# Electrochemical Synthesis of a 6-Coordinate Cadmium(II) Complex with N-Methylisatin N(4)-cyclohexylthiosemicarbazone

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Cadmium metal was oxidized in the presence of N-methylisatin N(4)-cyclohexylthiosemicarbazone (HMeIs4Chex) in an acetonitrile solution, which produced a complex of the formula [Cd(MeIs4Chex)<sub>2</sub>]. The two MeIs4Chex ligands are at an angle close to 90° from each other, and there is hydrogen bonding to two adjacent molecules by the anionic ligands remaining NH groups. The complex crystallizes in the monoclinic space group P2<sub>1</sub>/c with *a* = 11.820(4), *b* = 11.491(4), *c* = 27.834(4) Å,  $\beta$  = 106.82(2)°, V = 3618.7(17) Å<sup>3</sup> and Z = 4.

## Introduction

Interest in compounds related to 1-methylisatin thiosemicarbazone, methisazone, is based on its antiviral activity [1-3]. It has been suggested that thiosemicarbazone drugs inhibit virus growth by binding to copper ions which are constituents of the virus [4]. Along with other molecular modifications, replacement of hydrogen atoms at the N(4)position of the thiosemicarbazone moiety, Fig. 1, has been explored [5]. A single phenyl or methyl group attached to N(4) results in a total loss of antismallpox activity, and a propenyl group reduced activity to 4% of that of the unsubstituted thiosemicarbazone, while substitution of two alkyl groups at N(4) yielded compounds with activity against ectromelia and type 2 polio [6]. However, in other series of thiosemicarbazones possessing biological activity, no predictable structure/activity relationship for the N(4) substituent has been found to date [7]. Therefore, structural studies of a variety of thiosemicarbazones coordinated to various different metal centers continues to be of considerable interest. Although there have been a number of structure determinations of 5-coordinate cadmium complexes with one tridentate thiosemicarbazone ligand and two halogen ligands in the coordination sphere [8-11], to our knowledge there has been only one of a 6-coordinate bis(thiosemicarbazone) complex of cadmium reported to date, a  $CdN_4S_2$  species [8]. We report here the structure of a  $CdO_2N_2S_2$  complex of N-methylisatin N(4)-cyclohexylthiosemicarbazone, HMeIs4Chex, which is the first complex with a metal center for this ligand.



Fig. 1. Depiction of HMeIs4Chex showing intramolecular hydrogen bonding between the thiosemicarbazone moiety and the isatin amide oxygen atom, as well as the N4-H $\cdots$ N1 hydrogen bonding common to N(4)-alkylthiosemicarbazones.

#### Experimental

#### Reagents, materials and syntheses

HMeIs4Chex was prepared by condensation of 1methylisatin (0.05 mols, 8.05 g, Aldrich) with a 2:1 molar excess of hydrazine monohydrate (Aldrich) in EtOH under reflux, and then reacting 0.005 mol (0.875 g) of the

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Table 1. Crystal data and structure refinement for metal complexes of N-methylisatin N(4)-cyclohexylthiosemicarbazone.

Table 2. Selected bond distances (Å) and angles (°) for  $[Cd(MeIs4Chex)_2]$ .

		Cd-N12	2.301(9)	Cd-N22	2,300(9)
Empirical formula	$C_{32}H_{38}CdN_8O_2S_2$	Cd-S1	2.569(4)	Cd-S2	2.569(4)
Color, habit	yellow, plate	Cd-O1	2.505(1) 2.514(8)	Cd-02	2.505(1)
Formula weight	743.22	S1-C9	1.705(13)	S2-C29	1.711(13)
Temperature, K	293(2)	N12-C8	1.305(11)	N22-C28	1.292(13)
Crystal system	monoclinic	N12-N13	1.351(12)	N22-N23	1.345(11)
Space group	$P2_1/c$ (#14)	N13-C9	1.357(14)	N23-C29	1.343(13)
a [Å]	11.820(4)	N14-C9	1.339(13)	N24-C29	1.344(13)
<i>b</i> [Å]	11.491(4)	01-C1	1.229(13)	O2-C21	1.209(14)
<i>c</i> [Å]	27.834(4)	N12 CH N22	157.2(2)	S2 C4 S1	107.14(12)
$\alpha$ [°]	90(0)	N12-Cd-N22	137.5(3) 121.6(2)	52-Cu-51	107.14(12) 118.0(2)
$\beta$ [°]	106.82(2)	N12-Cd-52	7121.0(2)	N22-Cd-S1	74.7(2)
$\gamma$ [°]	90(0)	N12-Cd-S1	74.0(3)	N22-Cd-52	74.7(3)
Volume [Å <sup>3</sup> ]	3618.7(17)	N12-Cd-O1	70.4(3)	N22-Cd-O2	70.5(3)
Z	4	N12-Cu-02	91.0(3) 143.8(2)	N22-Cd-O1	92.3(3)
Density [Mg/m <sup>3</sup> ]	1.364	SI-Cd-O1	143.8(2)	S2-Cd-O2	143.0(2)
Absorption coefficient $[mm^{-1}]$	0.758	S1-C1-O2	91.2(2)	32-Cu-O1	98.9(2)
Crystal size [mm]	0.25  imes 0.15  imes 0.15	$C_1 C_1 C_2$	80.8(3)	C20 52 C4	06.4(5)
$\theta$ Range for data collection [°]	2.34 - 24.40	C9-S1-Ca	97.0(3)	C29-52-Cd	90.4(3)
Index ranges	-13 < h < 13		109.1(9)	C21-02-Cd	109.0(10)
C	$-13 \leq k \leq 0$	C8-N12-Cd	117.3(9)	C28-N22-Cd	118.6(9)
	$-32 \le l \le 13$	N13-N12-Cd	125.1(7)	N23-N22-Cd	126.1(8)
Reflections collected	5939	C8-N12-N13	117.5(11)	C28-N22-N23	115.1(11)
Unique reflections	5805	N12-N13-C9	112.2(11)	N22-N23-C29	111.1(11)
Absorption correction	$\Psi$ -scan	N13-C9-N14	112.5(14)	N23-C29-N24	113.1(12)
Max / min transmission	0.963/0.910	N13-C9-S1	129.6(11)	N23-C29-S2	131.5(10)
Data / parameters	5805 / 408	N14-C9-S1	117.9(11)	N24-C29-S2	115.3(11)
Goodness-of-Fit on $F^2$	0 904	01-C1-N11	127.7(13)	O2-C21-N21	129.1(15)
Final <i>R</i> indices $[I > 2\sigma(I)]$	$R_1 = 0.0676$	O1-C1-C8	124.4(14)	O2-C21-C28	125.8(15)
[1 > 20(1)]	$wR_2 = 0.0931$				
R indices (all data)	$R_1 = 0.3926$				
A marces (an data)	$wR_2 = 0.1468$	C32 C31 0			
Largest diff. peak/hole $[eÅ^{-3}]$	0.601  and  -1.033		30 0		C15 C14

resulting hydrazone with an equimolar amount (0.706 g) of cyclohexyl isothiocyanate (Aldrich) in EtOH with warming. The resulting yellow product (yield = 72%) was washed with isopropanol followed by diethyl ether and stored in a vacuum desiccator over calcium sulfate. [Cd(MeIs4Chex)<sub>2</sub>] was prepared by electrochemical oxidation of cadmium in a solution of HMeIs4Chex (0.19 mmol, 59 mg) in CH<sub>3</sub>CN (40 ml) containing 10 mg of tetramethylammonium perchlorate for 1 h at 5 mA. A loss of 10.5 mg of the anode resulted.

### X-ray data collection and processing

A yellow plate crystal of  $[Cd(MeIs4Chex)_2]$  was mounted on a glass fibber and used for data collection with a Nonius MACH3 automatic diffractometer. The cell constants and an orientation matrix for data collection were obtained by least-squares refinement of the diffraction data from 25 reflections in the range of 7.491 <  $\theta$  <



Fig. 2. Perspective drawing of  $[Cd(MeIs4Chex)_2]$  at 50% probability.

11.286°. Data were collected at 293(2) K using MoK $\alpha$  radiation ( $\lambda = 0.71073$  Å) and the omega-scan technique, and corrected for Lorentz and polarization effects [12]. A semi-empirical absorption correction,  $\Psi$ -scan, was carried out [13]. The structure was solved by direct methods [14] and subsequent difference Fourier maps, and refined on F<sup>2</sup> by a full-matrix least-squares procedure using anisotropic displacement factors [15]. All hydrogen

Donor N14 N24	Acceptor <sup>a</sup> S2 <sup>#1</sup> S1 <sup>#2</sup>	D-H 0.86 0.86	H…A 2.76 3.00	D····A 3.578(10) 3.626(10)	∠D-H…A 159.3 131.4
Plane			Rms dev.	∠ w	vith previous plane
C1-C2-C3-C4-C5-C6-C7-C8-N11 C8-N12-N13-C9-N14-S1 C28-N22-N23-C29-N24-S2 C21-C22-C23-C24-C25-C26-C27-C28-N21			0.0262 0.0539 0.0585 0.0096	18. 82. 4.	23(0.41) 30(0.21) 59(0.42)

Table 3. Hydrogen bonding, root mean square plane deviations and angles between planes for [Cd(MeIs4Chex)<sub>2</sub>].

<sup>a</sup>Symmetry transformation used to generate equivalent atoms:  $\frac{1}{x} - x + 1$ ,  $y + \frac{1}{2}$ ,  $-z + \frac{1}{2}$ ;  $\frac{1}{x} - x + 1$ ,  $y - \frac{1}{2}$ ,  $-z + \frac{1}{2}$ .

Table 4. A comparison of thiosemicarbazone moiety bond distances for isatin thiosemicarbazones, isatin thiosemicarbazone bazone complexes and bis(thiosemicarbazone)cadmium(II) complexes.

Compound	C8-N12	N12-N13	N13-C9	C9-S1	C9-N14	Ref.
HIs4E <sup>a</sup> HIs4pT <sup>b</sup> HIshexim <sup>c</sup> [Zn(Ishexim) <sub>2</sub> ] [Pb(Ishexim) <sub>2</sub> ] [Cd(MeIs4Chex) <sub>2</sub> ]	$\begin{array}{c} 1.285(5) \\ 1.288(4) \\ 1.305(5) \\ 1.306(4) \\ 1.304(6) \\ 1.298(12) \end{array}$	$\begin{array}{c} 1.348(5) \\ 1.346(4) \\ 1.362(6) \\ 1.337(4) \\ 1.342(6) \\ 1.348(12) \end{array}$	1.383(5) 1.383(4) 1.375(4) 1.364(5) 1.357(7) 1.350(14)	$\begin{array}{c} 1.676(5) \\ 1.662(4) \\ 1.672(4) \\ 1.711(4) \\ 1.726(6) \\ 1.708(13) \end{array}$	$\begin{array}{c} 1.321(6) \\ 1.333(5) \\ 1.339(6) \\ 1.345(5) \\ 1.342(7) \\ 1.341(13) \end{array}$	21 21 21 20 20
$[Cd(Fo4DH)_2]^d$	1.29(1)	1.36(1)	1.33(1)	1.72(1)	1.36(2)	8

<sup>a</sup> isatin N(4)-ethylthiosemicarbazone; <sup>b</sup> isatin N(4)-*p*-tolylthiosemicarbazone; <sup>c</sup> isatin 3-hexamethyleneiminylthiosemicarbazone; <sup>d</sup> bis(2-formylpyridine N(4)-methylthiosemi-carbazonato)cadmium(II); <sup>e</sup> this work.

atoms were located in their calculated positions (C-H 0.93 - 0.97 Å) and refined using a riding model. Atom scattering factors were taken from the International Table for X-ray Crystallography [16] and molecular graphics are from PLATON99 [17].

### **Results and Discussion**

Table 2 lists selected bond distances and angles for[Cd(MeIs4Chex)<sub>2</sub>]. The cadmium atom is 6-coordinate with each ligand bonding via its thiolato sulfur [Cd-S, 2.569(4) Å], imine nitrogen [Cd-N, 2.301(9), 2.300(9) Å] and the isatin moiety's amide oxygen atom [Cd-O, 2.514(8), 2.515(9) Å]; the bonding of the two ligands is essentially equivalent. The previously reported 6-coordinate bis(thiosemicarbazone)cadmium(II) complex, [Cd(Fo4DH)<sub>2</sub>], where Fo4DH is the anion of 2-formylpyridine thiosemicarbazone, has similar Cd-donor atom distances [8]. For the two complexes the average bond distances with the thiolato sulfur atoms are similar [Cd-S, 2.569(4) *vs.* 2.577(3) Å] for [Cd(MeIs4Chex)<sub>2</sub>] and [Cd(Fo4DH)<sub>2</sub>], but the imine nitrogen atoms in  $[Cd(MeIs4Chex)_2]$  form shorter bonds, Cd-N, 2.301(9) vs. 2.352(8) Å. This difference probably results from the difference between the amide oxygen of MeIs4Chex and the pyridyl nitrogen of Fe4DH, even though both are involved in 5-membered, conjugated chelate rings with their imine nitrogen atoms.

The coordination polyhedron for [Cd(MeIs4-Chex)2] may be regarded as derived from an octahedron in which the two ligands are bonded in a meridional arrangement. The deviation from octahedral symmetry is due to the short bite of the ligands; the S1-Cd-O1 and S2-Cd-O2 "trans" angles are 143.8(2) and 145.0(2)°, respectively, which are similar to  $143.2(2)^{\circ}$  found for [Cd(Fo4DH)<sub>2</sub>] [8]. The N-Cd-S bite angles, 74.6(3) and  $74.7(3)^{\circ}$ , are larger than the N-Cd-O angles, 70.4(3) and  $70.3(3)^{\circ}$ . This difference in the two 5-membered chelate rings can be attributed to the differences in atomic volume of sulfur and oxygen. The best planes of the two thiosemicarbazone moieties, Table 3, approach orthogonality,  $82.30(21)^\circ$ , but this dihedral angle is smaller than  $92.4(2)^{\circ}$  found for  $[Cd(Fo4DH)_2]$  [8].

The isatin portions of the two ligands have small deviations from planarity, 0.0262 and 0.0096 Å, and these planes are at angles of 18.23(41) and  $4.69(42)^{\circ}$  to their thiosemicarbazone moieties.

There is intermolecular hydrogen bonding between the N-H groups (N14-H and N24-H) of the thiosemicarbazone moiety and a sulfur atoms on adjacent molecules, Table 3. The non-bonding N-H···S distances, 3.578(10) and 3.626(10) Å, are longer than the 3.348(3)-3.523(4) Å range found for nine substituted thioureas [18], as well as the 3.357(5) and 3.429(4) Å reported for 2pyridineformamide N(4)-methylthiosemicarbazone [19]. However, [Pb(Ishexim)<sub>2</sub>], where Ishexim is the anion of isatin 3-hexamethyleneiminylthiosemicarbazone, has an N-H···S non-bonding distance between the isatin nitrogen and a sulfur atom of a neighbouring molecule of 3.758(5) Å [20].

Unfortunately, we have not been able to grow a crystal of HMeIs4Chex or any other N-methylisatin thiosemicarbazone to compare changes in the bonding of the thiosemicarbazone moiety upon coordination. However, structures have been solved for three isatin thiosemicarbazones [21], and Table 4 is a compilation of bond distances of these thiosemicarbazones and related complexes including [Cd(Fo4DH)<sub>2</sub>] [8]. The increase in the bond distance of C9-S1 is in agreement with its change from a double bond to a single bond on complexation of the anion; the increase is much greater with transition metal ions [19]. Among the other bonds C13-C9 formally changes from a single to a double

bond on complexation of the anion, and the complexes tend to have a shorter bond than the three uncomplexed thiosemicarbazones. Again the change is greater for transition metal complexes [19].

The present study expands our knowledge of 6-coordinate cadmium(II) complexes by providing data for a new type of chelating thiosemicarbazone with ONS bonding. This structure of a bis(thiosemicarbazone)cadmium(II) complex is the first reported for an N-methyl-isatin thiosemicarbazone. It should be emphasized that electrochemical synthesis employing a low current density has provided a diffractable crystal of this new complex, and this technique is currently being used to produce additional metal complexes containing only the desired ligand.

#### **Supplementary Material**

Crystallographic data for  $C_{32}H_{38}CdN_8O_2S_2$ , [Cd(MeIs4Chex)<sub>2</sub>], CCDC#, 136015 have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1003/m. Copies of available material can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

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