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Synthesis, characterization and crystal structure of 1-(4-methylbenzoyl)-3-(4 aminosulfonylphenyl)thiourea

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ABSTRACT

An efficient synthesis of the title compound, 1-(4-methylbenzoyl)-3-(4-aminosulfonyl phenyl)thiourea, was carried out by reaction of 4-methylbenzoyl chloride with potassium thiocyanate in acetone to afford 4-methylbenzoyl isothiocyanate *in situ* followed by treatment with sulfanilamide. The structure was confirmed by spectroscopic data and elemental analyses. The molecular structure was determined from single crystal X-ray diffraction data. It crystallizes in the monoclinic space group $P2_1/n$ with unit cell dimensions of a = 4.8116(9) Å, b = 17.150(3) Å, c = 18.677(3) Å, γ = 96.487(4) °, and V = 1531.4(5) Å^3.

1. Introduction

1,3-disubstitued thioureas are extremely versatile building blocks for the synthesis of a variety of heterocyclic compounds and exhibit a wide spectrum of bioactivities. *N*,*N*-Dialkyl-*N*-aroyl thioureas are efficient ligands for the separation of platinum group metals [1]. 1,3-Dialkyl or diaryl thioureas exhibit significant antifungal activity against plant pathogens *Pyricularia oryzae* and *Drechslera oryzae* [2]. 1-Benzoyl-3-(4,6-disubstituted-pyrimidin-2-yl)thioureas display excellent herbicidal activity [3]. Acyl thioureas are well known for their superior pesticidal, fungicidal, antiviral and plant growth regulating activities [4]. 1-Aroyl-3-arylthioureas have recently been used in the synthesis of imidazole-2-thiones and imino thiazolines [5,6].

Sulfanilamide and its derivatives are still widely used in chemotherapy effectively against a broad range of microorganisms [7-8]. These are true anti-metabolites; they block a specific step in the biosynthetic pathway of folic acid [9]. More than 12000 sulfonyl thiourea derivatives are known and some of them are very potent hypoglycemic agents due to their ability to stimulate the release of insulin from the pancreatic islets. Examples of the first generation sulfonylureas include carbutamide, the first sulfonylurea used as an effective oral hypoglycemic agent which is more effective than IPTD, tolbutamide, chlorpropamide, tolazamide and those as the second generation are glyburide and glipizide. The present work aimed at appending the sulfanilamide moiety to thiourea nucleus in order to combine their beneficial effects in a single structure with expected bioactivities including anticancer activity.

The title compound, 1-(4-methylbenzoyl)-3-(4-amino sulfonylphenyl)thiourea, belong to a unique class of thioureas in which the free aniline nitrogen is incorporated into the thiourea structure compared to all other known urea derivatives which involve the sulfonamide amino group as part of the thiourea moiety.

2. Experimental

2.1. Instrumentation

Melting points were recorded using a digital Gallenkamp (SANYO) model MPD.BM 3.5 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were determined as chloroform-d solutions using a Bruker AM-300 spectrophotometer. FTIR spectra were recorded on an FTS 3000 MX spectrophotometer. Mass spectra was acquired (EI, 70eV) on a MAT 312 instrument, and elemental analyses were conducted using a LECO-183 CHNS analyzer. Crystallographic data were collected on a Bruker-AXS SMART APEX CCD diffractometer. The crystal structure was solved by direct methods. H-atoms were located from difference Fourier maps and then refined at idealized positions with riding model. Details on data collection and refinement are given in Table 1.

2.2. Synthesis

A solution of 4-methylbenzoyl chloride (10 mmol) in acetone (50 mL) was added dropwise to a suspension of potassium thiocyanate (10 mmol) in acetone (30 mL) and the reaction mixture was refluxed for 30 min. After cooling to room temperature, a solution of sulfanilamide (10 mmol) in acetone (10 mL) was added and the resulting mixture was refluxed for 3 h (Scheme 1). The reaction mixture was poured into cold water and the precipitated thiourea was recrystallized using aqueous methanol. Yield = (1.33 g, 64%). R_f = 0.7; M.p.: 209-210°C. IR (cm^{-1}): 1590 (arom. C=C), 1663 (C=O), 3317 (N–H), 1263 (C=S), 1158 (C–N), 1334 (S=O).

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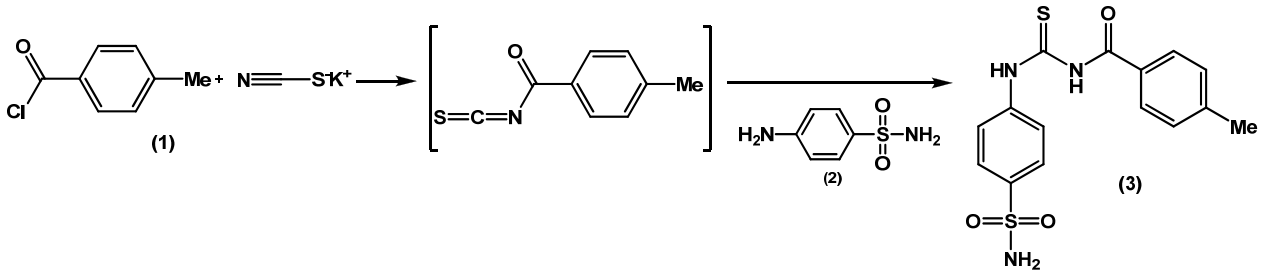

Scheme 1

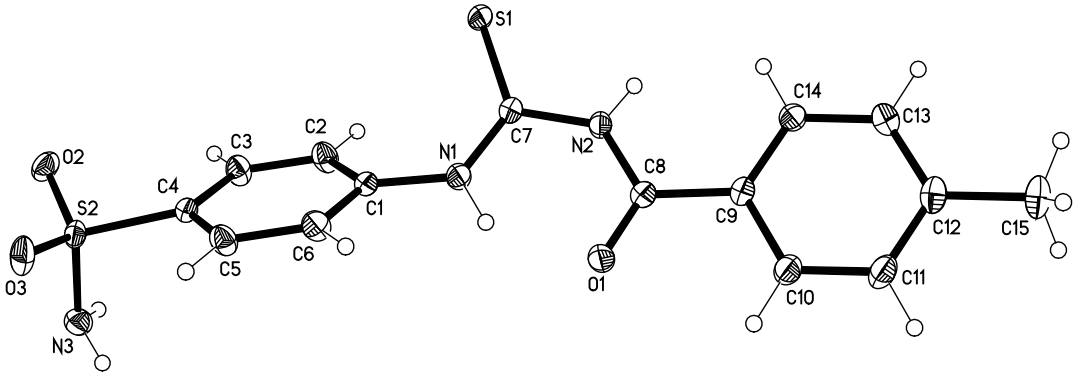

Figure 1. Molecular structure of the title compound with the atom-numbering scheme. Displacement ellipsoids plotted at 50% probability level.

Table 1. Crystal data and structure refinement for 1-(4-methylbenzoyl)-3-(4-aminosulfonylphenyl)thiourea.

Empirical formula	$C_{15}H_{15}N_3O_3S_2$
Formula weight	349.42
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group, Z	P 2_1/n, 4
Unit cell dimensions	a = 4.8116(9) Å.
	b = 17.150(3) Å
	c = 18.677(3) Å.
	β= 96.487(4)°.
Volume	1531.4(5) Å^3
Density (calculated)	1.516 Mg/m^3
Absorption coefficient	0.366 mm^{-1}
F(000)	728
Crystal size	0.49 x 0.20 x 0.05 mm^3
Theta range for data collection	1.62 to 27.87°
Index ranges	-6 ≤ h ≤ 6
	-22 ≤ k ≤ 22
	-17 ≤ l ≤ 24
Reflections collected	13460
Independent reflections	3665 [R(int) = 0.0435]
Completeness to theta = 27.87°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9819 and 0.8409
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3665 / 1 / 217
Goodness-of-fit on F^2	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0437, wR2 = 0.1012
R indices (all data)	R1 = 0.0602, wR2 = 0.1089
Largest diff. peak and hole	0.409 and -0.263 e.Å^{-3}
Measurement	Bruker SMART APEX CCD diffractometer
Program system	SAINT
Structure determination	Direct methods (SHELXL-97, SHELXTL)
CCDC	679109

3. Results and Discussion

4-Methylbenzoyl chloride (**1**) was obtained from the corresponding acid according to the standard procedure. It was then treated in a 1:1 molar ratio with potassium thiocyanate in dry acetone to afford the 4-methylbenzoyl isothiocyante intermediate which was not separated. Condensation of the latter with an equimolar quantity of sulfanilamide (**2**) in anhydrous acetone furnished the 1-(4-methylbenzoyl)-3-(4-aminosulfonylphenyl)thiourea (**3**) in 91% yield (Scheme 1).

Colorless crystals of 1-(4-methylbenzoyl)-3-(4-amino sulfonylphenyl)thiourea, suitable for X-ray analysis, were obtained by slow evaporation from ethyl acetate/petroleum ether (1:2) solvent mixture. The thiourea was characterized by typical IR stretching vibrations of N–H at 3318 cm^{-1}, C=O at 1663 cm^{-1}, C=S at 1263 cm^{-1}, C–N at 1154 cm^{-1}, and S=O at 1334 cm^{-1} in addition to the aromatic ring at 1590 cm^{-1}.

In ^{1}H NMR the singlet for the aromatic methyl appeared at δ 2.43 and the characteristic broad singlets at δ 9.19 and δ 12.76 for the protons of N_1 and N_3 respectively. The signals for the aromatic protons were also noted. ^{13}C NMR showed peaks at δ 23.9 for the aromatic methyl and at δ 170.3 and δ 179.4 for C=O and C=S respectively. Mass spectrum of the compound showed the molecular ion peak at m/z 304. The major fragment at m/z 168.9 (50 %) was derived from the N-McLafferty rearrangement and the base peak at m/z 119 originated from the 4-methylbenzoyl cation.

The molecular structure of the title compound is depicted in Figure 2. Table 1 gives the crystal data and the structure refinement; selected bond lengths and angles as well as hydrogen bonds are presented in Table 2. The torsion angles C7-N2-C8-O1 of 2.3(3)° and C8-N2-C7-N1 of –6.1(3)° reflect the almost planar conformation of the molecule with respect to the thiocarbonyl and carbonyl parts. The two aromatic rings form a dihedral angle of 42.82(8)° and the associated N2-C8-C9-C10 torsion angle is 9.6(3)°. Bond parameters (Table 1) in general are typical for this type of a compound. Similar geometric parameters are valid for the related molecular structures of 1-(4-Methylbenzoyl)-3-(4-nitro/halogeno-phenyl)thiourea [9-11]; the most distinct difference is reflected by the dihedral angles between the aryl rings: for the nitro compound [11] it is 28.1(1)°, for the Br [12] and the Cl compounds [10] it measures 14.3(1)° and 30.5(1)°, respectively. Strong intermolecular N(3)-

H…O(2) hydrogen bonds link molecules to head-to-head dimers that are stacked along [100] (Table 2).

Table 2. Selected geometric parameters (Å, °) for 1-(4-methylbenzoyl)-3-(4-aminosulfonylphenyl)thiourea.

Bond lengths	
S1-C7	1.656(2)
C1-N1	1.411(3)
C7-N1	1.346(2)
C7-N2	1.394(2)
C8-N2	1.374(2)
C8-O1	1.230(2)
C8-C9	1.479(3)
S2-C4	1.7607(19)
S2-N3	1.6172(19)
H3-H2	0.88(3)
H2….O2	2.18(3)
N3….O2	3.016(3)
Bond Angles	
C1-N1-C7	128.50(17)
N1-C7-N2	114.38(17)
C7-N2-C8	128.47(16)
N2-C8-C9	117.40(17)
N3-H2….O2	158(2)

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Supplementary material

CCDC-679109 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: +44(0)1223-336033.

References

[1]. Koch, K.R. *Coord. Chem. Rev.***2001**, *216-217*, 473-488
[2]. Krishnamurthy, R.; Govindaraghavan, S.; Narayanasamy, J. *Pesticide Science* **1999**, *52*, 145-151.
[3]. Sijia, X.; Liping, D.; .Shaoyong, C.; Liangbin, J**.** *Chem. J. Internet* **2003**, *5*, 67-70.
[4]. Wang, X-C.; Wang, V.; Quan, Z-J.; Wang, M-G.; Li, Z. *J. Chem. Res.,* **2005**, *61*, 689-690.
[5]. Saeed, A.; Parvez, M. *J. Heterocyl. Chem.* **2006**, *43***,** 1027-1030.
[6]. Snieckus, V; *Chem. Rev***. 1990**, *90*, 879-933
[7]. Bestmann, H.J.; Kern, F.; Schafer, D.; Witschel, M.C. *Angew. Chem. Int. Ed. Engl.* **1992** *31*, 795-796.
[8]. Stokstad, E. L. R.; Jãoekes, T. H. *J. Nutr.* **1987,** *117*; 1335-1341.
[9]. Botet, J.; Mateos, L.; Revuelta, J. L; Santos, M. A. *Eukaryotic Cell*, **2007**, 2102–2111.
[10]. Saeed, A.; Flörke, U. *Acta Cryst.* **2006,** *E62*, o2924- o2924.
[11]. Yusof, M. S. M.; Hamid, M. A.; Ramli, R. N. H. R.; Yamin, B. M. *Acta Cryst.* **2006,** *E62*, o2131- o2131.
[12]. Saeed, A.; Flörke, U. *Acta Cryst.* **2006,** *E62*, o5036-o5036.