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Supramolecular self-assembly of a coumarine-based acylthiourea synthon directed by π-stacking interactions: Crystal structure and Hirshfeld surface analysis

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ABSTRACT

The structure of 1-(2-oxo-2*H*-chromene-3-carbonyl)-3-(2-methoxy-phenyl)thiourea (**1**) has been determined by single-crystal X-ray crystallography. This compound crystallizes in the monoclinic space group $P2_1/c$ with $a = 7.455$ (2) Å, $b = 12.744$ (3) Å, $c = 16.892$ (4) Å, $\beta = 90.203$ (6)° and $Z = 4$. Both, the coumarin and the phenyl rings are nearly coplanar with the central 1-acylthiourea group, with the C=O and C=S bonds adopting an opposite orientation. Intramolecular N–H···O, C–H···O, and C–H···S hydrogen bonds are favored by the planar conformation. The molecules are packed through C–H···O, C–H···S and C–H···C hydrogen bonds, and two π···π interactions with offset arrangement. Inter-centroid distance of 3.490 (2) Å, slip angles of 18.5 and 20.9°, and vertical displacements of 1.10 and 1.24 Å are the stacking parameters corresponding to the stronger π···π interaction. Hirshfeld surface analysis was performed for visualizing, exploring and quantifying intermolecular interactions in the crystal lattice of compound **1**, and compared with two closely related species. *Shape index* and *Curvedness* surfaces indicated π-stacking with different features in opposed sides of the molecule. Fingerprint plot showed C···C contacts with similar contributions to the crystal packing in comparison with those associated to hydrogen bonds. Enrichment ratios for H···H, O···H, S···H and C···C contacts revealed a high propensity to form in the crystal.

1. Introduction

Thioureas and acyl-substituted thiourea derivatives are amongst the most promising compounds in synthetic chemistry due to their versatile applications [1–3]. These compounds have been shown to exhibit a broad range of coordination modes toward metal complexes [4,5], representing good candidates as single-source of metal sulfides for photovoltaic devices [6,7].

Structural evaluations of 1-acyl-3-substituted thiourea derivatives have attained immense attention in current years [8,9]. They show intramolecular hydrogen bonding [10] which greatly affect their behavior toward complexation [11], cyclization reactions [12], and other useful applications. Very recently, we have demonstrated [13] that the Hirshfeld surfaces analysis [14–16] provides a powerful technique for analyzing intermolecular interactions in a series of 1-(adamantane-1-carbonyl) thioureas.

The molecular structure around the acylthiourea group depends on the degree of substitution on the nitrogen atoms. Accordingly, 3-(mono-substituted) species form a pseudo six-membered ring, which is favored by a C=O···H–N intramolecular hydrogen bond, leading to a local planar structure of the acylthiourea group with opposite orientation between the C=O and C=S double bonds [17]. It is anticipated that the inclusion of substituent with acceptor hydrogen bond groups can strongly affect the conformational

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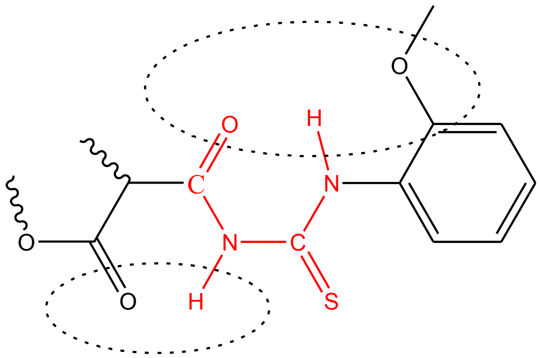
properties [18], [19,20]. It was previously demonstrated that the inclusion of a 2-methoxy-phenyl group on the 3-possition offers the possibility of increasing the acidity of the N–H group by the formation of a N–H···O intramolecular hydrogen bond [21–24]. It can be rationalized that further substitution at the nitrogen 1-position with especially designed acyl substituents can also affect the hydrogen bonding network around the second N–H group, facilitating the formation of more complex and varied intra- and intermolecular interactions. For example, coupling the 1-acyl thiourea nucleus with the ferrocene group conducts to compounds with salient electrochemical [25], as well as structural properties [26].

We focus our attention on the coumarin group [27,28] as substituent at the 1-acyl position, leading to the general structure showed in Scheme 1. Very recently, a series of coumarin-linked thioureas were synthetized and their inhibition activity against acetyl- and butyryl-cholinesterases were evaluated, showing promising *in vitro* results [29]. Related chromene-based compounds have a high degree of chemical diversity leading to a broad array of biological activities. For example, the chromone-3-(phenyl) carboxamide derivatives are promising compounds for the management of neurodegenerative diseases [30]. It has been proposed that π···π and C–H···π intermolecular interactions in the crystal packing of coumarins are associated with high lipophilicity parameter values and the ability for the transport of these compounds through membranes [31].

From the structural point of view, we rationalize that introducing a substituent bearing a second C=O group can, in principle, affect the intramolecular hydrogen bond into the thiourea moiety. Moreover, the extended electronic conjugation of the coumarin ring could also favor the formation of π-directed intermolecular interactions [32], for which an increasing number of theoretical and experimental studies have been recently accomplished and could be used as tools in crystal engineering for the design of crystalline thioureas [33–35]. We report here the spectroscopic and structural study by X-ray diffraction and a detailed analysis of intermolecular interactions by Hirshfeld surfaces computational method of 1-(2-oxo-2*H*-chromene-3-carbonyl)-3-(2-methoxyphenyl)thiourea. The surfaces are mapped with d_{norm}, 2D-fingerprint plots, *shape-index* and *curvedness* properties [14–16], in order to analize packing features, and determine the main descriptors of distinct π-stacking in the opposed faces of the aromatic rings for title compound and related structures.



Scheme 1. Representation of different N–H···O intramolecular hydrogen bonds prompted by specific substitutions at the 1-acyl-thiourea group (in red).

2. Experimental

2.1. Synthesis of 1-(2-oxo-2H-chromene-3-carbonyl)-3-(2-methoxyphenyl)thiourea

The preparation of the target molecule was achieved according to the method reported very recently [29].

Conversion of coumarin-3-carboxylic acid to its acid chloride was followed by treatment with potassium thiocyanate to obtain coumarin-3-carbonylisothiocyanate. The *in situ* reaction with 2-methoxyaniline in dry acetone gave the crude product which on recrystallization from ethanol afforded the desired product as light yellow crystals. All commercial reagents were purchased from Aldrich Chemical Company.

2.2. Instrumentation

Fourier transform infrared spectroscopy (FTIR), recorded using a NICOLET 6700 spectrophotometer using attenuated total reflectance (ATR) technique. Solid-phase (in KBr pellets) infrared spectra were recorded with a resolution of 2 cm^{-1} in the 4000-400 cm^{-1} range on a Bruker EQUINOX 55 FTIR spectrometer.

2.3. Computational details

Molecular quantum chemical calculations have been performed with the GAUSSIAN 03 program package [36] by using the B3LYP DFT hybrid methods employing Pople-type basis set [37]. The valence triple-ξ basis set augmented with diffuse and polarization functions in both the hydrogen and weighty atoms [6–311++G(d,p)] has been used for geometry optimization and frequency calculations. The calculated vibrational properties corresponded in all cases to potential energy minima for which no imaginary frequency was found. The Potential Energy Distribution (PED) analysis are computed from the B3LYP/6–311++G(d,p) calculated vibrational frequencies using VEDA4 program [38,39].

2.4. X-ray data collection and structure refinement

The crystal and refinement data for title compound are listed in

Table 1
Crystal data and structure refinement for 1-(2-oxo-2H-chromene-3-carbonyl)-3-(2-methoxyphenyl)thiourea.

Empirical formula	$C_{18}H_{14}N_2O_4S$
Formula weight	354.37
Temperature/K	130 (2)
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	$a = 7.455$ (2) Å
	$b = 12.744$ (3) Å
	$c = 16.892$ (4) Å
	$\beta = 90.203$ (6)°
Volume/$Å^3$	1604.8 (7)
Z	4
ρ calc./mg mm^{-3}	1.467
μ/mm^{-1}	0.229
F (000)	736
Crystal size/mm^3	0.15 x 0.16 x 0.45
Theta range for data collection	2.0–27.9°
Index ranges	$-9 \le h \le 9$, $-16 \le k \le 16$, $-22 \le l \le 20$
Reflections collected	14701
Independent reflections	3807 [R (int) = 0.083]
Data/restraints/parameters	3807/0/227
Goodness-of-fit on F^2	0.98
Final R indexes [$I > 2\sigma(I)$]	$R1 = 0.063$, $wR2 = 0.154$
Largest diff. peak/hole/e $Å^{-3}$	0.38/-0.36