



## Synthesis, Characterization and Crystal Structure of N-(3-((2-Chlorothiazol-5-yl)methyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene)nitramide

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N-(3-[(2-chlorothiazol-5-yl)methyl]-5-methyl-1,3,5-oxadiazinan-4-ylidene)nitramide (**I**), *i.e.*, thiamethoxam, it is a broad-spectrum insecticide that effectively controls insects, being a second generation neonicotinoid compound belonging to the chemical subclass the thianicotinyls. It was prepared from 5-(chloromethyl)-2-(phenylthio)thiazole (**1**) *via* chlorination by Cl<sub>2</sub>/HCl system and then condensation by K<sub>2</sub>CO<sub>3</sub>/CsI. The product was characterized by NMR and LC-MS. The crystal structure of compound **I** was investigated using X-ray diffraction and SHELXTL-97 software. The result indicated that compound **I** crystallized in the monoclinic system, space group P 21/n with a = 6.488(13), b = 28.786 (6), c = 6.804(14) Å, V=1225.1 (5) Å<sup>3</sup>; Z4.

**Keywords:** Thiamethoxam, Synthesis, Characterization, Crystal structure.

### INTRODUCTION

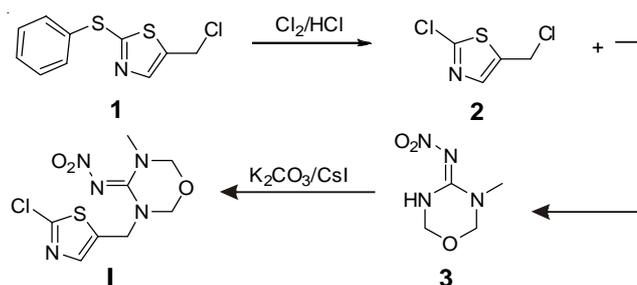
Triazole compounds have been found to show wide spread biological activities, many of them have been developed and used as fungicides, plant growth regulators and medicine. Triazole compounds are the most important types of fungicides in nitrogen heterocyclic compounds. Different structures of triazole compounds have different biological activities, developing novel structural triazole compounds is the research focus at present<sup>1-3</sup>.

Thiamethoxam, is an important kind of triazole compounds. It was developed by Syngenta Company in 1991. It is a broad-spectrum insecticide that effectively controls insects, being a second generation neonicotinoid compound belonging to the chemical subclass the thianicotinyls<sup>4</sup>.

N-(3-[(2-Chlorothiazol-5-yl)methyl]-5-methyl-1,3,5-oxadiazinan-4-ylidene)nitramide (**I**) *i.e.*, thiamethoxam is reported and synthesized in several steps<sup>5-7</sup>. The last 2 steps were shown as below in **Scheme-I**. The quality and purity of the final product is determined by the last steps.

In some literatures, compound **I** is prepared from 5-(chloromethyl)-2-(phenylthio) thiazole and N-(3-methyl-1,3,5-oxadiazinan-4-ylidene)nitramide by condensation reaction with K<sub>2</sub>CO<sub>3</sub>/DMF, K<sub>2</sub>CO<sub>3</sub>/Me<sub>4</sub>N<sup>+</sup>OH<sup>-</sup> or K<sub>2</sub>CO<sub>3</sub>/KI system, then chlorination by Cl<sub>2</sub>/HCl, but the product phase is not good and the purity and quality of product is not high either<sup>8-10</sup>.

Herein, we report the synthesis of **I** from compound **1** with an overall yield of about 79.2 %. Meanwhile, the crystal structure of **I** also was investigated. The synthetic route of compound **I** was presented as **Scheme-I**.



**Scheme-I:** Route for the synthesis of compound **I**

### EXPERIMENTAL

5-(Chloromethyl)-2-(phenylthio)thiazole (**1**), N-(3-methyl-1,3,5-oxadiazinan-4-ylidene)nitramide (**3**), were supplied by Well Chemical Co. Ltd. of Jiangsu(Yancheng, People's Republic of China), its mass content is 98.8 % determined by LC. HCl solution, Cl<sub>2</sub> and CsI was supplied by Sinopharm Chemical Reagent Co. Ltd of China. All other chemicals were of reagent grade and used without purification as received.

<sup>1</sup>H NMR spectrum was obtained with Bruker AV-300 spectrometer at 300.13 MHz and measured in CDCl<sub>3</sub> solution

at  $25 \pm 0.5$  °C. The sample was dissolved in a 5 mm diameter tube at a concentration of about 20 mg/mL. X-ray diffraction was performed on a Bruker APEX-II CCD diffractometer. Mass spectrum of (**I**) was analyzed using Trace DSQ LC/MS (Thermo Electron Co., USA).

**Synthesis of compound 2:** In a 1 L four-necked flask, HCl solution (300 g, 30 %, 2.47 mol), compound **1** (30 g, 0.124 mol) were added. Then chlorobenzene (150 g, 1.33 mol) was added in as solvent. Stirring is carried out at room temperature for 0.5 h, then  $\text{Cl}_2$  (124 g, 1.75 mol) was added into the system by air tube in 4 h. Stirring is carried out at 25 °C for a further 2 h. After that, the excess chlorine gas is blown off with nitrogen. Then the inorganic phase is filtered, pH value was adjusted to 5 by NaOH solution (30 %). The solid was filtered and washed twice with water and saturated brine. The pale yellow power is filtered off and dried. In this manner, 18.77 g (m.p. 31-32 °C) of compound **2** (90 %) are obtained.

**Synthesis of compound I:** In a 250 mL four-necked flask, compound **2** (10 g, 0.0595 mol) and  $\text{K}_2\text{CO}_3$  (9.1 g, 0.0655 mol) in ethylmethyl ketone (40 mL) was added in cesium iodide (1.55 g, 0.006 mol) was added into the system as catalyst. Compound **3** (9.53 g, 0.0595 mol) in ethylmethyl ketone (30 mL) is added dropwise at 60 °C. Stirring is carried out at 60 °C for another 10 h, followed by cooling to room temperature, separating off the organic solvent. Dichloromethane ( $\text{CH}_2\text{Cl}_2$ ) (100 mL) was added in and the inorganic salt is filtered off and the filtrate is concentrated by evaporation. In this manner, 15.274 g (m.p. 139-140 °C) of the compound **I** (88 %) are obtained in the form of a pale yellow powder which crystallizes from toluene.

Crystals of (**I**) that suitable for X-ray diffraction were obtained by slow evaporation of 1,2-dichloroethane solution of (**I**).

**X-ray crystallography:** A colorless block-like crystal of compound (**I**) grown in 1,2-dichloroethane with dimensions of  $0.30 \times 0.20 \times 0.10$  mm was used for structural determination. Diffraction data were collected on a Bruker APEX-II CCD diffractometer by using graphite monochromated  $\text{MoK}_\alpha$  radiation ( $\lambda = 0.71073$  Å). The structure was solved by direct methods with SHELXS-97 and refined on the  $F^2$  by full-matrix least-squares method with SHELXL-97. All non-hydrogen atoms were refined anisotropically<sup>11-14</sup>.

## RESULTS AND DISCUSSION

**Identification of resonance in the spectra:**  $^1\text{H}$  NMR and LC-MS spectra of purified compound **I** were presented. In the  $^1\text{H}$  NMR of compound **I**, the peak at 3.04 ppm was ascribed to the proton of methyl group. The other data was described as below,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.04 (3H, s), 4.76 (2H, s), 4.89 (2H, s), 4.90 (2H, s), 7.49 (1H, s).

In the LC spectrum peak at 3.258 min ascribed to the compound **I**. In the MS spectrum, the existence of the peaks at right end showed the compound **I**,  $m/z$  291.75 was ascribed to molecular ion peak ( $M^+$ ).

The crystal configuration of compound **I** was confirmed by X-ray structural analysis. Experimental details for X-ray data collection were presented in Table-1 and the geometric parameters for compound **I** were listed in Table-2. Molecular structure and packing plot of compound **I** were showed in Figs. 1 and 2, respectively.

TABLE-1  
CRYSTALLOGRAPHIC DATA FOR COMPOUND (**I**)

Item	Data or description
m.f.	$\text{C}_8\text{H}_{10}\text{N}_5\text{O}_3\text{SCl}$
Formula weight	291.72
Temperature (K)	293 (2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P 21/n
a (Å)	6.4880(13)
b (Å)	28.786 (6)
c (Å)	6.8040(14)
Volume (Å <sup>3</sup> )	1225.1(4)
Z	4
Calculated density (g/cm <sup>3</sup> )	1.582
Absorption coefficient (mm <sup>-1</sup> )	0.49
F(000)	600
Crystal size (mm)	0.30 × 0.20 × 0.10
Theta range for data collection (°)	1.4 to 25.4
Reflections collected/unique	2247/1551 [ $R_{\text{int}} = 0.058$ ]
Completeness to theta = 25.38 (%)	99.9
Max. and min. transmission	0.867 and 0.953
Refinement method	Full-matrix least-squares on $F^2$
Data/restraints/parameters	2247/0/164
Goodness-of-fit on $F^2$	1.001
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0582$ , $wR_2 = 0.1567$
R indices (all data)	$R_1 = 0.0942$ , $wR_2 = 0.1567$
Largest diff. peak and hole (e. Å <sup>-3</sup> )	0.34 and -0.34

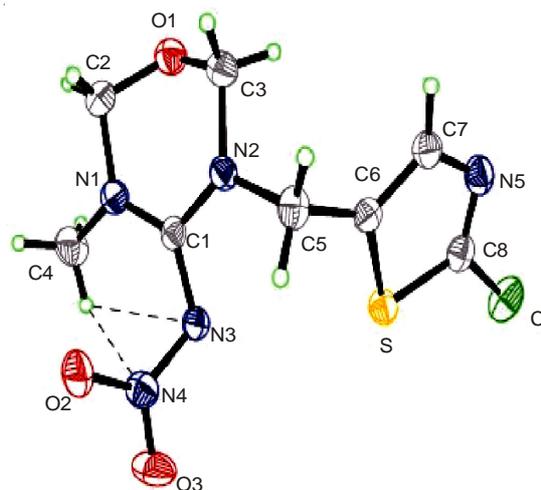


Fig. 1. General appearance of compound **I** with the atoms represented by thermal vibration ellipsoids of 50% probability.

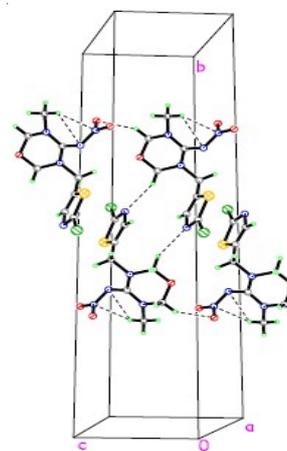


Fig. 2. Packing diagram for compound **I**

TABLE-2  
GEOMETRIC PARAMETERS FOR COMPOUND (I)

Bond	Dist. (Å)	Bond	Dist. (Å)
S—C6	1.719 (4)	N3—N4	1.333 (5)
S—C8	1.720 (5)	O3—N4	1.233 (5)
C1—C8	1.714 (5)	C3—H3B	0.9700
O1—C3	1.396 (6)	C3—H3C	0.9700
O1—C2	1.405 (6)	C4—H4A	0.9600
N1—C1	1.327 (5)	C4—H4B	0.9600
N1—C2	1.450 (6)	C4—H4C	0.9600
N1—C4	1.467 (6)	C5—C6	1.497 (6)
C1—N2	1.328 (5)	C5—H5A	0.9700
C1—N3	1.369 (5)	C5—H5B	0.9700
N2—C5	1.466 (5)	C6—C7	1.349 (6)
N2—C3	1.475 (5)	C7—N5	1.378 (6)
O2—N4	1.250 (5)	C7—H6A	0.9300
C2—H2A	0.9700	N5—C8	1.282 (6)
C2—H2B	0.9700		
Angle	Data (°)	Angle	Data (°)
C6—S—C8	88.7 (2)	O3—N4—N3	117.3 (4)
C3—O1—C2	109.5 (4)	O2—N4—N3	121.4 (4)
C1—N1—C2	117.5 (4)	N1—C4—H4A	109.5
C1—N1—C4	123.7 (4)	N1—C4—H4B	109.5
C2—N1—C4	118.6 (4)	H4A—C4—H4B	109.5
N1—C1—N2	117.9 (4)	N1—C4—H4C	109.5
N1—C1—N3	124.9 (4)	H4A—C4—H4C	109.5
N2—C1—N3	116.8 (4)	H4B—C4—H4C	109.5
C1—N2—C5	122.1 (4)	N2—C5—C6	112.8 (3)
C1—N2—C3	122.5 (4)	N2—C5—H5A	109.0
C5—N2—C3	115.3 (3)	C6—C5—H5A	109.0
O1—C2—N1	108.7 (4)	N2—C5—H5B	109.0
O1—C2—H2A	110.0	C6—C5—H5B	109.0
N1—C2—H2A	110.0	H5A—C5—H5B	107.8
O1—C2—H2B	110.0	C7—C6—C5	127.5 (4)
N1—C2—H2B	110.0	C7—C6—S	108.8 (3)
H2A—C2—H2B	108.3	C5—C6—S	123.7 (3)
N4—N3—C1	114.6 (3)	C6—C7—N5	117.2 (4)
O1—C3—N2	110.9 (4)	C6—C7—H6A	121.4
O1—C3—H3B	109.5	N5—C7—H6A	121.4
N2—C3—H3B	109.5	C8—N5—C7	108.7(4)
O1—C3—H3C	109.5	N5—C8—C1	123.4(4)
N2—C3—H3C	109.5	N5—C8—S	116.6(4)
H3B—C3—H3C	108.0	C1—C8—S	120.0(3)
O3—N4—O2	121.2(4)		
C2—N1—C1—N2	-4.8 (6)	C1—N3—N4—O3	167.2(4)
C4—N1—C1—N2	170.3(4)	C1—N3—N4—O2	-15.9(6)
C2—N1—C1—N3	-176.8(4)	C1—N2—C5—C6	98.0(5)
C4—N1—C1—N3	-1.7 (7)	C3—N2—C5—C6	-78.1(5)
N1—C1—N2—C5	168.8(4)	N2—C5—C6—C7	97.0(5)
N3—C1—N2—C5	-18.5(6)	N2—C5—C6—S	-84.4(4)
N1—C1—N2—C3	-15.4(6)	C8—S—C6—C7	0.6(3)
N3—C1—N2—C3	157.3(4)	C8—S—C6—C5	178.2(4)
C3—O1—C2—N1	-66.2(5)	C5—C6—C7—N5	178.7(4)
C1—N1—C2—O1	45.3(6)	S—C6—C7—N5	0.0 (5)
C4—N1—C2—O1	-130.1(5)	C6—C7—N5—C8	-0.8 (6)
N1—C1—N3—N4	-60.0(6)	C7—N5—C8—C1	-177.6(3)
N2—C1—N3—N4	127.8(4)	C7—N5—C8—S	1.3 (5)
C2—O1—C3—N2	46.8(5)	C6—S—C8—N5	-1.2 (4)
C1—N2—C3—O1	-6.3 (6)	C6—S—C8—C1	177.8(3)
C5—N2—C3—O1	169.7(4)		

Symmetry code: (i) x, y, z; (ii) x-1/2, -y-1/2, z-3/2; (iii)-x+2, -y, -z

According to the data from X-ray crystallographic analysis, compound (I) crystallized in a P 21/n space group of the monoclinic system. All H atoms were positioned geometrically and constrained to ride on their parent atoms, with C-H = 0.93 Å for aromatic H. Other H atoms were positioned geometrically and refined using a riding model, with C-H = 0.96 Å for alkyl H, with Uiso (H) = 1.2 Ueq (C) for aromatic H and Uiso (H) = 1.5 Ueq (C) for other H. There are C-H...N intramolecular and C-H...O, C-H...N intermolecular hydrogen bonds in the structure, hydrogen-bond geometry for compound I was listed in Table-3. Unit cell parameters: a = 6.488 (13), b = 28.786 (6), c = 6.804 (14) Å, V = 1225.1 (5) Å<sup>3</sup>; Z<sub>4</sub>.

TABLE-3  
HYDROGEN-BOND GEOMETRY FOR COMPOUND (I)

D—H...A	D—H	H...A	D...A	D—H...A
C2—H2A...O2	0.97 Å	2.47 Å	3.342 (7) Å	149°
C2—H2B...O2	0.97 Å	2.55 Å	3.231 (6) Å	127°
C3—H3C...N5	0.97 Å	2.50 Å	3.392 (6) Å	152°
C4—H4A...N3	0.96 Å	2.50 Å	2.924 (7) Å	106°
C4—H4A...N4	0.96 Å	2.41 Å	3.034 (7) Å	122°

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