Synthesis and Structural Characterization of N-[4-(2-Hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-benzamide and its Mercury(II) Chloride Adduct

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Z. Naturforsch. **60b,** 945 – 950 (2005); received June 16, 2005

The synthesis of N-[4-(2-hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-benzamide (**2a**) and N-[4-(2-hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-2-fluorobenzamide (**2b**) by oxidation of the corresponding 1,1-bis(2-hydroxyethyl)-3-aroylthioureas with potassium iodate in aqueous solution is reported. Variable temperature ^{1}H NMR spectra of **2a** prove that the heterocyclic 1,2,4-(O, S,N) six-membered ring is involved in a dynamic chair-boat conformational interconversion. Molecular mechanic calculations show that the chair conformation is more stable than the boat conformation by 3.0 kcal/mol. The synthesis of the adduct [(**2a**)·0.5 $HgCl_2$] **3** as well as the X-ray structural characterization of **2a** and **3** are also reported.

Key words: Oxathiazinanes, Mercury(II) Chloride Adduct, Synthesis, Crystal Structure, NMR Data

Introduction

During the last years our research interest has been directed towards the chemistry of N',N'-disubstituted N-acylthiourea derivatives. Several articles dealing with spectroscopic, electronic, structural and reactivity properties of N-acylthiourea ligands and related metal complexes have been published [1 – 4].

Interestingly, the reaction of N-acylthioureas with oxidizing reagents can lead to different products. So it has been found that 1-[5-(2-chlorophenyl)-2-furoyl]-3-acylthioureas undergo reaction with potassium iodate to give 1-[5-(2-chlorophenyl)-2-furoyl]-3-acylureas [5].

In contrast, the reaction of 1-(2-hydroxyethyl)-1-methyl-3-benzoylthiourea with bromine leads to N-(4-methyl-1,2,4-oxathiazinan-3-ylidene)-benzamide [6] by formation of a heterocyclic six-membered ring. Special interest in this structure results from the nature of the bonding in the O–S···O region [7]. Following these results, the present investigation was directed to explore the reaction products of 1,1-bis(2-hydroxyethyl)-3-benzoylthiourea **1a** with potassium iodate and with mercury(II) chloride as oxidizing reagents.

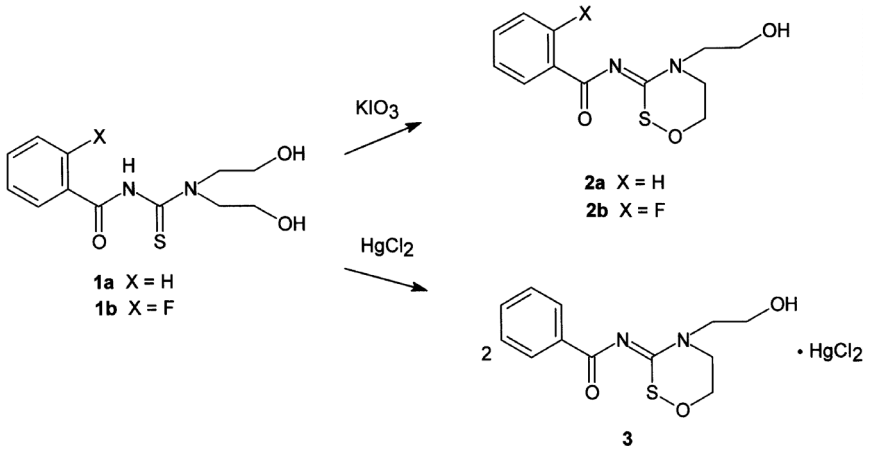
Results and Discussion

Synthesis

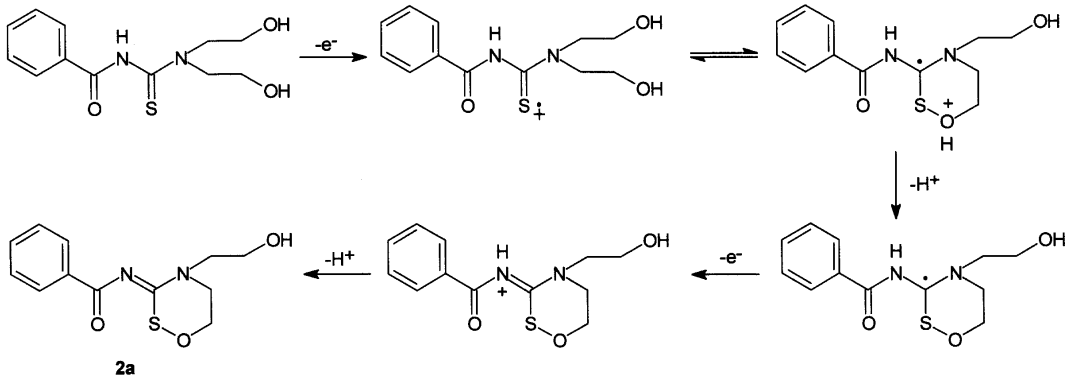
Treatment of 1,1-bis-(2-hydroxyethyl)-3-aroylthioureas **1a** (aryl = phenyl) and **1b** (aryl = 2-fluorophenyl) with potassium iodate afforded **2a** and **2b** in high yields (Scheme 1).

A plausible mechanism is depicted in Scheme 2.

The first step is an oxidative one-electron transfer reaction leading to a cation-radical species. The less electronegative sulphur atom appears to stabilize the SOMO of the cation-radical. Nucleophilic attack of the terminal oxygen at the sulphur atom leads to cyclization. Successive deprotonation, one-electron oxidation and deprotonation afford **2a**. The overall process is an "oxidative dehydrogenation reaction" (*i.e.* $-2e^-$ $-2H^+$). This reaction also takes place with $HgCl_2$ as an oxidant, which is reduced to Hg_2Cl_2 (Scheme 1).



Scheme 1.



Scheme 2.

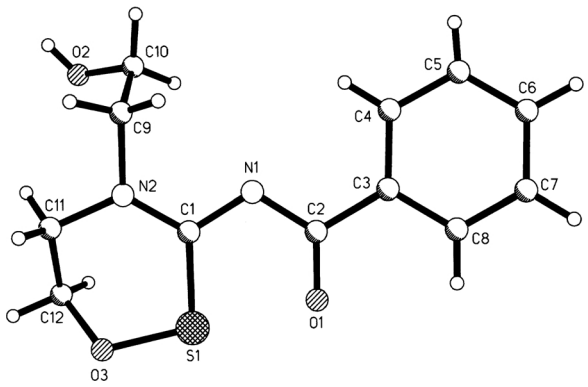


Fig. 1. Molecular structure of **2a**.

Structural characterization by X-ray structure analysis

Molecular structure of **2a**

The molecular structure of **2a** is shown in Fig. 1. Selected bond lengths and angles are found in Table 1.

The oxathiazinane ring has a distorted chair conformation. Remarkably, the three bonds N1–C1 (1.339(2) Å), N1–C2 (1.341(2) Å) and N2–C1 (1.328(2) Å) have nearly the same lengths, which point to a partial double bond character of all these bonds and to a π-electron delocalization in which the bond O1–C2 (1.251(2) Å) is also included.

The torsion angles τ(S1C1N1C2) = 1.7(2)° and τ(O1C2N1C1) = −2.7(2)° prove a Z,Z' configuration of the fragment S1C1N1C2O1.

In the crystal intermolecular hydrogen bonds exist between the atom O2 of the hydroxyl group and the atom O1 of the keto group (O2–H2···O1[1/2 + *x*, 3/2 − *y*, 1/2 + *z*] with O2···O1 2.776(2) Å, O2–H2 0.78(3) Å, H2···O1 2.02(3) Å and O2–H2···O1 162(3)°). These hydrogen bridges lead to the formation of chains of molecules in the crystal.

The results of the structure determination of **2a** are in good agreement with the structure of the analogous N-(4-methyl-1,2,4-oxathiazinan-3-ylidene)benzamide [7], where likewise no localized exocyclic (with respect to the oxathiazinane ring) C–N double bond exists but a delocalized multiple bond system including all bonds in the fragment

Table 1. Selected bond lengths (Å) and angles (°) for **2a** and **3**.

Atom	**2a**	**3**
Hg1–Cl1		2.270(2)
Hg1–Cl2		2.276(2)
Hg2–Cl3		2.307(1)
S1···O1	2.307(1)	2.296(3)
S1–O3	1.662(1)	1.680(3)
S1–C1	1.759(2)	1.767(3)
O1–C2	1.251(2)	1.253(4)
O2–C10	1.411(3)	1.426(4)
O3–C12	1.424(2)	1.433(4)
N1–C1	1.339(2)	1.329(4)
N1–C2	1.341(2)	1.341(4)
N2–C1	1.328(2)	1.331(4)
N2–C9	1.468(2)	1.474(4)
N2–C11	1.468(2)	1.470(4)
C9–C10	1.502(3)	1.507(4)
C11–C12	1.478(3)	1.480(6)
Cl1–Hg1–Cl2		180
Cl3–Hg2–Cl3a		180
O3–S1–C1	101.2(1)	99.7(1)
S1–O3–C12	113.8(1)	113.7(2)
C1–N1–C2	115.9(1)	115.8(3)
C1–N2–C11	125.1(1)	125.9(3)
S1–C1–N1	121.1(1)	120.8(2)
S1–C1–N2	121.1(1)	121.2(2)
O1–C2–N1	122.4(1)	122.9(3)
N2–C11–C12	112.3(1)	112.2(3)
O3–C12–C11	108.4(2)	108.0(3)

N2C1N1C2O1. In this reference compound the distance S1···O1 is 2.245(3) Å.

Structure of **3**

The crystal structure of **3** is shown in Fig. 2. Selected bond lengths and angles have also been included in Table 1. The atom labeling of the ligand in **3** is the same as for **2a** in Fig. 1.

Mercury(II) chloride forms with **2a** an adduct with two neutral ligand molecules per $HgCl_2$ unit. In the crystal the linear $HgCl_2$ units are arranged parallel to the *z* direction of the unit cell in channels of the ligand substructure. The unit cell contains 8 ligand and 4 $HgCl_2$ molecules. Two crystallographically independent Hg atoms Hg1 (site symmetry 4) and Hg2 (site symmetry $\bar{4}$) form linear $HgCl_2$ units with Hg–Cl distances of 2.270(2), 2.276(2) and 2.307(1), 2.307(1) Å, respectively, which are in accordance with the Hg–Cl bond lengths in $HgCl_2$ (2.284(12), 2.301(14) Å) [8].

Weak interactions are observed between the atoms Hg1 and Hg2 and the donor atoms O2 and O3 of the ligands: Hg1···O3 2.787(2) Å and Hg2···O2 2.762(3) Å. Therefore both Hg atoms are octahedrally surrounded by two Cl and four O atoms.

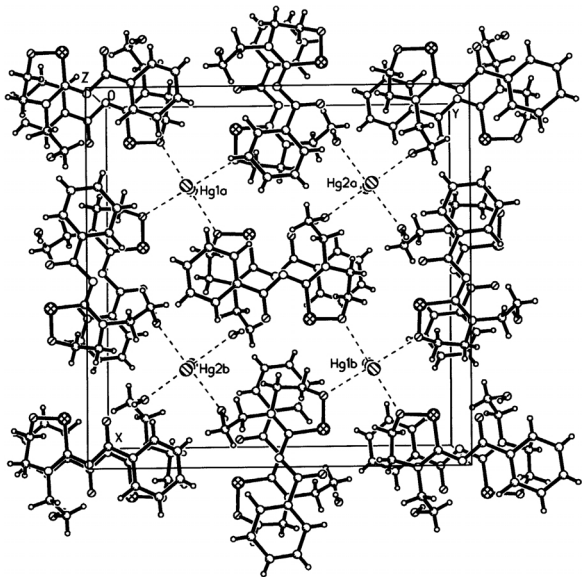


Fig. 2. Crystal structure of **3**. View along [001].

In the $HgCl_2$ adduct **3** the bond lengths and angles of the coordinated ligand are nearly unchanged in comparison with the free ligand **2a** indicating that **2a** is not strongly influenced by the adduct formation. Likewise unchanged are the distance S1···O1 (2.296(3) Å) and the torsion angles τ(S1C1N1C2) = 1.6(4)° and τ(O1C2N1C1) = −2.1(4)°. In the crystal structure intermolecular hydrogen bonds exist again between the atom O2 of the hydroxyl group and the atom O1 of the keto group (O2–H2···O1 [$1-x$, $1-y$, $1-z$] with O2···O1 2.787(3) Å, O2–H2 0.77(4) Å, H2···O1 2.02(4) Å and O2–H2···O1 173(4)°). Here these hydrogen bridges lead to the formation of pairs of ligand molecules.

Adducts of $HgCl_2$ with neutral molecules or salts have been known for a long time and show a great structural variety [9]. The angle Cl–Hg–Cl often deviates from linearity.

Structural characterization in solution and molecular mechanic calculations

Variable temperature ^{1}H NMR spectra of **2a** displayed a broadening of the signals at 4.02 and 4.06 ppm assigned to the $–CH_2–CH_2–$ group in the heterocyclic ring. The broadening remained unresolved even for the lowest temperature accessible in our experiment (−80 °C). This behaviour is consistent with a low energy barrier chair-boat conformational change of the heterocyclic 1,2,4-(O, S, N) six-membered

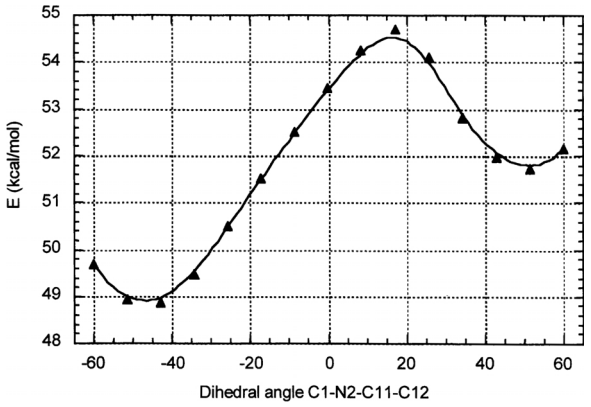


Fig. 3. Plot of energy versus dihedral angle in the chair-to-boat conformational change of the heterocyclic 1,2,4-(O,S,N) six-membered ring in **2a**.

ring. The chair-boat interconversion involves modifications in the dihedral angle τ(C1N2C11C12). Mechanic molecular calculations at MMFF94 [10] level are plotted in Fig. 3.

It has been found that the chair is the most stable conformation by 3.0 kcal/mol and the barrier to reach boat conformation is 5.81 kcal/mol. Both values are very small and account for the observed behaviour.

Experimental Section

All starting chemicals were used as commercially obtained. ^{1}H NMR spectra were recorded either on Varian VXR200S, Varian GEMINI-2000, Bruker ARX 300, Varian Unity Inova-400, and Bruker DRX-600 spectrometers. Chemicals shifts are in ppm relative to $SiMe_4$ (TMS) as external standard. The XPS spectra were recorded on VG ESCALAB 200i XL (Vacuum Generators), the elemental analyses on Leco CHNS 932 instruments.

*Synthesis of 1,1-bis(2-hydroxyethyl)-3-benzoylthiourea (***1a***) [11,12] and 1,1-bis(2-hydroxyethyl)-3-(2-fluorobenzoyl)thiourea (***1b***)*

To potassium thiocyanate (19.44 g, 0.2 mol) was added 100 ml of acetone followed quickly by benzoylchloride (28.11 g, 0.2 mol) [*2-fluorobenzoylchloride* (31.71 g, 0.2 mol)]. The mixture was refluxed for 2 h with stirring at nearly 50 °C. After cooling the mixture, a solution of diethanolamine (22.08 g, 0.21 mol) in 40 ml of acetone was added dropwise. After warming up, stirring for 30 min and filtration the precipitate was washed with warm acetone. The solution was concentrated to a smaller volume and kept in the refrigerator. The light yellow precipitate was collected and recrystallized from methanol (**1a**) and acetone (**1b**). Yield: 57% (**1a**), 51% (**1b**).

1a: M. p. 118 – 120 °C. – ^{1}H NMR (600 MHz, DMSO-d_6, H,H-COSY): δ = 3.70 (2H, CH_2-O), 3.72 (2H, N-CH_2), 3.77 (2H, CH_2-O), 3.99 (t, 2H, N-CH_2), 4.87 (t, 1H, OH), 5.65 (s(br), 1H, OH), 7.51 (2H, *m*-Ar), 7.60 (1H, *p*-Ar), 7.86 (2H, *o*-Ar), 10.88 (1H, NH). – ^{13}C NMR (150 MHz, DMSO-d_6, HMQC, HMBC): δ = 54.98 (N-CH_2), 55.09, 57.58 (CH_2-OH), 59.23, 127.86 (*o*-Ar), 128.60 (*m*-Ar), 132.36 (*p*-Ar), 133.52 (*i*-Ar), 164.53 (C=O), 181.15 (C=S).

1b: M. p. 110 – 112 °C. – ^{1}H NMR (600 MHz, DMSO-d_6, H,H-COSY): δ = 3.71 (2H, CH_2-OH), 3.74 (2H, CH_2-OH), 3.79 (t, 2H, N-CH_2), 3.94 (t, 2H, N-CH_2), 4.89 (t, 1H, OH), 5.71(s(br), 1H, OH), 7.28 (1H, Ar-H(3)), 7.29 (1H, Ar-H(5)), 7.56 (1H, Ar-H(4)), 7.62 (1H, Ar-H(6)), 10.86 (1H, NH). – ^{13}C NMR (150 MHz, DMSO-d_6, HMQC, HMBC): δ = 54.92 (N-CH_2), 55.02, 57.62 (CH_2-OH), 59.22, 116.19 (Ar-C(3), d, $^2J_{C,F}$ = 21.7 Hz), 123.47 (Ar-C(1), d, $^2J_{C,F}$ = 13.4 Hz), 124.58 (Ar-C(5), d, $^4J_{C,F}$ = 3.4 Hz), 130.26 (Ar-C(6), d, $^3J_{C,F}$ = 2.7 Hz), 133.33 (Ar-C(4), d, $^3J_{C,F}$ = 8.8 Hz), 159.24 (Ar-C(2), d, $^1J_{C,F}$ = 250.3 Hz), 163.02 (C=O, d, $^3J_{C,F}$ = 1.3 Hz), 180.44 (C=S). – ^{19}F NMR (564 MHz, DMSO-d_6): −112.3 (1F). – MS: *m/z* (%) = 286.0 (1.72) [M^+], 123.1 (100), 94.9 (34.77), 44.9 (6.62). – $C_{12}H_{15}FN_2O_3S$ (286.3): calcd. C 50.34, H 5.28, N 9.78, S 11.20; found C 50.10, H 5.67, N 9.68, S 11.70.

*Synthesis of N-[4-(2-hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-benzamide (***2a***) and N-[4-(2-hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-2-fluorobenzamide (***2b***)*

To an aqueous solution of 1,1-bis-(2-hydroxyethyl)-3-benzoylthiourea (**1a**) (1.34 g, 5.0 mmol; 135 ml water) [*1,1-bis-(2-hydroxyethyl)-3-(2-fluorobenzoyl)thiourea* (**1b**) (1.43 g, 5.0 mmol; 80 ml water)] was added KIO_3 (1.61 g, 7.5 mmol) at room temperature. The mixture was refluxed for 1.5 h to form a white precipitate in an orange-yellow solution with evolution of violet vapours. After cooling to room temperature the precipitate was filtered and washed with small portions of water. The crude product was dissolved in hot methanol (20 ml) and filtered. A very small amount of an insoluble yellow precipitate remained. Colourless crystals of **2a** [**2b**] formed on cooling the filtrate in the refrigerator. A single crystal of **2a** suitable for X-ray diffraction was obtained by covering a solution of the compound in ethanol with a layer of *n*-hexane. Yield: 95% (**2a**), 94% (**2b**).

2a: M. p. 142 – 144 °C. – ^{1}H NMR (400 MHz, CD_3COCD_3, RT): δ = 3.89 (2H, t, J = 5.0 Hz, CH_2), 4.02 (2H, m), 4.06 (2H, m), 4.17 (2H, t, J = 5.0 Hz), 4.22 (1H, t, J = 5.2 Hz), 7.44 (2H, m), 7.53 (1H, m), 8.11 (2H, m). – $C_{12}H_{14}N_2O_3S$ (266.3): calcd. C 54.12, H 5.30, N 10.52, S 12.04; found C 53.92, H 5.66, N 10.48, S 11.99.

2b: M. p. 90 – 92 °C. – ^{1}H NMR (200 MHz, DMSO-d_6, H,H-COSY, RT): δ = 3.81 (2H, N-CH_2), 3.81(2H, CH_2O), 3.89 (2H, N-CH_2), 4.14 (t, 2H, CH_2OS), 4.99 (s(br),

Table 2. Crystal data and details of structure determinations.

	2a	**3**
Empirical formula	$C_{12}H_{14}N_2O_3S$	$C_{12}H_{14}N_2O_3S{\cdot}0{,}5HgCl_2$
Formula weight [g/mol]	266.31	402.06
Colour, habit	colourless prisms	colourless prisms
Crystal system	monoclinic	tetragonal
Space group	$P2_1/n$	$P4/n$
a [Å]	7.904(2)	18.265(1)
b [Å]	11.011(4)	18.265(1)
c [Å]	14.494(4)	8.621(1)
β [°]	97.44(2)	
V [Å^3]	1250.8(6)	2875.9(4)
Z; $F(000)$	4; 560	8; 1576
ρ_{calc} [g/cm^3]	1.414	1.857
Crystal size [mm]	$0.6\times0.6\times0.4$	$0.5\times0.2\times0.2$
2θ Range [°]	4.6 – 56.0	3.2 – 58.7
Temperature [K]	293(2)	220(2)
μ(Mo-K$_\alpha$) [mm^{-1}]	0.261	5.729
Measured reflections	7604	18527
Unique reflections	2776	3660
Observed reflections ($I > 2\sigma(I)$)	2336	3289
Refined parameters	219	235
R_1 (observed reflections)	0.0416	0.0343
wR_2 (unique reflections)	0.1159	0.0568
Largest difference peak and hole [e/Å^3]	0.17/−0.27	0.72/−1.22

1H, OH), 7.24 (1H, Ar-H(3)), 7.28 (1H, Ar-H(5)), 7.55 (1H, Ar-H(4)), 7.96 (1H, Ar-H(6)). – ^{13}C NMR (50 MHz, DMSO-d$_6$, HETCOR, RT): δ = 50.38 (N-CH_2), 57.50 (N-CH_2), 58.48 (CH_2OH), 65.52 (CH_2OS), 116.87 (Ar-C(3), d, $^2J_{C,F}$ = 22.1 Hz), 122.65 (Ar-C(1), d, $^2J_{C,F}$ = 9.2 Hz), 124.24 (Ar-C(5), d, $^4J_{C,F}$ = 3.8 Hz), 131.92 (Ar-C(6), d, $^3J_{C,F}$ = 1.2 Hz), 133.21 (Ar-C(4), d, $^3J_{C,F}$ = 8.8 Hz), 161.01 (Ar-C(2), d, $^1J_{C,F}$ = 256.7 Hz), 173.48 (C=O, d, $^3J_{C,F}$ = 3.4 Hz), 175.72 (C-S). – ^{19}F NMR (188 MHz, DMSO-d$_6$): −111.5 (1F). – XPS [eV]: N1s 398.1 (-N=), 399.9 (>N-); O1s 531.2 (>C=O), 532.6 (C-OH); C1s 284.6 (sp^3), 285.9 (sp^2), 287.2 (C=O); S2p$_{3/2}$ 163.9 (C-S-O); F1s 686.9 (F). – $C_{12}H_{13}FN_2O_3S$ (284.3): calcd. C 50.70, H 4.61, N 9.85, S 11.28; found C 50.30, H 4.57, N 9.86, S 12.1.

*Synthesis of the adduct of N-[4-(2-hydroxyethyl)-1,2,4-oxathiazinan-3-ylidene]-benzamide with mercury(II) chloride (**3**)*

To a solution of 1,1-bis(2-hydroxyethyl)-3-benzoylthiourea (**1a**) (0.54 g, 2.0 mmol) in hot methanol (15 ml) was added mercury(II) chloride $HgCl_2$ (0.27 g, 1.0 mmol) dissolved in 15 ml of methanol. The mixture was heated with stirring for 20 min. After 30 min a white precipitate of mercury(I) chloride Hg_2Cl_2 was obtained which was filtered. The solution was kept in the refrigerator. Crystals of **3** were obtained which were suitable for X-ray diffraction. Yield: 37%.

M. p.: decomposition with taking on a black colour. – XPS [eV]: N1s 398.2 (-N=), 400.1 (>N-); O1s 531.4 (>C=O), 532.5 (C-OH); C1s 284.6 (sp^3), 285.7 (sp^2), 287.2 (C=O); S2p$_{3/2}$ 164.0 (C-S-O); Hg4f$_{7/2}$101.1; Cl2p$_{3/2}$ 198.1 (Cl).

Crystal structure determinations

The data for the crystal structure determinations were collected on Bruker SMART CCD area-detector diffractometers with Mo-K$_\alpha$ radiation (λ = 0.71073 Å) at temperatures of 293 K (**2a**) and 220 K (**3**). The intensities were corrected for Lorentz and polarization effects and for absorption using SADABS (**3**). The structures were solved by direct methods and refined by least-squares on weighted F^2 values for all reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters [13]. The positions of the hydrogen atoms were taken from difference syntheses and refined with isotropic displacement parameters. Details of crystal data and structure determinations are given in Table 2.

Further details of the crystal structure determinations are available on request from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK, on quoting the deposition numbers CCDC-279414 (**2a**) and CCDC-279415 (**3**), the name of the authors, and the journal citation.

Acknowledgement

We thank Dr. K.-H. Hallmeier for recording and discussing the XPS spectra.

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