5 | H4 |
| 1 | 8.17 | 7.58/1.5 | 7.92/2.4 | 6.33 m | 7.08 m | 7.59/5.1 | 7.08 m |
| 2a | 8.70 | 8.00/2.2 | 8.41/2.3 | 6.67 m | 6.71/3.7 | 7.53/5.1 | 6.98 m |
| 2b | 8.71 | 8.07/2.2 | 8.47/2.6 | 6.73 m | 6 61/3 7 | 7.54/5.1 | 6.98 m |
| 2c | 8.73 | 8.14/2 2 | 8.51/2.6 | 6 77 m | 6.51/3.7 | 7.53/5.1 | 6.97 m |

*Structure determination*

The bromo complex 2b yielded good crystals which were used to elucidate the molecular nature of the compounds 2. All crystallographic details are given in 'Experimental'. Figure 1 shows a view of the molecule. Table 3 lists pertinent structural data. It is obvious that the zinc ion has only fourfold coordination and that the thiophene ring does not participate in the zinc–ligand bonding.

The geometry around zinc is highly distorted tetrahedral with the Br–Zn–Br angle (116°) having the largest and the N–Zn–N angle (90°) having the smallest value. The latter seems to be characteristic for the pyrazole-containing ligand, as it is observed regularly in zinc complexes of pyrazolylborates [5, 6]. The zinc–ligand bond lengths are in the normal range. The Zn–N bond lengths (2.05–2.06 Å) are typical for zinc in a tetrahedral environment [1] and for zinc in pyrazolylborate complexes [6]. Zn–Br distances like the ones in 2b (2.33–2.36

Å) have been observed, e.g. in [HB(3-tBupz)$_3$Zn-Br] [16] and in [BBMA·ZnBr$_2$] (BBMA = bis[(benzimidazolyl)methyl]methylamine [17].

Although the thiophene part of the molecule is not coordinating, the geometry of the ligand 1 in complex 2b seems to be strain-free. The most obvious indication for this rests in the normal tetrahedral angles at the central C1 atom. Thus, as the thiophene ring is attached to an aliphatic carbon atom, there is no electronic reason for it to be oriented in a plane maximizing its distance from the zinc ion. Accordingly the geometry and coordination number in 2b are controlled by the preference of zinc for the bromine and nitrogen ligands.

As mentioned above, the bonding situation in 2b resembles that in [SBI·ZnCl$_2$] (SBI = (1,3-bis(5′-methyl-4′-imidazolyl)-2-thiapropane) [13]. The thioether sulfur atom in this complex is also non-coordinating, and the coordination geometry of zinc is close to ideally tetrahedral. The low affinity for thioethers, however, seems to be specific for zinc, as the corresponding copper complex is trigonal-bipyramidal with a normal Cu–S bond [14].

**Conclusions**

This paper shows that pyrazolylmethanes can form zinc complexes of which the pyrazolyl part resembles that in pyrazolylborates. Two factors make the obtained complexes 2 less favourable than their pyrazolylborate counterparts: (i) the lack of an anionic charge on the ligand as an important contribution to the complex stability, and (ii) the presence of the thiophene sulfur as a donor of too low efficiency. In order to obtain L$^3$Zn–X complexes with an (N,N,S) donor set, a preferable property of the L$^3$ ligand would be a negative charge resulting either from the presence of a thiol sulfur or of a bis(pyrazolyl)(thienyl)borate ligand.



Fig 1. Molecular structure of 2b.

TABLE 3. Selected bond lengths (Å) and angles (°) for 2a

| Zn–Br1 | 2.328(2) | Br1–Zn–Br2 | 116.1(1) |
|---|---|---|---|
| Zn–Br2 | 2.358(3) | Br1–Zn–N12 | 113.9(3) |
| Zn–N12 | 2.06(1) | Br1–Zn–N22 | 115.3(4) |
| Zn–N22 | 2.05(1) | Br2–Zn–N12 | 107.6(4) |
| N12–N11 | 1.36(2) | Br2–Zn–N22 | 110.7(3) |
| N22–N21 | 1.34(2) | N12–Zn–N22 | 90.3(5) |
| N11–C1 | 1.46(2) | N11–C1–N21 | 109.7(12) |
| N21–C1 | 1.46(2) | N11–C1–C31 | 112.6(12) |
| C1–C31 | 1.50(2) | N21–C1–C31 | 111 8(12) |

**Supplementary material**

All details of the crystal structure determination are available upon request from the Fachinformationszen-

trum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, Germany, quoting the depository no. CSD 400046, the authors and the journal citation.

## Acknowledgements

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