

Synthesis, Characterization and Crystal Structure of 1-(2-benzamidophenyl)-3-benzoylthiourea Hemihydrate

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Abstract: The dissymmetric compound $C_{21}H_{17}N_3O_2S \cdot 0.5H_2O$ obtained by a reaction of 1,2-diaminobenzene, potassium thiocyanate and benzoyl chloride in 1/1/2 ratio is characterized by elemental analyses, IR, and NMR spectroscopies. The structure is elucidated by X-ray diffraction technic. The compound crystallizes in the monoclinic system with a space group of *I*2. The asymmetric unit contains one hemihydrate organic molecule. The title thiourea derivative, features an almost planar, C_2N_2S (S1/N1/N2/C7/C8) moiety, with a maximum deviation from the least-squares plane of 0.0422 (3) Å. This moiety is flanked by a disubstituted and a monosubstituted phenyl rings. The dihedral angles between the thiourea and the monosubstituted phenyl ring and the thiourea and the central disubstituted phenyl ring are respectively 10.418 (7)° and 60.292 (2)°, indicating twist in the molecule. On the other arm, a phenyl ring supported by an amide function, which is linked to the central ring through the nitrogen atom, is present. The dihedral angle between this phenyl group and the central disubstituted phenyl is 76.862 (7)° showing that their mean planes are not coplanar. Intramolecular S(thiono)—H...O(water) hydrogen bonds which close in *S*(6) and *S*(7) rings consolidate the conformation. Intermolecular N(amido)—H...O(carbonyl) which form layers parallel to the *ac* plane stabilized the structure.

Keywords: 1,2-diaminobenzene, Benzoyl Chloride, Potassium Thiocyanate

1. Introduction

Compounds derived from thiourea are molecules largely used in pharmaceutical industry for the preparation of heterocyclic derivatives. The importance of these compounds is widely demonstrated in the scientific literature. Thiourea derivatives are reported as molecules with biological properties such as antiviral [1], antifungal [2], antibacterial [3] and antitumoral [4, 5]. Isoxyl which is a molecule derived from thiourea is an effective drug against tuberculosis [6]. The thiourea derivatives also exhibit catalytic activities [7, 8] and can interact with DNA [9]. Yusof et al. [10] demonstrated that biological activities of these kind of compounds may be enhanced by the presence of substituent such as chloro, bromo or nitro groups [11]. Thiourea derivatives are also reported as organic inhibitors for corrosion. This property is due to the

easily protonation of the sulfur atom in acidic medium [12, 13]. In the recent past we have started to study the coordination of some ligands derived from thiourea having a number of interesting properties. It is in this context that we have reported two thioureidos ligands whose two arms are bridged by ethane-1,2-diyl group [14] and 1,2-phenyl ring [15] respectively. We have continued to search for ligands of this type. In this article, we report the synthesis, the characterization and the X-ray structure of an asymmetric molecule in which a 1,2-phenyl ring bridges a thioureido group and an amido group yielding the compound (I).

2. Materials and Methods

2.1. General Information

Potassium Thiocyanate, benzoyl chloride,

1,2-diaminobenzene and acetone were purchased from Sigma-Aldrich and used as received without further purification. Elemental analyses of C, H and N were recorded on a VxRio EL Instrument. The ^1H and ^{13}C NMR spectra were recorded with a Bruker AM-400 spectrometer, using tetramethylsilane as the internal standard. The solid-state IR spectra were recorded from KBr discs on a FTIR Spectrum Two of Perkin Elmer spectrophotometer in the $4000\text{--}400\text{ cm}^{-1}$ range.

2.2. Synthesis and Characterization of (I)

To a mixture of 4.859 g (50 mmol) of potassium thiocyanate and 100 mL of acetone was added dropwise a solution of 14.071 g (100 mmol) of benzoyl chloride in 50 mL of acetone. The resulting mixture was stirred under reflux for 1 h and cooled to room temperature. A solution of 5.407 g (50 mmol) of 1,2-diaminobenzene in 20 mL of acetone was added. The yellow solution obtained was stirred at room temperature during 2 h. 300 mL of 1 N HCl was added to dissolve the precipitated KCl. A white solid appeared after five minutes. The compound was filtered and washed with 3 x 50 mL of water and dried under vacuum. Recrystallization from a mixture of methanol and chloroform (1:1) gave 18.52 g (85.7%) of the title compound. Mass spectrum, $m/z = 384$ (M^+). Analysis calculated for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_2\text{S} \cdot 0.5\text{H}_2\text{O}$: C 65.61, H 4.72, N 10.93, S 8.34%; found: C 65.59, H 4.71, N 10.914, S 8.32%. d 6.44–7.95 (m, 14H, ArH), 8.195 (s, 1H, NH), 9.25 (s, 1H, NH); 9.60 (s, 1H, NH). ^{13}C NMR (CDCl_3): δ 122.1, 124.9, 125.1, 126.8, 127.6, 129.2, 129.6, 132.8, 133.3, 134.7, 164.9, 169.5, 177.9. IR (cm^{-1} , KBr): 3210, 1673, 1596, 1470, 1319, 1262, 1149, 857, 688. Monocrystals suitable for X-ray analysis was obtained from slow evaporation of a dimethylformamide solution of the product.

2.3. Crystal Structure Determination

Crystals suitable for single-crystal X-ray diffraction, of the reported compounds, were grown by slow evaporation of MeOH solution of the compound. Details of the crystal structure solution and refinement are given in Table 1. Diffraction data were collected using a Rigaku AFC11 007-HF diffractometer with graphite monochromatized $\text{CuK}\alpha$ radiation ($\lambda = 1.54184\text{ \AA}$). All data were corrected for Lorentz and polarization effects. Scattering factors were taken from the program package SHELXTL [16]. The structures were solved by direct methods, which revealed the position of all non-hydrogen atoms. All the structures were refined on F^2 by a full-matrix least-squares procedure using anisotropic displacement parameters for all non-hydrogen atoms [17]. The hydrogen atoms of water molecules and NH groups were located in the Fourier difference maps and refined. Others H atoms (CH and CH_3 groups) were geometrically optimized and refined as riding model by AFIX instructions. Molecular graphics were generated using ORTEP-3 [18]

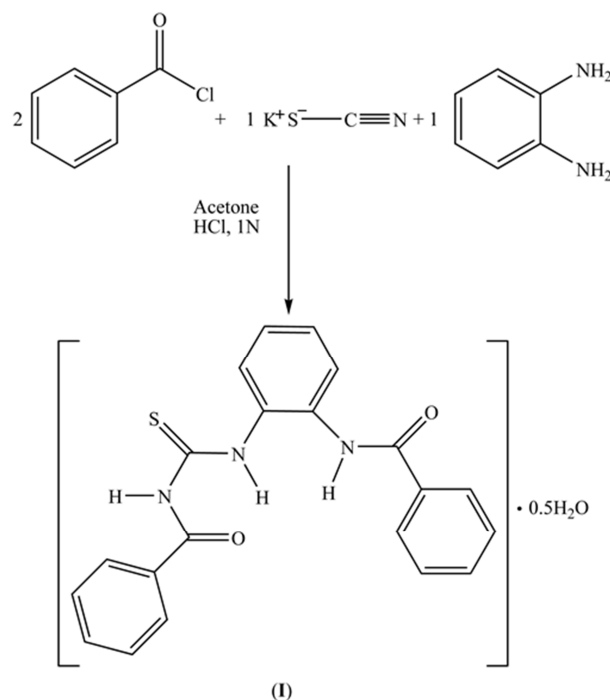


Figure 1. Synthesis scheme of the compound (I).

3. Results and Discussion

3.1. General Study

The dissymmetrical compound 1-(2-benzamidophenyl)-3-benzoylthiourea hemihydrate (I) ($\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_2\text{S} \cdot 0.5\text{H}_2\text{O}$) was prepared by a reaction of 1,2-diaminobenzene, potassium thiocyanate and benzoyl chloride in acetone in 1/1/2 ratio (Figure 1). The elemental analyses results are in accordance with the proposed chemical formulae. The FTIR spectrum of the compound exhibits a band centered at 3210 cm^{-1} assigned to N—H stretching of the thiourea and the amid moieties [19]. The band due to the amidic C=O is pointed at 1673 cm^{-1} as observed for similar Schiff base [20, 21]. Additional bands revealed in the range $1596\text{--}1470\text{ cm}^{-1}$ are attributed to the phenyl rings. Band due to the thione C=S function appears at 1169 cm^{-1} [22]. The ^1H and ^{13}C NMR spectra of the compound 1-(2-benzamidophenyl)-3-benzoylthiourea were recorded in CDCl_3 . The ^1H NMR spectra of the compound reveals three singlets at δ 8.19, 9.25 and 9.60 ppm assignable to three —N—H groups in the dissymmetrical compound. These observations are in accordance with the ^{13}C spectrum of compound. The signals at δ 164.9 and 169.5 ppm attributed to carbon atom of the C=O groups and the signal at 177.9 ppm attributed to carbon atom of the C=S bond are indicative of the successful of the reaction [23]. Additional signals are pointed for the aromatic carbon atoms in the range 122.10–134.70 ppm.

3.2. Crystal Structure

The X-ray structure determination reveals that the compound (I) crystallizes in the monoclinic space group $I2$

with one molecule in the asymmetric unit. The molecular geometry is illustrated in Figure 2 and selected bond lengths and angles are listed in Table 2. The N—H atoms of the thiourea moiety adopt an *anti* conformation. The benzoyl group of the thiourea subunit is *trans* with respect to the thiono S atoms across the C7—N2 bond, while the 1-amino-2-benzamidobenzene fragment adopts a *cis* conformation with respect to the thiono S atom across the C7—N1 bond. For the thiohydrazino arm, the S1—C7 [1.661 (4) Å] and the O1—C8 [1.236 (5) Å] distances indicates that these correspond to double bonds and are comparable to those observed for 1,2-Bis(N'-benzoylthioureido)benzene [1.660 (2) Å for C—S, and 1.222 (2) Å for C—O respectively [15]. The C—N bond length are 1.344 (5) Å for C7—N1, 1.352 (5) Å for C15—N3 and 1.373 (5) Å for C8—N2. These values are in normal range observed for a nominal C(sp²)—N(sp³) [24]. The angles around C7, C8 and C15 which are in the range [115.2 (4)—126.0 (3)°] are close proximity for the ideal angle of 120° around C(sp²). The side arms with the thione function is slightly twisted as reflected by the two torsion angles C7—N2—C8—O1 [−1.43 (7)°] and C8—N2—C7—N1 [−6.1 (6)°]. The other side arm contains only an amide function with bond length distances of 1.234 (5) Å [C15—O2] and 1.352 (5) Å [C15—N3]. The thiourea fragment S1/N1/N2/C7/C8 is planar, with a maximum deviation from the least-squares plane of 0.0422 (3) Å for the N1 atom. The dihedral angle between this plane and that of the monosubstituted thiureidobenzene ring (rms deviation = 0.004 Å) is 10.418 (7)° versus 26.95 (5)° in the analogous Schiff base *N,N'*-(ethane-1,2-diyl)bis(azanediylcarbonothioyl)]bis(benzamide) [14]. The thiourea and the central disubstituted phenyl ring are not coplanar with dihedral angle value of 60.292 (2)°. The central phenyl ring mean plan (rms 0.0157 Å) is not coplanar with the mean plans of the two terminal phenyl rings with respective dihedral angle values of 70.565 (8)° (phenyl (rms 0.0044 Å) on the thioureido moiety) and 76.862 (7)° (phenyl (rms 0.0010 Å) on the amido moiety).

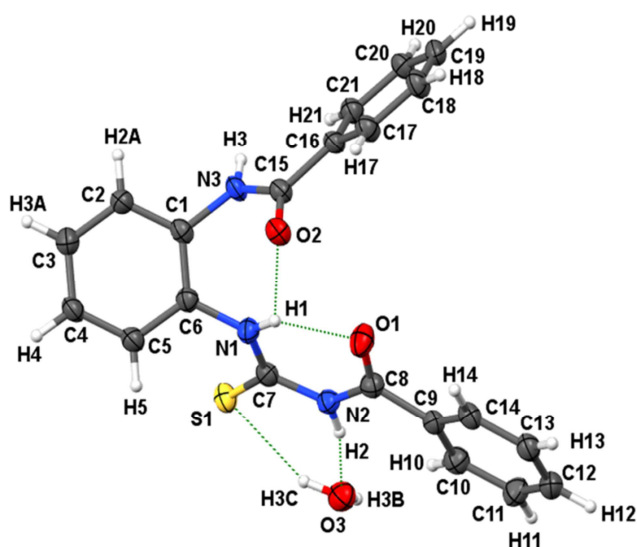


Figure 2. Crystal structure of the compound (I).

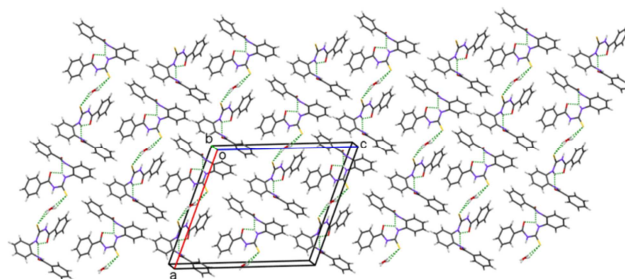


Figure 3. The packing of the compound (I) in the crystal structure.

The molecule features intramolecular hydrogen-bond contacts involving the NH of the thiourea group and the O atoms of the amide groups, which close an *S*(6) and *S*(7) rings. Additional intramolecular hydrogen bonds N(thiourea)—H...O(water) and HO—H...S(thiourea) which close in *S*(6) ring are observed. Intermolecular hydrogen-bond is observed between the NH of the amido groups and the O atoms of the amide groups which form layers parallel to the *ac* plane (Figure 3, Table 3).

Table 1. Crystal data and structure refinement for compound (I).

Formula	4(C ₂₁ H ₁₇ N ₃ O ₂ S)·H ₄ O ₂
Mr	1537.79
Crystal shape/color	Block/colorless
Crystal system, Space group	Monoclinic, <i>I</i> 2
Temperature (K)	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	18.1868 (6), 5.2493 (1), 20.5286 (6)
β (°)	110.434 (3)
<i>V</i> (Å ³)	1836.50 (9)
<i>Z</i>	1
<i>D</i> _{calc} (g cm ^{−3})	1.390
<i>F</i> (000)	804
Radiation type	λ = 1.54184 Å
μ (mm ^{−1})	1.78
Crystal size (mm)	0.23 × 0.02 × 0.01
Data collection	
Diffractometer	XtaLAB AFC12 (RCD3): Kappa single
Absorption correction	Multi-scan
<i>T</i> _{min} , <i>T</i> _{max}	0.658, 1.000
Limiting indices	
<i>h</i>	−22 → 21
<i>k</i>	−6 → 6
<i>l</i>	−23 → 20
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	10200, 3404, 3038
<i>R</i> _{int}	0.060
Refinement	
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²)	0.047, 0.128
No. of parameters/restraints	252, 1
Goodness-of-fit (Gof) on <i>F</i> ²	1.06
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å ^{−3})	0.33, −0.26

Table 2. Bond lengths [Å] and angles [°] for (I).

S1—C7	1.661 (4)	O2—C15—N3	122.5 (3)
O2—C15	1.234 (5)	O2—C15—C16	120.9 (4)
O1—C8	1.236 (5)	N3—C15—C16	116.6 (3)
N1—C7	1.344 (5)	O1—C8—N2	122.2 (4)
N3—C15	1.352 (5)	O1—C8—C9	119.6 (4)
N2—C8	1.373 (5)	N1—C7—S1	126.0 (3)
N1—C7	1.407 (5)	N1—C7—N2	115.2 (4)
		N2—C7—S1	118.8 (3)

Table 3. Hydrogen-bond geometry (\AA , $^\circ$) for (I).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$O3-H3C\cdots S1$	0.85	2.57	3.270 (2)	131.0
$N1-H1A\cdots O2$	0.86	2.22	2.841 (5)	129.2
$N1-H1A\cdots O1$	0.86	1.92	2.615 (4)	136.9
$N3-H3\cdots O2^i$	0.86	2.32	3.069 (5)	145.0
$N3-H3\cdots O1^i$	0.86	2.43	2.979 (5)	122.3
$N2-H2\cdots O3$	0.86	2.29	3.108 (3)	159.5

Symmetry code: (i) $x, y-1, z$.

4. Conclusion

The novel 1-(2-benzamidophenyl)-3-benzoylthiourea hemihydrate (I) was synthesized by treatment of 1,2-diaminobenzene with potassium thiocyanate and benzol chloride in 1/1/2 ratio. The isolated compound was characterized by elemental analyses, FTIR and NMR spectroscopies. The X-ray single crystal diffraction confirmed the structure. The X-ray structure reveals that the benzoyl and 1-amino-2-benzamidobenzene groups adopt, respectively, a trans conformation and a cis conformation with respect to the S atom ($S1=C7$) through the corresponding $C7-N$ bond. The conformation was stabilized by intramolecular $N-H\cdots O$ and $S-H\cdots O$ hydrogen bonds which close in $S(6)$ and $S(7)$ rings. The structure is consolidated by intermolecular hydrogen bonds $N-H\cdots O$ developing layers parallel to the *ac* plane.

Supplementary Materials

CCDC-2036811 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via <https://www.ccdc.cam.ac.uk/structures/>, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Conflicts of Interest

The authors declare that they no competing interest.

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