# SÍNTESE, ESTRUTURA CRISTALINA E ANÁLISE DE SUPERFÍCIE HIRSHFELD DO 1-ACETIL-5- (2-METILPROPIL) -2-TIOXO-IMIDAZOLIDIN-4-ONA

# SYNTHESIS, CRYSTAL STRUCTURE AND HIRSHFELD SURFACE ANALYSIS OF 1-ACETYL-5-(2-METHYLPROPYL)-2-THIOXO-IMIDAZOLIDIN-4-ONE

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## RESUMO

Os heterociclos de hidantoína e tio-hidantoína estão presentes numa ampla gama de compostos biologicamente ativos incluindo fármacos terapêuticos para o tratamento de convulsões e compostos antitumorais. Tio-hidantoína também foram utilizados como agentes anticonvulsivante e estão presentes em fungicidas, herbicidas e produtos naturais. No entanto, o principal interesse atual vem da aplicação de tio-hidantoínas para o tratamento de câncer de próstata. A caracterização estrutural da hidantoína e da tio-hidantoína é importante para compreender seus mecanismos de efeito devido aos seus consideráveis efeitos biológicos. Neste trabalho, obteve-se um derivado de tio-hidantoína, 1-acetil-5-(2-metilpropil)-2-tioxo-imidazolidin-4-ona (I) pela reação de ácido 2-amino-4-metilpentanóico com KSCN em Amido de anidrido acético-ácido acético. O composto heterocíclico foi caracterizado por análise de difração de raios X de FTIR, RMN, pó e de cristal único. Este composto cristaliza no sistema triclinico, grupo espacial P-1 (Nº2), Z = 4, com duas moléculas independentes na unidade assimétrica. A tio-hidantoína (I) forma cadeias unidimensionais ligadas ao hidrogênio através de uma única ligação de hidrogênio entre os oxigênios da carbonila e a posição N3 do anel de amina, que corre ao longo da direção [100], com o motivo C (6) do conjunto de gráficos. A natureza das interações intermoleculares foi analisada através de superfícies de Hirshfeld e impressão digital 2D.

**Palavras-chave**: heterocíclico, tio-hidantoína, difração de raios X, ligação de hidrogênio, análise de Hirshfeld





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## ABSTRACT

The hydantoin and thiohydantoin heterocycles are present in a wide range of biologically active compounds including therapeutic drugs for the treatment of seizures and anti-tumor compounds. Thiohydantoins, have also been used as anti-convulsant agents and are present in fungicides, herbicides and natural products. However, the principal current interest comes from the application of thiohydantoins for the treatment of prostate cancers. Structural characterization of hydantoin and thiohydantoin are important to comprehend their effect mechanisms because of their considerable biological effects. In this work a thiohydantoin derivative, 1-acetyl-5-(2-methylpropyl)-2-thioxo-imidazolidin-4-one (**I**), has been obtained by the reaction of 2-amino-4-methylpentanoic acid with KSCN in acetic anhydride-acetic acid mixture. The heterocyclic compound was characterized by FTIR, NMR, powder and single-crystal X-ray diffraction analysis. This compound crystallizes in the triclinic system, space group P-1 (Nº2), Z=4, with two independent molecules in the unit asymmetric. The thiohydantoin (**I**) forms one-dimensional hydrogen bonded chains, via a single hydrogen bond between the carbonyl oxygens and the amine ring N3 position, that run along [100] direction, with graph-set motif C(6). The nature of intermolecular interactions has been analyzed through Hirshfeld surfaces and 2D fingerprint plots.

**Keywords:** heterocyclic compound, thiohydantoin, x-ray diffraction, hydrogen bond, Hirshfeld analysis

## INTRODUCTION

The hydantoin and thiohydantoin heterocycles are present in a wide range of biologically active compounds including therapeutic drugs for the treatment of seizures and anti-tumor compounds (Mutschler and Derendorf, 1995; Dylag *et al*., 2013; Carmi *et al*., 2006; Singh *et al*., 2005; Kaindl *et al*., 2006)]. The best knwonhydantoin, phenytoin, is the most widely used antiepileptic drug (Merrit and Putman, 1938). Thiohydantoins, have also been used as anti-convulsant agents and are present in fungicides, herbicides and natural products [7 – 9]. However, the principal current interest comes from the application of thiohydantoins for the treatment of prostate cancers [10, 11].

Both of these heterocycles are commonly used as templates in combinatorial chemistry libraries, due its very reactive nucleus which provides four possible points of diversity [12, 13], and recently, there has been interest in the search of new synthetic routes for the preparation of these types of compounds [14 – 16].

Structural characterization of hydantoin and thiohydantoin are important to comprehend their effect mechanisms because of their considerable biological effects. It is because of that we are interested in hydantoin and thiohydantoin derivatives of amino acids [17 – 27], and therefore report here the synthesis and structure of the thiohydantoin derivative 1-acetyl-5-(2-methylpropyl)-2-thioxo-imidazolidin-4-one. In order to understand the nature of the described non-covalent interactions in the supramolecular network of this material, we performed a Hirshfeld surface analysis [28].

## MATERIALS AND METHODS

### Synthesis

The title compound (**I**), which is the intermediate in the preparation of the thiohydantoin 5-(2-methylpropyl)-2-thioxo-imidazolidin-4-one (II) (see Scheme 1), was synthesized from 2-amino-4-methylpentanoic acid (dl-leucine). dl-leucine (5 mmol) and KSCN (5 mmol) was dissolved in a 9 ml acetic anhydride-1 ml acetic acid mixture and transferred in a 25 ml round-bottom flask. The mixture was warmed, with agitation, to 100 °C over a period of 30 min. The resulting solution was cooled in an ice/water mixture and stored in a freezer overnight. The resulting white solid was filtered off and washed with cool water (m.p. 131-132 °C). Crystal of (I) suitable for X-ray diffraction analysis were obtained by slow evaporation of a 1:1 ethanol-methanol solution. All the reagents used were obtained from Sigma-Aldrich (USA) and were used without any further purification.

### Spectroscopic studies

The Fourier transform infrared spectroscopy (FT-IR) absorption spectrum was obtained as KBr pellet using a Perkin-Elmer 1600 spectrometer (Perkin-Elmer, USA). $^{1}$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker Avance 400 model spectrometer (Bruker, Germany) in DMSO-$d_6$ solution.

FT-IR (KBr, ν, $cm^{-1}$): 3218 ν(N-H), 1765 ν(C=O), 1720 ν(C=O), 1434 ν(C-N), 1175 ν(C=S)
$^{1}$H-RMN (400 MHz, DMSO-$d_6$): δ=12.66 (H3, s), 4.71 (H5, d), 2.70 (H7, s), 1.76 (H8, H9, m), 0.85 (H10, H11, d).
$^{13}$C-RMN (100.6 MHz, DMSO-$d_6$): δ=182.5 (C2), 173.5 (C4), 169.7 (C6), 61.3 (C5), 38.1 (C8), 27.3 (C7), 23.7 (C9), 23.1 (C10), 21.9 (C11).

**X-ray powder diffraction**

The X-ray powder diffraction pattern of (**I**) was collected at room temperature in a Phillips PW-1250 (Phillips, Netherland) goniometer using monocromatized CuKα radiation. A small quantity of compound was ground mechanically in an agate mortar and pestle and mounted on a flat holder covered with a thin layer of grease. The sample was scanned from 3-50° 2θ, with a step size of 0.02° and counting time of 10s. Silicon was used as an external standard.

X-ray powder pattern of the thiohydantoin compound is show in Figure 1. The 20 first measured reflections were completely indexed using the program Dicvol04 [34], which gave a unique solution in a triclinic cell with parameters *a*= 7.185 Å, *b*= 9.725 Å, *c*= 16.431 Å, α= 101.1°, β= 94.0°, γ= 90.5°. In order to confirm the unit cell parameters, a Le Bail refinement [35] was carried out using the Fullprof program [36]. The Figure 1 shows a very good fit between the observed and calculated patterns.

**X-ray single-crystal crystallography**

Colorless rectangular crystal (0.3x0.2x0.1 mm) was used for data collection. Diffraction data were collected at 298(2) K by ω-2θ scan technique on a Siemens P4 four-circle diffractometer (Siemens, Netherland) equipped with graphite monochromatized CuKα radiation (λ = 1.54178 Å). The data were corrected for Lorentz-polarization and absorption effects. Three standard reflections were monitored every 100 reflections (intensity decay: none). The structure was solved by direct methods using the SHELXS program [29] and refined by a full-matrix least-squares calculation on $F^2$ using SHELXL [30].

All H atoms were placed at calculated positions and treated using the riding model, with C-H distances of 0.97-0.98 A, and N-H distances of 0.86 A. The $U_{iso}$(H) parameters were fixed at $1.2U_{eq}$(C, N) and $1.5U_{eq}$(methyls).

Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre (CCDC-860694).

**Hirshfeld surfaces analysis**

The packing of the title compound (**I**) was also investigated by an analysis of the Hirshfeld surfaces [28] with the aid of Crystal Explorer [31]. The two-dimensional fingerprint plots [32] were calculated for the crystal, as were the electrostatic potentials. The electrostatic potentials were mapped on the Hirshfeld surfaces using the STO-3G basis set at the level of Hartree-Fock theory over a range of ±0.075 au [33]. Crystallographic information file (CIF) of (**I**) was used as input for the analysis. For the generation of fingerprint plots the bond lengths of hydrogen atoms involved in interactions were normalized to standard neutron values (C-H = 1.083 Å, N-H = 1.009 Å, O-H = 0.983 Å).

The Hirshfeld surfaces can identify and quantify the intermolecular interactions [28]. The d*norm* surface is the distance in terms of d*e* and d*i*. In the plot, for each point of the Hirshfeld surface enveloping the molecule in the crystal, the distance d*i* to the nearest atom inside the surface and the distance d*e* to the nearest atom outside the surface are reported. The colour of each point in the plot is related to the abundance of that interaction, from blue (low) to green (high) to red (very high). The fingerprint plot is a graphical two-dimensional map that indicates the distribution of the interactions for a single molecule in the crystal [32].

## RESULTS AND DISCUSSION:

The heterocycle compound (**I**) crystallizes with two independent molecules (*R* and *S*) in the asymmetric unit, in the centrosymmetric space group P-1. The molecular structure and labeling scheme of the title compound (**I**) are shown in Fig. 2.Table 1 summarizes the crystal data, intensity data collection and refinement details for (**I**).Selected geometrical parameters are collected in Table 2. All bond distances and angles are in agreement with experimental average values found in 50 records with thiohydantoin ring fragments with N3 unsubstituted, searched in the Cambridge Structural Database (CSD, version 5.37, May. 2016) [37].

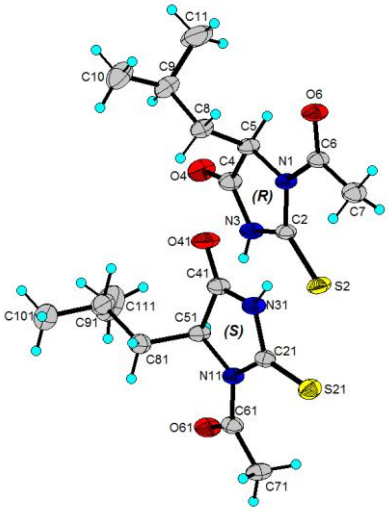


***Figure 2.****Asymmetric unit with anisotropic ellipsoid representations, together with atom labelling scheme of (**I**). The ellipsoids are drawn at 25% probability level, hydrogen atoms are depicted as spheres with arbitrary radii*

The thiohydantoin ring, in both molecules, is planar with a maximum deviations of 0.034 (3) Å in C4 and -0.037 (3) Å in C4, in molecule *R* and 0.039(3) Å in C41 and -0.038(3) Å in C51, for molecule *S*.

N-acetylation affects the external angles flanking the C=S group, with S2-C2-N1 (131.5°) becoming wider and S2-C2-N3 narrower (122.8°). This difference is also observed in the other seven 1-acetyl thiohydantoin compounds reported in the CSD; rac-1-acetyl-5-methyl-2-thioxoimidazolidin-4-one (131.5-122.2°) [18], rac-1-acetyl-5-benzyl-2-thioxoimidazolidin-4-one (131.6-122.3°) [19], rac-1-acetyl-5-propionamide-2-thioxo-imidazolidin-4-one (130.6-123.7°) [22], S-(1-(3-acetyl-5-oxo-2-thioxo-2,3,4,5-tetrahydro-1H-imidazol-4-yl)ethyl) ethanethioate (130.6-123.4°) [38], 1-acetyl-5-(4-fluorophenyl)-2-thioxoimidazolidin-4-one (130.3-123.4°) [39] and the two polymorphs of 1-acetyl-2-thioxoimidazolidin-4-one (average 132.0-121.9°) [40, 41].

Two intermolecular main hydrogen bonds N3--H3···O6 (1+x, y, z) and N31--H31···O61 (-1+x, y, z) were identified in the crystal of (**I**) (Table 3). The thiohydantoin (**I**) forms one-dimensional hydrogen bonded chains, via a single hydrogen bond between the carbonyl oxygens and the amine ring N3 position, that run along [100] direction, and can be described in graph-set notation as C(6) [42] (see Figure 3).

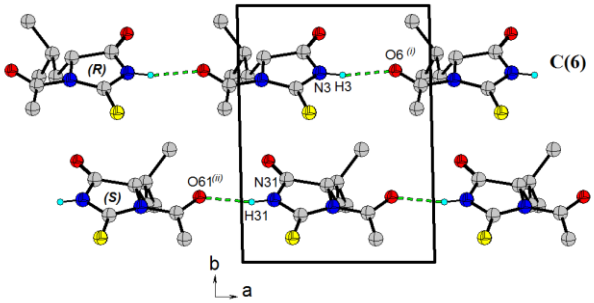


***Figure 3.****Packing view of (**I**) viewed in the ba plane, showing the chains of (R) and (S) tapes along the a axis. Intermolecular hydrogen bonds, N--H···O and O--H···O, are indicated by dashed lines. H atoms not involved in hydrogen bonding have been omitted for clarity*

This lineal packing is also appreciated in the structure of 1-acetyl-5-benzyl-2-thioxo-imidazolidin-4-one [19]. The steric bulk of the 2-methylpropyl group appears to inhibit formation of rings, as in the structures rac-1-acetyl-5-methyl-2-thioxo-imidazolidin-4-one [18], rac-5-(2-methylthio-ethyl)-2-tioxo-imidazolidin-4-one [22], rac-1-acetil-5-propionamida-2-tioxo-imidazolidin-4-ona [24] and (S)-5-secbutyl-2-thiohydantoin [25]. A comparison of these structures suggests increased steric bulk in the 5-position favours chain formation.

In order to assess possible packing differences involving the two independent molecules, we have examined their Hirshfeld surfaces [28].

The d*norm* surfaces plots for *R* and *S* molecules of (**I**) are shown in Figure 5. The d*norm* surfaces plots of two molecules are consistent with the analysis of the packing patterns as discussed in the previous section. Dark-red spots close to O6 and O61 atoms are a result of a close contact between these atoms resulting in strong N--H···O hydrogen bonds.

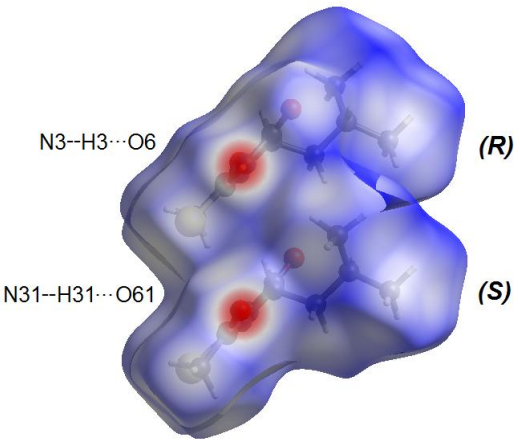


***Figure 4.****dnorm mapped on Hirshfeld surfaces in (I)*

The Hirshfeld fingerprint plots of the two independent molecules are illustrated in Figure 6. A distinctive feature of each plot is represented by the two spikes at d*e* + d*i*~ 1.8 Å, pointing to the lower left of the plots and symmetrically disposed with respect to the diagonal. They correspond to the strong hydrogen bonds present in the crystal packing. Another common feature is the sting along the diagonal, at d*e* = d*i*~ 1.25 Å, which reflects points on the Hirshfeld surface that involve nearly head-to-head H···H contacts. Two plots look very similar, thus indicating that the packing around each molecule is similar, consistent with the hydrogen-bonds analysis by X-ray diffraction.

## CONCLUSIONS:

The thiohydantoinderivative1-acetyl-5-(2-methylpropyl)-2-thioxoimidazolidin-4-one was synthesized and characterized by FTIR and NMR spectroscopy, and X-ray diffraction techniques. This material crystallize in the triclinic system with space group P-1 (Nº2), Z=4, with two independent molecules in the unit asymmetric. In the crystal structure of (**I**), the crystal packing is governed by N--H···O hydrogen bond-type intermolecular interactions, forming infinite one-dimensional chains with graph-set motif C(6).

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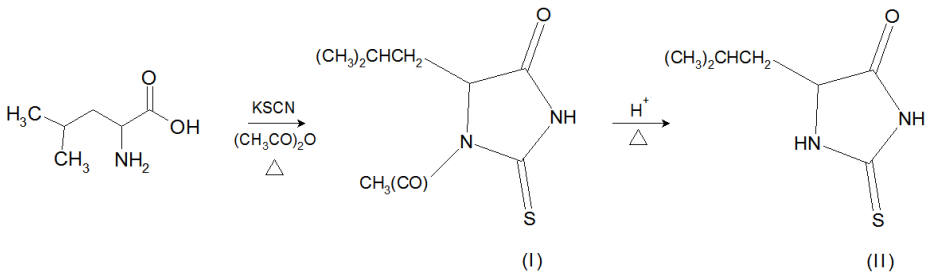
## REFERENCES:

1. Mutschler, E., Derendorf, H. *Drug actions, basic principles and therapeutic aspects*, Medpharm Scientific Publishers, Stuttgart, 1995.
2. Dylag, T., Zygmunt, M., Maciag, D., Handzlik, J., Bednarski, M., Filipek, B., Kiec-Kononowicz, K. *Eur. J. Med. Chem.***2004**, 39, 1013.
3. Carmi, C., Cavazzoni, A., Zuliani, V., Lodola, A., Bordi, F., Plazzi, P.V., Alfieri, R.R., Petronini, P.G., Mor, M. *Bioorg. Med. Chem. Let.***2006**, 16, 4021.
4. Singh, G., Driever, P.H., Sander, J.W., Sander, L.*Brain J. Neurol.***2005**, 128, 7.
5. Kaindl, A.M., Asimiadou, S., Manthey, D., Hagen, H.V.D., Turski, V.D., Ikonomidou, C.*Cell. Mol. Life Sci.*, **2006**, 63, 399.
6. Merrit, H.H., Putnam, T.J. *Arch. Neurol.Psychiat.***1938**, 39, 1003.
7. Marton, J. Enisz, J. Hosztafi, S. Timar, T., *J. Agric. Food Chem.***1993**, 41, 148.
8. Al-Madi, S., Al-Obaid, A.M., El-Subbagh, H., *Anti-Cancer Drugs*, **2001**, 12, 835.
9. Takahashi, A., Matsuoka, H., Yamada, K.,Uda Y.*FoodChem.Toxicol.***2005**, 43, 521.
10. Harrison, C.*Nature Rev. Drug Disc.***2009**, 8, 452.
11. Shen H.C., Balk,S.P., *Cancer Cell*, **2009**, 15, 461.
12. Park, K.H., Ehrler, J., Spoerri, H., Kurth, M. J.*J. Comb. Chem.***2001**, 3, 171.
13. Muccioli, G.G., Poupaerta, J.H., Wouters, J., Norberg, B.,Poppitzc, W., Gerhard K.E Scribad, G.K.E.,Lamberta, D.M., *Tetrahedron*, **2003**, 59, 1301.
14. Vázquez, J., Royo, M., Albericio, F., *Letters Org. Chem.***2004**, 1, 224.
15. Reyes, S., Burges, K., *J. Org. Chem.***2006**, 71, 2507.
16. Wang, Z.D., Sheikh, S.O., Zhang, Y.L., *Molecules*, **2006**, 11, 739.
17. Delgado, G.E., Mora, A.J., Uzcátegui, J., Bahsas, A., Briceño, A., *Acta Cryst.***2007**, C63, o448.
18. Sulbaran, M.E., Delgado, G.E., Mora, A.J., Bahsas, A., Novoa de Armas, H., Blaton, N., *Acta Cryst.***2007**, C63, o543.
19. Uzcátegui, M.C., Delgado, G.E., Mora, A.J., González, T., Briceño. A.,*ActaCryst.***2009**, E65, o104.

20. Seijas, L.E., Mora, A.J., Delgado, G.E., Brunelli, M., Fitch, A.N., *Powder Diffr.* **2010**, 25, 342.
21. Delgado, G.E., Seijas, L.E., Mora, A.J., *J. Chem.Cryst.***2012**, 42, 968.
22. Delgado, G.E., Varela, K.N., Araque, R.V., Rodríguez, J.A., Mora, A.J.,Seijas, L.E. *Av. Quím.***2014**, **9**, 3.
23. Seijas, L.E., Almeida, R., Mora, A.J., Delgado G.E., *J. Comp.MethodsSci.Eng.***2014**, 14, 5.
24. Delgado, G.E.,Seijas, L.E., Mora, A.J., Almeida, R., González, T., *Mol.Cryst. Liq.Cryst.***2015**, 607, 192.
25. Delgado, G.E., Hernández, M., Mora, A.J., Bahsas, A., Lobaton, R., González, T.,*Mol.Cryst. Liq.Cryst.***2015**, 616, 187.
26. Delgado, G.E., Mora, A.J., Contreras, J.E., Chacón C., *PowderDiffr.***2015**, 30, 178.
27. Delgado, G.E., Rodríguez, J.A., Mora, A.J., Bruno-Colmenárez, J., Uzcátegui, J., Chacón, C.,*Mol.Cryst. Liq.Cryst.***2016**, 629, 96.
28. Spackman, M.A., Jayatilaka, D.,*CrystEngComm*, **2009**, 11, 19.
29. Sheldrick, G.M.,*ActaCryst.***2008**, A64, 112.
30. Sheldrick, G.M., *ActaCryst.* **2015**, C71, 3.
31. Turner, M.J., McKinnon, J.J., Wolff, S.K., Grimwood, D.J., Spackman, P.R., Jayatilaka, D., Spackman, M.A. CrystalExplorer17, University of Western Australia, 2017.
32. Spackman, M.A., McKinnon, J.J., *CrystEngComm*, **2002**, 4, 378.
33. Spackman, M.A., McKinnon, J.J., Jayatilaka, D., *CystEngComm*, **2008**, 10, 377.
34. Boultif, A. Louër, D., *J. App. Cryst.***2004**, 37, 724.
35. Le Bail, A., *Powder Diffr.***2015**, **20**, 316.
36. Rodriguez-Carvajal, J.: Fullprof, version 5.7, LLB, CEA-CNRS, France, 2017.
37. Groom, C. R., Allen, F. H. *Angew. Chem. Int. Ed.***2014**, **53**, 662.
38. Mackay, M.F., Duggan, B.M., Laslett, R.L., Wilshire, J.F.K., *ActaCryst.***1992**, C48, 334.
39. Casas, J.S., Castañeiras, A., Couce, D., Playá, N., Sordo, J., Varela, J.M. *Acta Cryst.***1998**, C54, 427.
40. Kitoh, S., Feng, Y., Fujinami, S., Ichitani, M., Honda, M., Kunimoto, K.K., *Acta Cryst.***2013**, E69, o1699.
41. Taniguchi, K., Okumura, H., Honda, M., Suda, M., Fujinami, S., Kuwae, A., Hanai, K., Maeda, S., Kunimoto, K.K., *X-ray Struc. Anal. Online*, **2009**, 25, 93.
42. Etter, M.C.,*Acc. Chem. Res.***1990**, 23, 120.




***Scheme 1.****Synthesis of 1-acetyl-5-(2-methylpropyl)-2-thioxo-imidazolidin-4-one (**I**)*

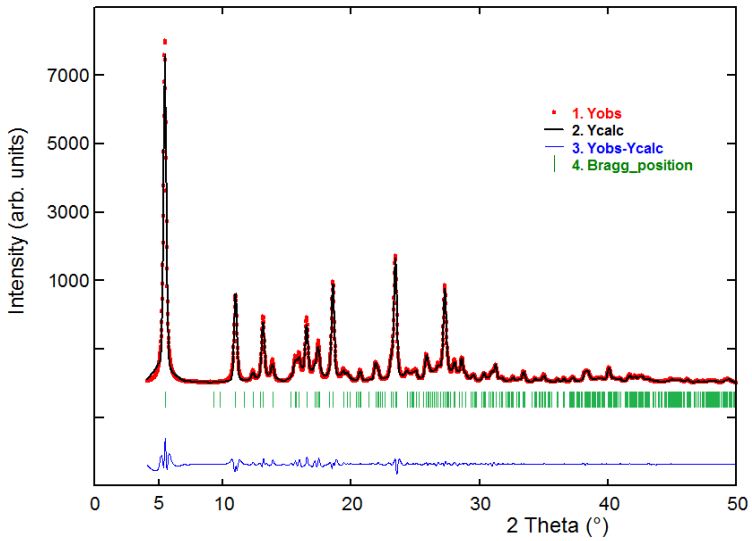



***Figure 1.*** *X-ray powder diffraction data for (**I**). The powder pattern was refined without structural model to confirm the unit cell parameters*

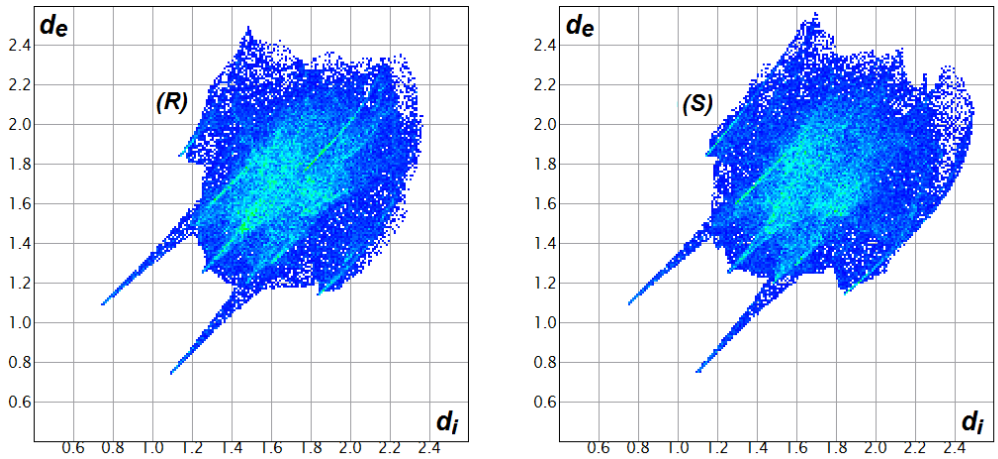



***Figure 5.****Hirshfeld fingerprint plots of the two crystallographically independent molecules (R and S) of (**I**). de is the closest external distance from a given point on the Hirshfeld surface and di is the closest internal contacts*

***Table 1.*** *Crystal data, data collection and structure refinement of* ***(I)***

| | | | |
|---|---|---|---|
| Chemical formula | $C_9H_{14}N_2O_2S$ | CCDC | 860694 |
| Formula weight | 214.28 | Radiation (MoKα) | λ = 0.71073 Å |
| Crystal system | Triclinic | μ($mm^{-1}$) | 0.27 |
| Space group | P-1 | hkl range | -1, 8; -11, 11; -18, 19 |
| a(Å) | 7.1855(4) | Reflections | |
| b(Å) | 9.7300(4) | Collected | 4921 |
| c(Å) | 16.442(1) | Unique ($R_{int}$) | 3991 (0.088) |
| α (°) | 101.13(1) | With I > 2σ(I) | 3003 |
| β(°) | 94.00(1) | Refinement method | Full-matrix ls on $F^2$ |
| γ (°) | 90.49(1) | Number of parameters | 260 |
| V(Å3) | 1125.0(1) | $R(F^2)[I > 2\sigma(I)]$ | 0.0782 |
| Z | 4 | $wR(F^2)[I > 2\sigma(I)]$ | 0.1998 |
| dx (g $cm^{-3}$) | 1.265 | Goodness of fit on $F^2$ | 1.11 |
| F(000) | 456 | Max/min Δρ (e $Å^{-3}$) | 0.73/-0.71 |

***Table 2*** *Selected geometrical parameters (Å, º) for* ***(I)***

| Molecule *R* | | Molecule *S* | |
|---|---|---|---|
| S2-C2 | 1.6340(3) | S21-C21 | 1.6480(3) |
| O4-C4 | 1.2050(4) | O41-C41 | 1.2070(4) |
| O6-C6 | 1.2130(4) | O61-C61 | 1.2190(4) |
| N1-C2 | 1.3860(4) | N11-C21 | 1.3860(4) |
| N3-C2 | 1.3770(4) | N31-C21 | 1.3650(4) |
| N3-C4 | 1.3700(4) | N31-C41 | 1.3780(4) |
| S2-C2-N1 | 131.5(2) | S21-C21-N11 | 130.8(2) |
| S2-C2-N3 | 122.8(2) | S21-C21-N31 | 122.6(2) |
| O4-C4-N3 | 125.5(3) | O41-C41-N31 | 125.8(3) |
| O4-C4-C5 | 128.2(3) | O41-C41-C51 | 127.9(3) |
| C6-N1-C2-S2 | 4.10(5) | C61-N11-C21-S21 | -6.90(5) |
| C4-N3-C2-S2 | -174.80(2) | C41-N31-C21-S21 | 176.50(2) |

***Table 3*** *Hydrogenbondsgeometry (Å, °). (D-donor; A-acceptor; H-hydrogen)*

| D--H···A | D--H | H···A | D···A | D--H···A | Symmetrycodes |
|---|---|---|---|---|---|
| N3--H3···O6 | 0.860 | 1.981(1) | 2.825(3) | 166.6 | 1+x, y, z |
| N31--H31···O61 | 0.860 | 1.988(2) | 2.834(3) | 167.7 | -1+x, y, z |