Understanding the conformational changes and molecular structure of furoyl thioureas upon substitution

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ABSTRACT

1-Acyl thioureas [R'C(O)NHC(S)NR2R3] are shown to display conformational flexibility depending on the degree of substitution at the nitrogen atom. The conformational landscape and structural features for two closely related thioureas having R1 = 2-furoyl have been studied. The un-substituted 2-furoyl thiourea (I) and its dimethyl analogue, i.e. 1-(2-furoyl)-3,3-dimethyl thiourea (II), have been synthesized and fully characterized by spectroscopic (FT-IR, 1H and 13C NMR) and elemental analysis. According to single crystal X-ray diffraction analysis, compounds I and II crystalize in the monoclinic space group P21/c. In the compound I, the trans-cis geometry of the almost planar thiourea unit is stabilized by intramolecular N–H⋯O = C hydrogen bond between the H atom of the cis thioamide and the carbonyl O atom. In compound II, however, the acyl thiourea group is non-planar, in good agreement with the potential energy curve computed at the B3LYP/6-311+G(d,p) level of approximation. Centrosymmetric dimers generated by intramolecular N–H⋯S–N= C hydrogen bond forming R2(8) motif are present in the crystals. Intermolecular interactions have been rationalized in terms of topological partitions of the electron distributions and Hirshfeld surface analysis, which showed the occurrence of S⋯H, O⋯H and H⋯H contacts that display an important role to crystal packing stabilization of both thiourea derivatives.

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reported by Becker and coworkers [15], the S form prevails for 1-(acyl/aroyl)-3-(mono-substituted) thiourea derivatives with R2 = H, because the formation of intramolecular C⋯H–N hydrogen bond strongly stabilize this conformation [16–18]. On the other hand, 1-(acyl/aroyl)-3,3-(di-substituted) thioureas tend to adopt the U form since in this case R3 and R2 ≠ H and thus, the formation of a intramolecular hydrogen bond is disallowed [19].

Thiourea derivatives containing the 2-furoyl group were synthesized [20–24] and the complexation ability of these ligands toward various metal ions was investigated [25–28], with salient analytical applications [29]. In particular, 1-(2-furoyl)-3-substituted thioureas were probed as useful intermediates used in environmental control and as ionophores in ion selective electrodes [26,30]. Recently, mesoporous silica hybrid materials functionalized with 1-(2-furoyl) thioureas exhibited good usefulness as useful intermediates used in environmental control and as ionophores in ion selective electrodes [26,30]. Recently, mesoporous silica hybrid materials functionalized with 1-(2-furoyl) thioureas exhibited good ability to remove Hg(II) from aqueous solutions [31].

In this article the effect of substitution at the 2-furoyl thiourea core is analyzed by studying two closely related species, i.e. the “parent” and the novel 3,3-dimethylated thioureas (compounds I and II in Scheme 2, respectively). Structural characterization includes experimental spectroscopic (FT-IR and Raman) and X-ray diffraction studies, complemented with a detailed analysis of intermolecular interactions by Hirshfeld surfaces and Atom in Molecule (AIM) topological analysis of the electron charge density.

2. Experimental

2.1. Material and Measurements

Thin layer chromatography (TLC) was performed on 0.25 mm silica gel pre-coated plastic sheets (40/80 mm) (Polygram SIL G/UV254, Macherey & Nagel, Düren, Germany) using benzene/methanol (9/1) as eluent. The IR spectra were recorded on a FT-IR Bomem-Michelson 102 spectrometer, in KBr pellets with a resolution of 2 cm−1 in the 4000–400 cm−1 range. Raman spectra for compounds I and II were recorded using a Horiba Jobin Yvon T64000 Raman spectrometer equipped with a liquid N2-cooled back-thinned CCD detector. Spectra were recorded as the co-addition of up to 16 individual spectra with CCD exposure times of 10–20 s each. 1H and 13C NMR spectra were recorded on a Bruker DRX 400 MHz, internally referenced to TMS.

2.2. Quantum Chemical Calculations

Optimization of molecular geometries was accomplished within the frame work of the density functional theory [32,33] as implemented in the Gaussian 03 package [34]. Contracted Gaussian basis sets of triple-zeta quality plus polarized and diffuse functions 6–311 + + (G,d,p) for all atoms were used throughout the present work [35]. The corresponding vibrational analyses were performed for the optimized geometries (Cartesian coordinates are given in Tables S1 and S2 in the Supporting information) to verify whether they are local minima or saddle points on the potential energy surface of the molecule. Calculated normal modes were also used as an aid in the assignment of experimental frequencies. Natural Bond Orbital (NBO) population analysis were performed and the energy of the donor–acceptor interactions estimated by the second order perturbation theory [36].

Periodic calculations were performed at the B3LYP/6–31G(d,p) level with Crystal14 code [37]. Using the experimental estimations as the starting point, the coordinates of the hydrogen atoms in the crystal were optimized to minimize the crystal energy with heavy atom coordinates and cell parameters fixed at their experimental values. The topology of the resulting electron density was then analyzed using the TOPOND14 code [38,39].

2.3. Synthesis of 2-Furoyl Thioureas

Detailed descriptions of syntheses and characterization of related furoyl thioureas have been previously reported [13]. A solution of an appropriately acyl chloride (30 mmol) in acetonitrile (50 mL) was added drop wise to a suspension of KSCN (30 mmol) in acetone (30 mL). The mixture was stirred until a precipitate appeared (KCl), indicating the formation of 2-furoyl isothiocyanate. Ammonia [31] or dimethyl amine (30 mmol), dissolved in acetonitrile was slowly added with constant stirring of the resulting solution (Scheme 3). The solution was cooled in an ice-water bath and the stirring was continued at room temperature during 2–9 h, until the reaction was completed (the reaction progress was monitored by TLC). The reaction mixture was then poured into 600 mL of cold water. The solid thioureas were collected by filtration and finally purified by recrystallization from acetone:water mixture. The identity of the products was confirmed by the analysis of the 1H and 13C NMR spectra (given in Figs. S1–S4 of the Supplementary information) in comparison to similar compounds previously reported in the literature [13].

2-Furoyl thiourea (I): yield 79%, mp 146–147 °C. FT-IR [ATR (solid), ν·cm−1]: 3336, 3320, 3302, 3200, 1679, 1606, 1529, 1530, 1178, 883, 756. 1H NMR (400 MHz, DMSO-d6): 10.92 (s, 1H, NH, D2O exchangeable); 9.58 (s, 1H, NH, D2O exchangeable); 8.02 (dd, 2H, Ar), 7.79 (dd), 6.73 (dd). 13C NMR (400 MHz, DMSO-d6): 181.5 (C=S); 157.1 (C=O), 148.1, 144.7, 118.2 and 112.5. Anal. Calc. for C8H10N2O2S (198.05): C, 48.47; H, 4.07; N, 5.08; S, 9.07. Found: C, 48.00; H, 5.30; N, 4.50; S, 8.50%.

1-(2-furoyl)-3,3-dimethyl thiourea (II): yield 82%, mp 146–147 °C. FT-IR [ATR (solid), ν·cm−1]: 3161, 2923, 1697, 1571, 1473, 1263, 1178, 929, 761. 1H NMR (400 MHz, CDCl3): 8.63 (s, 1H, NH, D2O exchangeable), 7.56 (dd), 7.27 (dd), 6.58 (dd), 3.40(s, CH3), 2.88 (s, CH3). 13C NMR (400 MHz, CDCl3): 179.0 (C=S); 153.4 (C=O), 146.1, 145.5, 117.3, 112.8. Anal. Calc. for C12H16N2O2S (342.40): C, 48.47; H, 5.08; N, 4.13; S, 8.17%: Found: C, 48.00; H, 5.30; N, 4.50; S, 8.50%.
2.4. Crystal Structure Determination

Single crystals suitable for X-ray diffraction were obtained by slow evaporation of CHCl₃-n-hexane (3:1) solutions of the furoyl thioureas I and II. Diffraction data were collected on an Enraf-Nonius Kappa-CCD diffractometer with graphite-monochromated MoKα radiation (λ = 0.71073 Å). The final unit cell parameters were based on all reflections. Data collections were performed using the COLLECT program [40]. Integration and scaling of the reflections were performed with the HKL Denzo–Scalepack system of programs [41]. Absorption corrections were carried out using the Gaussian method [42]. The structures were solved by direct methods with SHELXS-97 [43]. The models were refined by full-matrix least-squares on F² by means of SHELXL-97. The projection views of the structures were prepared using ORTEP-3 for Windows [44]. Hydrogen atoms were stereochemically positioned and refined with the riding model. The crystal and refinement data for title compounds are listed in Table 1 with the CCDC deposit numbers for supplementary crystallographic data.

3. Results and Discussion

3.1. Synthesis and Characterization

2-Furoyl thioureas I and II were synthesized according to the general method early reported by Douglass and Dains [45] and further optimized for 2-furoyl substitutions [13,31]. The one-pot procedure involves the in situ reaction between 2-furoyl chloride and KSCN and the reaction of the intermediate 2-furoyl isothiocyanate with the appropriated amine. The reaction proceeds via a nucleophilic addition of the amine to the isothiocyanate with good yields (79 and 82%, for I and II, respectively). The synthesized compounds were purified by recrystallization from an acetone-water mixture (1:2) and characterized by elemental analysis, ¹H NMR, ¹³C NMR, and FT-IR spectroscopy. In ¹H NMR, the compounds exhibited broad signals in the range of 10.92, 9.58 and 8.63 ppm, which were assigned to the N—H protons. ¹³C NMR spectrum showed the peaks at about 8181.5 and 179.0 for C=O (thioamide) and 157.1 and 153.4 for C=O (amide), respectively. The elemental analyses closely corresponded to calculated values.

3.2. Vibrational Spectra

Infrared and Raman spectroscopies have shown to be very useful for analyzing the conformational properties, as well as intermolecular and intramolecular hydrogen bond interactions involving N—H donors of acyl thioureas [11,46–54]. As early noted by Reguera et al. [21] the joint analysis of both infrared and Raman spectroscopy are required for study the effect on the substitution for a series of mono- and disubstituted thioureas. Recently, we have shown the complementarily of both techniques for the analysis of 1-(adamantane-1-carbonyl)-3-(mono)- and 3,3-(di) substituted thioureas [55]. The 3N — 6 = 45 normal modes of vibration for compound I can be classified as 31 A’ in-plane modes and 14 A” out-of-plane modes in the C₃ point symmetry group.

In particular, the 1720–1050 cm⁻¹ region of the Raman spectrum of compounds I and II is shown in Fig. 1. The close examination of the ν(C=O) stretching mode region reveals a strong absorption at 1679 cm⁻¹, with a counterpart in the Raman spectrum at 1680 cm⁻¹ for compound I, whereas this mode appears shifted toward higher frequencies for compound II, with values at 1697 cm⁻¹ (IR) and 1693 cm⁻¹ (Raman), as shown in Fig. 1. These values are in good agreement with those previously reported for related acyl thioureas and 1-acyl,3,3-di-substituted thioureas [56]. The experimental values are well-reproduced by the quantum chemical calculations, with computed ν(C=O) frequency values of 1735 and 1760 cm⁻¹ for I (A’ symmetry species) and II, respectively. The lower force constant of the ν(C=O) stretching found for compound I is associated with the intramolecular N—H⋯O=C hydrogen bond.
Intense absorptions in the 1500–1600 cm\(^{-1}\) region due to the \(\delta(N–H)\) deformation modes are usually observed in the infrared and Raman spectra of thioureas [57], whereas only one \(\delta(N–H)\) band is expected for the 3,3-disubstituted species. The infrared spectra show very intense absorptions at 753 and 755 cm\(^{-1}\), whereas only one \(\nu(C–O)\) and 1571 cm\(^{-1}\) (Raman) and 1570 cm\(^{-1}\) (infrared) bands are observed for the 1-acyl thiourea compounds. The potential energy curve around the C–N bond for compound I and II have been computed at the B3LYP/6-31 + G(d,p) level of approximation, allowing geometry optimizations with the \(\delta(CN–CN)\) dihedral angle varying from 0 to 360° in steps of 20° (Fig. 3). For compound I, the most stable structure corresponds to the S form (see Scheme 1) with a dihedral angle of 0°. In this conformation the C2–O1 and H–N1 groups form a pseudo 6-membered ring, favoring an H-bond intramolecular interaction. For compound II, the minimum occurs at a dihedral angle ca. 60°, with mutual syndical orientation of the C1–N1 and C6–N2 bonds (see Figs. 4 and 5 for atoms numbering).

The structures with \(\delta(CN–CN) = 180°\) correspond in both cases to local maxima in the potential energy curve, the energy barriers being ca. 15 and 11 kcal/mol, higher for compound I. Two equivalent local minima are observed at \(\delta(CN–CN)\) values of ca. 150 and 210°. These conformers are located higher in energy and correspond to structures with a nearly antiplanar orientation between the C–N and C–N bonds.

It is recognized that remote donor-acceptor orbital interactions can play a decisive role on the peptide backbone conformation [63]. In particular, it has been proposed that C=O⋯H–N hydrogen bonds [64] can through the intramolecular, N–H⋯O=C, hydrogen bonds, as will be discussed below. The first step observed in the TG curve for compound I with a loss mass of 88.54%, is consistent with the removal (fragmentation) of furoyl C(O)NC(S) moiety (calculated loss weight of 89.90%). The second step observed in the TG curve with a loss mass of 9.76%, is probably due to the formation of NH\(_3\) as a result of a mechanisms simultaneous by a migrating of the NH hydrogen atoms and the cleavage (homolysis) of C–N bonds (loss of weight calculated 9.98%). This thermal fragmentation mechanism is in agreement with that suggested previously in the pyrolysis of related furyl thioureas studied by mass spectrometry methods [61,62].

### 3.4. Molecular Structure

#### 3.4.1. Theoretical Conformational and Natural Bond Orbital Analysis

A rich conformational landscape can be anticipated for the studied compounds. In particular, several conformations can be adopted depending on the relative orientation of the C–O and C=S double bonds of the acyl thiourea core. Based on previous works [11,12] the most relevant conformational changes are expected by differences in the relative orientations around the C–N bond joining the amide and thioamide groups [18]. The potential energy curve around the C–N bond for compounds I and II have been computed at the B3LYP/6-31 + G(d,p) level of approximation, allowing geometry optimizations with the \(\delta(CN–CN)\) dihedral angle varying from 0 to 360° in steps of 20° (Fig. 3). For compound I, the most stable structure corresponds to the S form (see Scheme 1) with a dihedral angle of 0°. In this conformation the C2–O1 and H–N1 groups form a pseudo 6-membered ring, favoring an H-bond intramolecular interaction. For compound II, the minimum occurs at a dihedral angle ca. 60°, with mutual syndical orientation of the C1–N1 and C6–N2 bonds (see Figs. 4 and 5 for atoms numbering).

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**Fig. 1.** Selected region of the Raman spectra for the solid phase of compounds I and II.

**Fig. 2.** TGs curves for compounds I (red) and II (blue).

**Fig. 3.** Calculated [B3LYP/6-31 + G(d,p)] potential function for internal rotation around the \(\delta(CN–CN)\) dihedral angle of thioureas I (−●−) and II (−○−).
be analyzed on the basis of the hyperconjugative interaction involving the partial transfer of a lone pair of electrons of the oxygen atom to the N—H antibonding orbital [65]. For benzenesulfonylamidic acid, lpO → σ*(N—H) interaction values of ca. 9.5 kcal/mol were computed by using DFT methods [66].

We applied the Natural Bond Orbital population analysis for determining electron donations in the studied compounds. For the compound I, the second-order perturbation analysis of the Fock matrix [B3LYP/6-311++G(d,p) level of approximation] indicates a lpO1 → σ*(N1—H) remote interaction, amounting to 8.1 kcal/mol for the S form. The hyperconjugative interaction increases the electronic population of the σ*(N1—H) orbital (0.031 e), as compared with that of the second N—H group, i.e. σ*(N2—H), with 0.010 e. For compound II, without the possibility of forming intramolecular hydrogen bond, the σ*(N1—H), shows an electronic population of 0.016 e.

The NBO analysis for the most stable conformers for compounds I and II, respectively, indicates the presence of pure p-type [lp(N)] lone pair orbitals on both amide and thioamide nitrogen atoms. These orbitals display low electron occupancies (1.675 and 1.650 for the N1 and N2 nitrogen atoms, respectively, in good agreement with reported values for other compounds [69]. The hyperconjugative interactions involve hydrogen atoms, their positions in the crystal were determined for the N—H antibonding orbital [68], two donor sites rich in electron density and the trans geometry of the thiourea unit is stabilized by intramolecular N1—H⋯O1 hydrogen bond, with N1⋯O1 distance of 2.676(2) Å and N1—H⋯O1 bond angle of 132°. The C1=S1 and O1⋯C1 bonds show a typical double bond character with bond lengths of 1.672(2) Å and 1.223(2) Å, respectively.

The Fig. 5 shows the molecular structure of the compound II. It is non planar forming a distorted “S”-shaped conformation type, this conformation where the carbonyl and thiourea groups are non-planar with mutual anticlinal (O=C / C=S = 112.8°) orientation of the C=S and C=O double bonds (see Fig. S5 in the Supporting information) [68]. The C1=S1 and O1⋯C1 bonds show a typical double bond character with bond lengths of 1.687(2) Å and 1.221(2) Å, respectively.

The amicd (O)C=N—H and thioamide NH2=N(C=S) and (S)C=N—H bonds for I and (O)C=N—H and thioamide NH1=N(C=S) and (S)C=N—H bonds for II are both shorter than a C—N single bond, typically ca. 1.472(5) Å. This fact indicates that these bonds have a pronounced double bond character. It is deduced that these thiourea derivatives make up a multi-electron conjugated π bond, in agreement with the NBO results discussed above. Other selected geometric parameters (Table 2) are between the ranges obtained for similar compounds [69].

3.5. Crystal Packing and Topology Analysis of the Electron Densities

Since many of the more relevant intra and intermolecular interactions involve hydrogen atoms, their positions in the crystal were optimized at the B3LYP/6-311G(d,p) level, keeping fixed at their crystallographic values the heavy atom positions and cell parameters. The electron density topology was analyzed and the values of the electron density and positive principal curvature of the Laplacian at the corresponding (3,−1) critical point were used as indicators of the interaction strength. Topological parameters of the predominant intermolecular interactions present in the crystal structures of I and II are reported in Tables 3 and 4, respectively.

In compound I, the basic crystal substructures are the centrosymmetric molecular pairs involving, each, a pair of N—H⋯S=C interactions with one of the hydrogen atom in the amino group as donor (I in Table 4), these being the most relevant from a topological point of view. This pair can be classified as an R2(8) motif forming a pseudo eight-membered ring, as shown in Fig. S6 (Supporting information). In the structure of I the H1B⋯S is separated by 2.622 Å.

The crystal structure of I, however, can be better described in terms of the infinite chains expanding in c axis direction (see Fig. 6a and Table 3), along which molecules are linked each other mainly through four interactions. The two strongest interactions link the carbonyl

![Fig. 4. The molecule structure of the compound I in the crystal. Ellipsoids represent 50% probability levels and dashed line indicates intramolecular hydrogen bond.](image1)

![Fig. 5. Molecular structure of compound II. Displacement ellipsoids are drawn at the 50% probability level.](image2)

### Table 2
Selected bond distances (Å) for compounds I and II.

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<th>Compound</th>
<th>Bond</th>
<th>Distance (Å)</th>
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<tr>
<td>I</td>
<td>S—C1</td>
<td>1.672(2)</td>
</tr>
<tr>
<td></td>
<td>O2—C3</td>
<td>1.371(2)</td>
</tr>
<tr>
<td></td>
<td>N1—C1</td>
<td>1.310(2)</td>
</tr>
<tr>
<td></td>
<td>N2—C2</td>
<td>1.386(2)</td>
</tr>
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<tr>
<td></td>
<td>O2—C2</td>
<td>1.372(2)</td>
</tr>
<tr>
<td></td>
<td>N1—C1</td>
<td>1.387(2)</td>
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<tr>
<td></td>
<td>N2—C6</td>
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<tr>
<td></td>
<td>N2—C8</td>
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<td>N1—C6</td>
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<td></td>
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<td></td>
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Table 3
Topological parameters (atomic units) of the close shell intermolecular (3,—1) critical points (electron density (ρ), Laplacian (ρλ) and positive curvature (λ₃)) and geometrical parameters (Å and °) of the interactions used in the structure description of compound I.

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<th>ρλ</th>
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<th>θ₂–H₄/N–S/N</th>
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<td>0.0400</td>
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<tr>
<td>II</td>
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<td>0.0444</td>
<td>0.0725</td>
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<td>168.6</td>
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<td>III</td>
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<td>0.0380</td>
<td>0.0642</td>
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<tr>
<td>V</td>
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<td>0.0312</td>
<td>0.0478</td>
<td>2.472</td>
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<td>VI</td>
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<td>0.0268</td>
<td>0.0388</td>
<td>2.768</td>
<td>159.2</td>
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Table 4
Topological parameters (atomic units) of the (3,—1) critical points (electron density (ρ), Laplacian (ρλ) and positive curvature (λ₃)) and geometrical parameters (Å and °) of the intermolecular interactions used in the structure description of compound II.

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<th>ρλ</th>
<th>λ₃</th>
<th>dₜ,N–S/N</th>
<th>θ₂–H₄/N–S/N</th>
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<td>0.0427</td>
<td>0.0810</td>
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<td>157.4</td>
</tr>
<tr>
<td>II</td>
<td>0.0116</td>
<td>0.0440</td>
<td>0.0671</td>
<td>2.300</td>
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<td>III</td>
<td>0.0104</td>
<td>0.0326</td>
<td>0.0534</td>
<td>2.431</td>
<td>150.5</td>
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<tr>
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<td>0.0494</td>
<td>2.463</td>
<td>157.79</td>
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<td>V</td>
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<td>0.0242</td>
<td>0.0378</td>
<td>2.850</td>
<td>150.5</td>
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3.6. Hirshfeld Surface Analysis

Intermolecular contacts were also explored using both Hirshfeld surfaces and fingerprint plots. In recent years, many research groups have used Hirshfeld surfaces [70,71] and their two-dimensional fingerprints as an important tool to visualize and analyze structural properties in relation to packing patterns [72], including those observed in thio-urea compounds [73,74]. The intermolecular interactions of I and II were analyzed using the Hirshfeld surface and the corresponding two-dimensional fingerprint plots [75] are shown in the Fig. 8.

The 3D dₜ,N–S Hirshfeld surfaces for I and II are represented in the Fig. 8A, in which the value of dₜ,N–S can be negative, positive or zero, when intermolecular contacts are shorter, longer or equal to van der Waals (vdW) radii, respectively. The dₜ,N–S values were mapped onto the Hirshfeld surface using a color gradient from blue to red indicates that region able to perform intermolecular interactions. Red regions represent closer contacts and a negative dₜ,N–S value, while blue regions represent longer contacts and a positive dₜ,N–S value. In the surface, white regions represent the distance of contacts equal to exactly the vdW separation with a dₜ,N–S value of zero. As can be seen in the Hirshfeld surfaces of the compounds I and II the most intense red

Fig. 6. (a) Two chains view along b axis direction, in the compound I. (b) Six chains view along c axis direction.

Fig. 7. (a) Layer view along a normal to [1,0,2]. (b) Two layers view along b axis direction in the compound II.

oxygen atom with the amide hydrogen atom and with a hydrogen atom of the furoyl ring (II and III in Fig. 6 and Table 3). The other two interactions link an amino hydrogen atom with a sulfur atom (IV) and a hydrogen atom of the furoyl group with the oxygen atom also from a furoyl ring (V). Chains, in turn, are linked each other through the above mentioned N–H⋯S interactions and the H₄–S ones (VI). Alternation in the molecule orientation along a chain (see Fig. 6b) ensures the main three dimensional interaction network is thus completed.

In compound II, the basic substructures are the centrosymmetric molecular pairs involving, each, a pair of N–H⋯S interactions (1 in Table 4 and Fig. 7). Linking of such pairs through C–H⋯O interactions (III) involving methyl groups and acting in almost perpendicular directions (see Fig. 7a), give rise to molecular layers parallel to [1,0,2]. The main three dimensional interaction network is completed by three interactions that link layers with each other (see Table 4 and Fig. 7b). Two of them involve carbonyl hydrogen atoms, a ring hydrogen atom (II) and a methyl hydrogen atom (IV) of the reference molecule being the donors. The remaining one is a H⋯S interaction (V).
Fig. 8. Hirshfeld surfaces (A) and fingerprint plots (B-E) for compounds I (left) and II (right). The full fingerprint is represented in (B), and graphics C, D and E depict the S⋯H, O⋯H and H⋯H intermolecular contacts, respectively.
regions occur near to C=S and N—H groups, due to bifurcate N—H⋯S hydrogen bonds present in both structures (see Fig. S6 in the Supporting information). The compound I also exhibits red regions close to both oxygen atoms of carbonyl and furoyl groups, as a result of N—H⋯O and C—H⋯O hydrogen bonds, respectively, such as illustrated in the Fig. 6a and discussed in the crystal packing analysis. Differently, when we look at to Hirshfeld surface of the compound II, it is observed that the oxygen atom of the furoyl group is not involved in any close intermolecular contact, resulting in a white-to-blue gradient color in the Hirshfeld surface. Meanwhile the less intense red color gradient in II is observed on oxygen atom of the carbonyl, because this group is involved in a non-classical C—H⋯O hydrogen bond, such as represented in Table 4 and Fig. 7.

The fingerprint plots of the two molecules show the presence of S⋯H, O⋯H and H⋯H intermolecular contacts (Fig. 8B). The relative contribution of the main intermolecular contacts present in each compound is listed in the Table S3 (Supporting information). The biggest contribution includes hydrophobic intermolecular contacts (H⋯H, C⋯H and C⋯C). In addition, the hydrogen bonding (S⋯H and O⋯H) form well defined contacts as represented in the Fig. 8C–D, acting as driving forces to stabilize the crystal packing. Therefore, the hydrophobic intermolecular contacts together with the N—H⋯S hydrogen bonds provide forces for self-assembly in the compounds.

4. Conclusions

Two 2-furoyl thiourea derivatives (I and II) were prepared and their structural and spectroscopic properties have been determined. Our results clearly show that the conformation of the central acyl-thiourea [−C(O)NHCS(−)] moiety depends on the substitution at the nitrogen atom. Thus, the simplest 2-furoyl thiourea (I) adopts a planar structure with the C=O and C=S double bonds mutually oriented in a pseudoantiperiplanar arrange, favoring a strong C=O⋯H⋯N intramolecular hydrogen bond. The same conformation was very recently found in the crystal of the mono-substituted 3-phenyl thiourea [76]. However, di-methylation of the —NH2 group leads to a different conformation.
of the thiourea group: planarity is absent in compound II and antical orientation of the C=S and C=O double bonds is observed. Inversion di- mers with an R(2) ring motif are observed for I and II, a supramolecular synthon that is assisted by strong N—H···S=C hydrogen bonds, as char- acterized by topological grounds and Hirshfeld surface analysis.

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Appendix A. Supplementary data

Cartesian coordinates of optimized structures [B3LYP/6-311 + +G(d,p)] for compounds I and II are given in Tables S1 and S2, re- spectively. In Table S3 the relative contribution to the Hirshfeld surfaces of the important intermolecular contacts present in each compound, I and II are given. 1H and 13C NMR spectra are given in Figs. S1–S4. Con- formations of molecules of compound II are shown in Fig. S5 and centro- symmetric dimer the studied compounds are shown in Fig. S6. Supplementary data associated with this article can be found in the on- line version, at [10.1016/j.saa.2016.12.038].

References
