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Synthesis of Zinc Dimethyldithiocarbamate by Reductive Disulfide Bond Cleavage of Tetramethylthiuram Disulfide in Presence of Zn^{2+}

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The zinc(II) complex $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ has been synthesized directly from thiram ligand, containing a disulfide bond {dmdtc = N,N-dimethyldithiocarbamate; thiram = N,N-tetramethylthiuram disulfide}, and characterized by elemental analysis and spectroscopic methods. Surprisingly thiram, undergoes a reductive disulfide bond scission upon reaction with Zn^{2+} in methanolic media to give the $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ complex. The crystal structure of Zn(II) complex has been determined by single crystal X-ray diffraction. Zinc is 4+1 coordinate, with four nearly identical tetrahedral bonds and a longer fifth bond being similar to some reported $[Zn(dtc)_2(L)]$ complexes. The crystal structure of this complex is built up of dimeric units, $[Zn(dmdtc)(\mu\text{-}dmdtc)_2]$, so that each unit has two thiocarbamate groups, one wholly bound to a zinc atom as a bidentate ligand and the other in a bridging coordination mode between the two Zn(II) atoms. This structure clearly shows scission of the disulfide bond in the thiram ligand to give two dimethyldithiocarbamate ligands coordinated to the Zn(II) ion.

Keywords: Zn(II) complex, Crystal structure, Disulfide cleavage, Dimethyldithiocarbamate

INTRODUCTION

Dithiocarbamates are an important class of compounds with a variety of chemical properties and biological effects that are utilized in agriculture as fungicides and pesticides, in rubber chemistry, and in therapeutic applications such as the treatment of alcoholics, acute metal poisoning, and Wilson's disease [1-5]. The most prevalent therapeutic application of these compounds is in the treatment of alcoholics with disulfiram (N,N-tetraethylthiuram disulfide). The reduced form i.e. dithiocarbamate has been identified as metabolic product after ingestion of disulfiram [5-7]. The biochemical activity of diethyldithiocarbamate is supposed to involve chelation to the copper containing enzyme aldehyde dehydrogenase [5].

On the other hand, zinc is an essential metal involved in a variety of biochemical functions necessary for normal neuronal activity [8]. Diethyldithiocarbamate as a chelating agent affects the distribution of zinc, leading to an increase in the brain level of zinc(II). Such redistribution of zinc may be explained based on the formation of lipophilic metal chelates [9].

In this work, we report the synthesis and characterization of zinc(II) dithiocarbamate complex using an analogue of disulfiram, *i.e.* thiram as the ligand source which undergoes concomitant S-S bond scission and coordination to Zn(II). The crystal structure of zinc(II) complex is built up of dimeric entities of $[Zn(dmdtc)(\mu\text{-}dmdtc)]$ (Scheme 1). The X-ray structure of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ has been previously reported [10].

EXPERIMENTAL

Materials and General Methods

All solvents and chemicals were of commercial reagent grade and were used as received from Aldrich and Merck.

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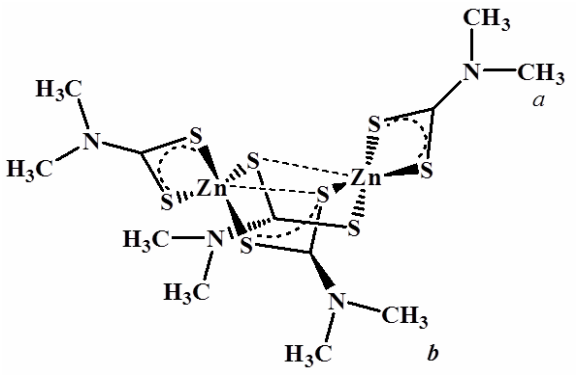


Scheme 1. The chemical formula of the $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$

Infrared spectra from KBr pellets were collected on a FT-IR JASCO 680 plus spectrophotometer in the range 4000-400 cm^{-1}. UV-Vis absorption spectra were recorded on a JASCO V-570 spectrophotometer. ^1H NMR spectra were obtained on a Bruker AVANCE III 400 spectrometer (400 MHz). Proton chemical shifts are reported in ppm relative to Me_4Si as internal standard. Elemental analyses were performed by using a Perkin-Elmer 2400II CHNS-O elemental analyzer.

Synthesis of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$, 1

To a solution of $Zn(OAc)_2{\cdot}2H_2O$ (22 mg, 0.1 mmol) in methanol (15 ml) was added a solution of thiram (24 mg, 0.1 mmol) in $CHCl_3$ (15 ml), and the mixture was stirred at room temperature for 24 h to give a colourless solution. Single crystals of complex 1 suitable for X-ray crystallography were obtained by slow evaporation of the solvents. Yield 58%. Anal. Calcd. for $C_6H_{12}N_2S_4Zn$: C, 23.56; H, 3.95; N, 9.16; S, 41.94. Found (%): C, 22.79; H, 3.89; N, 8.93; S, 42.13. FT-IR (KBr pellet, cm^{-1}) ν_{max}: 1389, 1241, 1145 (C=S, s). UV-Vis: λ_{max} (nm) (ε, M^{-1} cm^{-1}) (DMF): 303 (20400), 433 (1805). ^1H NMR (DMSO-d_6, 400 MHz): δ = 4.446 (s, 6H, H_a), 4.448 (s, 6H, H_b).

Crystal Structure Determination and Refinement

Suitable single crystals of Zn(II) complex were obtained by slow evaporation of a methanol-chloroform (1:1 v/v) solution at room temperature. X-ray data for 1 was collected at T = 100 K on a Bruker Kappa APEX-II CCD diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation. Cell refinement was performed with the help of the program SMART, and data reduction with the program SAINT [11]. Correction for absorption was carried out with the multi-scan method and program SADABS [12]. The structure of this complex was solved with direct methods using the program SHELXS-97 [12] and structure refinement on F^2 was carried out with the program SHELXL-97. Crystal data, together with other relevant information on the structure determination, are summarized in Table 1.

RESULTS AND DISCUSSION

Synthesis and Characterization

$[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ was directly synthesized by the reaction of tetramethylthiuram disulfide and $Zn(OAc)_2.2H_2O$ in a 1:1 molar ratio in methanol/$CHCl_3$ solution. Notably, the disulfide bond is reduced to two dimethyldithiocarbamate ligands, by the reductive solvent (methanol) in the presence of Zn(II) (Scheme 2) [13].

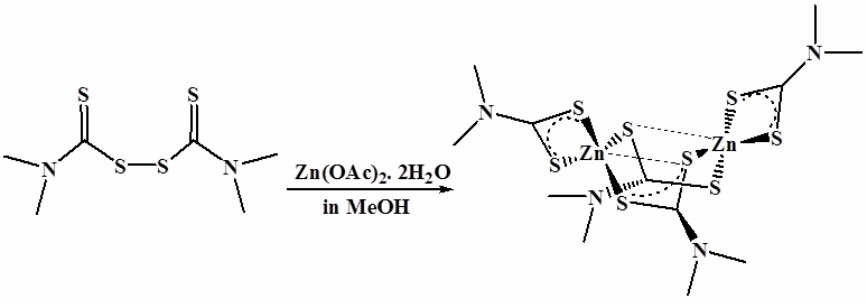
Description of the Structure of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$

The crystal structure of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ with atomic numbering scheme is presented in Fig. 1, and the selected bond distances and angles are listed in Table 2. This complex crystallizes in monoclinic space group *C2/c*. The crystal structure of this complex is built up of dimeric units, $[Zn(dmdtc)(\mu\text{-}dmdtc)_2]$, so that each unit has two thiocarbamate groups, one wholly bound to a zinc atom as a bidentate ligand and the other in a bridging coordination

Table 1. Crystal Data and Structure Refinement for $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$

Compound	$[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$
Empirical formula	$C_6H_{12}N_2S_4Zn$
Formula weight	305.79
Temperature (K)	100 (2)
Crystal system	Monoclinic
Space group	*C2/c*
a (Å)	8.26(3)
b (Å)	15.67(6)
c (Å)	18.14(7)
α (°)	90.00
β (°)	102.192(2)
γ (°)	90.00
V (Å^3)	2295.72(15)
Z	8
D_{calc} (mg m^{-3})	1.769
μ (mm^{-1})	2.82
Crystal size (mm)	0.45 × 0.38 × 0.25
F(000)	1248
Range (°)	2.3-30.0
Absorption correction	Multi-scan
Reflections collected	12665
R_{int}	0.021
Data/restraints/parameters	3361/0/122
Goodness-of-fit on F^2	1.048
Final *R* indices [$I > 2\sigma(I)$] [(a)]	$R_1 = 0.020$, $wR_2 = 0.050$
Largest diff. peak and hole (e Å^{-3})	0.5 and -0.25

[a] $R_1 = \sum||F_o|-|F_c||/\sum|F_o|$, $wR_2 = \{\sum[w(F_o^2-F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.



Scheme 2. Synthesis of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$

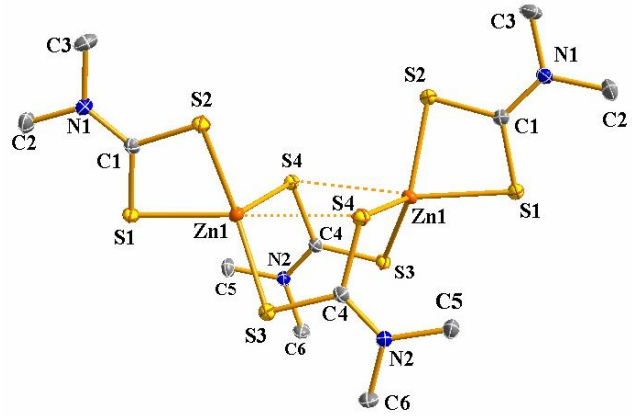
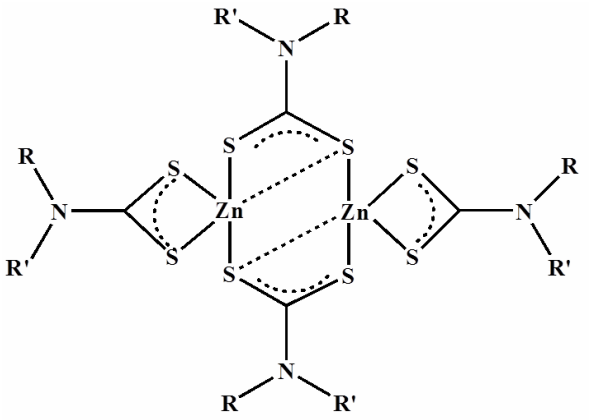


Fig. 1. The molecular structure of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ (1) with its atom labeling scheme.

Table 2. Selected bond lengths (Å) and angles (˚) for (1)

Bond lengths		Bond angles	
Zn1-S3	2.3216(3)	S3-Zn1-S2	136.327(13)
Zn1-S2	2.3384(3)	S3-Zn1-S4^{i}	110.465(12)
Zn1-S4^{i}	2.3765(3)	S2-Zn1-S4^{i}	105.051(12)
Zn1-S1	2.4273(3)	S3-Zn1-S1	109.156(11)
S4-Zn1	3.062(3)	S2-Zn1-S1	76.466(11)
S1-C1	1.7297(13)	S4^{i}-Zn1-S1	114.944(12)
S2-C1	1.7329(12)		
S3-C4	1.7268(12)		
S4-C4	1.7398(13)		

^{i}-x+2, y, -z+3/2



Scheme 3. The common unit of $[Zn_2(dtc)_2(\mu\text{-}dtc)_2]$ complexes

mode between the two Zn(II) atoms. This structure clearly shows that the thiram ligand has undergone scission of the disulfide bond to give two dimethyldithiocarbamate ligands coordinated to the Zn(II) ion in two different coordination modes. Zn is 4+1-coordinate, the four tetrahedral bonds are 2.332 to 2.427 Å, and the fifth bond (Zn1…S4) is 3.062 Å. In the reported $[Zn_2(dtc)_2(\mu\text{-}dtc)_2]$ complexes the four short bonds are between 3.31 and 3.48 Å while the fifth bonds are mostly 3.82-3.95 Å. The distortion of all coordination figures is always the same (distances, angles) and all complex cores $S_2 > Zn < (S\text{-}C\text{-}S)_2 > Zn < S_2$ are nearly identical; only $N(alkyl)_2$ groups show modest variations in orientation [10,14-19]. The common unit of $[Zn_2(dtc)_2(\mu\text{-}dtc)_2]$ complexes is shown in Scheme 3. Note also that some $Zn(dtc)_2$ complexes are mononuclear with two chelating dtc groups and relatively regular ZnS_4 tetrahedra with respect to Zn-S distances (narrower Zn-S range) [20-21]. Mono- as well as dinuclear $Zn(dtc)_2$ complexes react with donors like CH_3CN or pyridine or alike leading to the formation of usually $[Zn(dtc)_2(L)]$ complexes with two chelating dtc plus one terminal L generating 5-coordinated ZnS_4L-polyhedra [22].

Spectral Characterization

The FT-IR data of the spectra of thiram and $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ are presented in the supporting material. The FT-IR spectrum of the free thiram exhibits a band at 847 cm^{-1} corresponding to the ν(S-S) stretching vibration. This band is conspicuously absent in the spectrum of the Zn(II) complex, and it confirms cleavage of the disulfide bond during the synthesis process. The characteristic bands of (C=S) group in the thiram appear at 1147, 1234 and 1374 cm^{-1}. Similar features are observed in the IR spectrum of the Zn(II) complex, with the C=S stretching vibrations appearing at 1145, 1241 and 1389 cm^{-1} [23]. These spectroscopic data support the coordination of cleaved thiram to the zinc ion and conform to the structure of the complex obtained by X-ray diffraction (*vide supra*).

The electronic absorption spectra of thiram and $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ are recorded in DMF solution and the data are presented in supporting information. The absorption spectrum of thiram consists of an intense band appearing at 312 nm and is attributed to the intraligand transition. The Zn(II) complex shows two bands at 303 and 433 nm corresponding to the intraligand and charge transfer transitions. As in related d^{10} metal complexes, no d-d transition would be expected for this compound [24].

The ^1H NMR spectral measurements of $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$ was performed in DMSO-d_6 solution and the corresponding data are given in Section 2. The main features of the ^1H NMR spectrum of this complex are two singlet signals due to two different methyl groups at 4.446 and 4.448 ppm for bridging and terminal dimethyldithiocarbamate groups, respectively.

CONCLUSIONS

In this work, we have reported the direct synthesis of

zinc dimethyldithiocarbamate complex from tetramethyl-thiuram disulfide (thiram) ligand. The reaction of the disulfide ligand (thiram) with Zn(II) in reductive solvents (alcoholic medium) has led to the reductive cleavage of the S-S bond and formation of dimeric zinc complex, $[Zn_2(dmdtc)_2(\mu\text{-}dmdtc)_2]$. The similarity between thiram performance and that of disulfiram, therefore, makes it a suitable candidate to supersede disulfiram [25].

SUPPORTING MATERIAL

Crystallographic data for the structure of 1 reported in this article have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 1033786. Copies of the data can be obtained free of charge *via* www.ccdc.cam.ac.uk (or from the Cambridge Crystallographic Centre, 12 Union Road, Cambridge CB21EZ, UK; Fax: þ44 1223 336033; Email: deposit@ccdc.cam.ac.uk).

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