Synthesis and Characterization of (Z)-Furan-2-carbaldehyde Thiosemicarbazone at Low Temperature

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Abstract: The compound, C₆H₇N₃OS, has been prepared and characterized by condensation between thiosemicarbazide and furan-2-carbaldehyde and its structure was elucidated by x-ray analysis (at 150 K), NMR and IR spectroscopy methods (at ambient temperature). It crystallizes in the monoclinic space group *P*2₁/*c* (No. 14), *a* = 13.5099(3) Å, *b* = 5.67430(10) Å, *c* = 23.4755(6) Å, β = 117.367(2)°, *V* = 1598.20(7) Å³ and *Z* = 8. The crystal structure was solved and refined to *R* = 0.0290 with 2942 unique reflections. No significant π-π interactions are found in the crystal structure. There are C-H...π interactions and also different weak hydrogen bonds, stabilizing the three dimensional crystal structure.

Keywords: Thiosemicarbazide, Crystal structure, Synthesis, Furan.

Introduction

Thiosemicarbazones and their derivatives have been widely studied due to their various biological activities such as anticancer activities^{1,2}. Tridentate N-N-S ligand system of thiosemicarbazide seems to be a key for the antiviral, antibacterial and anticancer therapeutics^{3,4}.

Transition metal complexes of thiosemicarbazone and their derivatives attracted considerable interest for their wide range of pharmacological properties such as antimicrobial^{5,6}, antiameobic⁷, antitumor⁸⁻¹¹ and antiviral activity^{12,13}.

Therefore, many efforts were dedicated to investigate of the structure activity relationship of metal thiosemicarbazone complexes. Recently, thiosemicarbazone derivatives has been used for the determination of Cd(II) by using spectrophotometric method¹⁴.

However, heterocyclic thiosemicarbazones showed higher activity compared with aromatic thiosemicarbazones³. It has been shown that the *trans* thiosemicarbazone are the most active isomer¹. It seems likely that the oxygen atom of the furan ring plays an important role in determining the biological activity¹⁵. However, a much deeper study of the H-bonding and molecular interactions of these compounds would be needed for establishing the new activity aspects.

Therefore, a structural study in details for the title compound was of our interest. In this work, we first study the structure of the title compound at low temperature and compared with previous report at ambient temperature¹⁵.

Experimental

The crystallographic data were collected at low temperature by means of an x-calibur 3 equipped with a CCD area detector diffractometer, using graphite-monochromated Mo K α radiation ($\lambda = 0.71073$ Å) by ω scan mode. No intensity variations due to decomposition of the crystals were observed. Selected crystallographic and experimental details are summarized in Table 1.

Table 1. Crystal data and structure refinement for C₆H₇N₃OS at 150K

Molecular formula	C ₆ H ₇ N ₃ OS
Molecular weight	169.22
Temperature, K	150(2)
Radiation λ	0.71073
Crystal system	Monoclinic
Space group	P2 ₁ /c
a/Å	13.5099(3)
b/Å	5.67430(10)
c/Å	23.4755(6)
β (°)	117.367(2)
V/Å ³	1598.20(7)
Z	8
D _{calc} g cm ⁻³	1.407
Crystal size, mm	0.17 × 0.13 × 0.12
Crystal colour	Yellow
Absorption coefficient, cm ⁻¹	0.349
F(000)	704
Reflections collected/unique	6484/2942
Range/indices	-16 ≤ h ≤ 16, -6 ≤ k ≤ 6, -28 ≤ l ≤ 22
θ limit (°)	3.90-25.50
No. of observed data, I > 2 σ (I)	2290
No. of parameters	199
No. of restraints	0
Goodness of fit on F ²	0.931
R ₁ , wR ₂ [I ≥ 2 σ (I)] ^a	0.0290, 0.0621
R ₁ , wR ₂ (all data)	0.0424, 0.0646
Largest diff. peak and hole	0.194, -0.127

^a R values are defined as: $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$ $wR_2 = [\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]]^{1/2}$

CrysAlis program packages were used for indexing and integrating the single crystal reflections¹⁶. Absorption corrections were performed with the program x-RED and x-SHAPE¹⁷. In x-shape symmetry equivalent reflections were used to optimize the crystal shape and size. The structure was solved by direct methods using SHELXS-97 and refined using full-matrix least-squares method on F^2 , SHELXL-97¹⁸. Molecular graphics were drawn by Diamond and Mercury programs¹⁹ and PLATON²⁰ software was used to prepare materials for publication. All non-hydrogen atoms were refined anisotropically. Aromatic and methine H atoms were placed in calculated positions (C-H = 0.93 Å) and constrained to ride on their parent atoms, with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$. The rest of H atoms were located in difference electron density maps and their coordinates were refined freely with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{N})$.

NMR experiments were recorded at room temperature in CDCl_3 on a Bruker AV-500 spectrometer using an internal deuterated solvent lock. IR spectra were recorded as KBr disks on a Shimadzu IR instrument. Elemental analyses were performed using a Heraeus CHN-O rapid analyzer. All reagents and solvents used in this study were purchased from Merck & Aldrich.

(Z)-Furan-2-carbaldehyde thiosemicarbazone (**I**) was prepared according to the modified procedure described in the literature¹. A solution of thiosemicarbazide (0.91 g, 10 mmol) in 40 mL of dry methanol was prepared with stirring and warming (about 40 °C) during 1 h. To the warm thiosemicarbazide solution, furan-2-carbaldehyde (0.96 g, 10 mmol) in 10 mL of dry methanol was added following by a 12 h reflux (Figure 1). The mixture was then slowly cooled down to room temperature until the yellowish needle crystals suitable for crystallography were obtained. Yield: 1.31 g (77%). Anal. Calcd for $\text{C}_6\text{H}_7\text{N}_3\text{OS}$: C, 42.60; H, 4.16; N, 24.83; S, 18.94. Found: C, 42.41; H, 4.12; N, 24.76; S, 18.88 %. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3135 (s), 2887 (m), 1620 (s), 1612 (s), 1575 (s), 774 (m). ^1H NMR (δ , $\text{DMSO}-d_6$, 25 °C, ppm): 11.40 (s, 1H, NHCS), 8.41 (s, 1H, CH=N), 8.10 and 7.92 (2br s, 1H each, NH_2), 6.11–7.54 (m, 3H, aromatic); ^{13}C NMR (δ , $\text{DMSO}-d_6$, 25 °C, ppm): 177.60 (C=S), 139.54 (CH=N), 148.68, 142.8, 108.5, 109.01 (C-aromatic).

Figure 1. Synthetic and chemical structure of the compound (**I**)

Results and Discussion

(Z)-Furan-2-carbaldehyde thiosemicarbazone (**I**) was prepared by condensation between thiosemicarbazide and furan-2-carbaldehyde (Figure 1). The molecular structure of **I** and the atom-numbering scheme are shown in Figure 2. In the asymmetric unit there are two independent

molecules with similar bond distances and angles (Table 2), however, in one molecule the furan ring is almost coplanar with the least-squares plane defined by thiosemicarbazide by dihedral angle of 7.2° , while in the other molecule the furan is twisted to the corresponding thiosemicarbazide by 23.2° .

Figure 2. ORTEP structure of the compound (**I**), showing 50% probability ellipsoids (H atoms are shown as circles of arbitrary radii.)

Table 2. Selected bond distances (Å) for the compound (**I**)

D	H	A	D-H	H...A	D...A	D-H...A
N1	H1A	S1	0.86	2.695(3)	3.479(3)	152.09
N4	H4A	S1	0.86	2.497(2)	3.335(3)	164.84
N3	H7	S2	0.84	2.588(1)	3.426(2)	174.35
N6	H13	S2	0.87	2.465(1)	3.329(1)	171.26
C10	H10	O1	0.93	2.709(1)	3.497(2)	143.06

There are C-H... π interactions (*e.g.* C4-H3ⁱ ...Cg3 = 2.76 Å being the ring O1/C3/C6/C5/C4 with $i = -x, \frac{1}{2}+y, \frac{1}{2}-z$) and also different weak hydrogen bonds (Table 2), stabilizing the three dimensional crystal structure. No significant π - π interactions are found in the crystal structure.

The C1-S1 and C7-S2 bond lengths of 1.688(2) and 1.690(1) Å, respectively are consistent with C=S double bond. Likewise, the N2-C2 and N5-C8 bond distances with 1.277(2) and 1.271(2) Å, respectively, are in accordance with N=C double bond character, as well (Table 3). The bond angles for both furan rings are within normal ranges. As expected, the obtained data at low temperature have lower atomic movements, indicating lower thermal parameters in comparison to the data at room temperature¹³. Furthermore, in the current study we focused mainly structural and packing aspects, which was not specifically devoted before.

Table 3. Selected bond distances (Å) for the title compound.

S1-C1	1.6880(14)	N4-C7	1.3407(18)
S2-C7	1.6902(14)	N4-N5	1.3726(16)
O1-C3	1.3722(17)	N5-C8	1.2707(19)
O1-C4	1.3619(19)	N6-C7	1.3123(17)
O2-C9	1.3630(19)	C2-C3	1.434(2)
O2-C10	1.362(2)	C3-C6	1.346(2)
N1-C1	1.3432(17)	C4-C5	1.335(2)
N1-N2	1.3719(16)	C5-C6	1.417(2)
N2-C2	1.2768(17)	C9-C12	1.346(2)
N3-C1	1.3249(17)	C10-C11	1.319(3)
C11-C12	1.410(3)	C8-C9	1.434(2)

To gain new insight to the subject of supramolecular thiosemicarbazone arrays and to further extend the behavior antibacterial of metal complexes of the above amine substituted thiosemicarbazones with different metals, Further works on thiosemicarbazone derivatives is in progress in our laboratory. Moreover, to fundamentally understand how differences in the structures of thiosemicarbazone derivatives affect the intermolecular modes of thiosemicarbazone self-assembly, a more detailed available investigation of x-ray crystallography properties and supramolecular arrays directed by noncovalent bonding such as hydrogen bonding or π - π interactions needs to be done.

Supporting information materials

Crystallographic data for the title compound has been deposited to the Cambridge Crystallographic Data Centre (CCDC No. 704543). Copies of available materials can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (44)01223 336033); e-mail: deposit@ccdc.ac.uk).

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