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Molecular and crystal structure characteristics of 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride and 2-phenyliminohexahydro-1,3-thiazepine

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RESEARCH ARTICLE

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ABSTRACT

The current research includes the synthesis and crystallographic characterization of 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride (HPAT) and 2-phenyliminohexahydro-1,3-thiazepine (PIT) compounds. 2-Phenylaminotetrahydro-1,3-thiazepine hydrochloride was synthesized by cyclization of 1-(4-hydroxybutyl)-3-phenylthiourea in an acidic condition. The second compound, 2-phenyliminohexahydro-1,3-thiazepine, was obtained by neutralizing 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride with sodium hydrocarbonate. Both compounds were characterized by the single-crystal X-ray diffraction method. Crystal data for $C_{11}H_{17}N_2OClS$ (HPAT): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 4.97183(14) Å, b = 15.1169(4) Å, c = 17.7376(5) Å, V = 1333.14(6) Å^3, Z = 4, μ(CuKα) = 3.859 mm^{-1}, *Dcalc* = 1.299 g/cm^3, 9243 reflections measured (7.684° ≤ 2Θ ≤ 152.042°), 2749 unique (R_{int} = 0.0314, R_{sigma} = 0.0255) which were used in all calculations. The final R_1 was 0.0351 (I > 2σ(I)) and wR_2 was 0.0911 (all data). Crystal data for $C_{11}H_{14}N_2S$ (PIT): monoclinic, space group $P2_1/n$ (no. 14), a = 9.6303(9) Å, b = 9.8938(6) Å, c = 11.5627(9) Å, β = 103.419(8)°, V = 1071.62(14) Å^3, Z = 4, μ(CuKα) = 2.357 mm^{-1}, *Dcalc* = 1.279 g/cm^3, 3938 reflections measured (10.798° ≤ 2Θ ≤ 152.328°), 2172 unique (R_{int} = 0.0288, R_{sigma} = 0.0330) that were used in all calculations. The final R_1 was 0.0431 (I > 2σ(I)) and wR_2 was 0.1219 (all data). The asymmetric unit of HPAT contains one protonated amine, one chlorine anion, and one water molecule. Chlorine anion and water molecules play the role of the bridge in chain formation along the *a*- and *b*-axis through H-bonds with N-H hydrogen atoms. Furthermore, the Hirshfeld surface analyses are performed to determine the nature of the intermolecular contacts stabilizing the crystal structures of 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride and 2-phenyliminohexahydro-1,3-thiazepine.

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1. Introduction

The carbon-bridged nitrogen atoms -NH-C(R)=N- are known as the amidine group, which occurs in many biologically active compounds [1-4]. Hydrogenated derivatives of 2-phenyl amino-1,3-thiazoline, 2-phenylamino-1,3-thiazine and 2-phenylamino-1,3-thiazepine belong to one of the classes of compounds that contain an amidine group [4,5]. These compounds have been the subject of many investigations due to the presence of amine-imine tautomeric forms and biological activities [5,6]. 1,3-Thiazepines are studied less than their five- or six-membered analogs. A series of hydrogenated 1,3-thiazepine derivatives have been obtained by Ambartsumova *et al.* [7-10]], including 2-benzyliminohexahydro-1,3-thiazepine (imine form), which was reported as an amine form (2-benzyl aminotetrahydro-1,3-thiazepine) by Olszenko-Piontkowa and Urbanski [11]. The single-crystal X-ray diffraction method plays an important role to attribute a reaction product to an imine form [8]. Furthermore, the spatial arrangement of the atoms and the conformation of the seven-membered ring, which was obtained by X-ray diffraction analysis [8] or theoretical methods [12], is of great importance for amine-imine tautomeric chemistry. But only a few compounds that include the 1,3-thiazepine ring containing (with Refcodes in CCDC [13]: BEVNEW [14], BEVNIA [14], JEPYOS [15], QIBMET [16], QIBMET01, QIBMET02, QIBMET03, QIBMET04 [17], QOZMUO [18], RENVOV [8], RENVIP [8], and YUKPIE [19]) were characterized by the single-crystal XRD method. All of these deposited structures belong to an imine form. Amine forms of 1,3-thiazepines or their salts have not been deposited in CCDC till nowadays.

The accumulated experimental data on the stereochemistry of the seven-membered ring with nitrogen and sulfur atoms can

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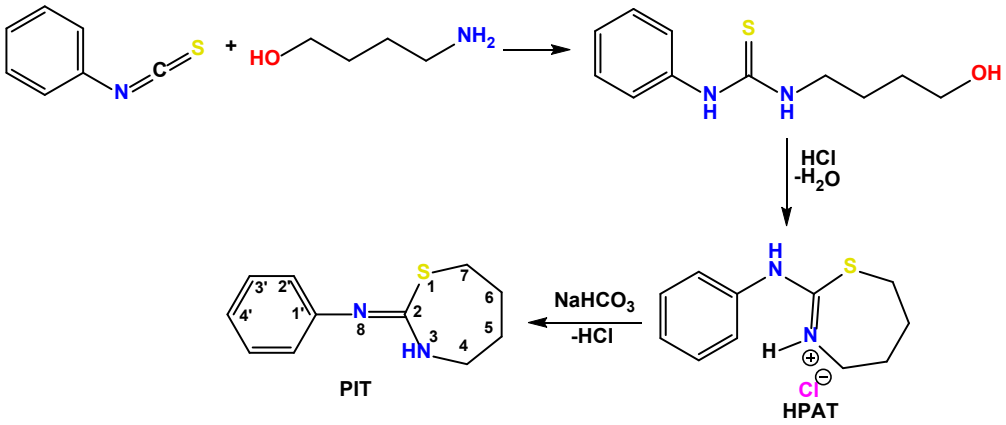

Scheme 1. Synthesis of 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride (HPAT) and 2-phenyliminohexahydro-1,3-thiazepine (PIT).

be useful in the theoretical modeling of biologically active derivatives of hydrogenated 1,3-thiazepine. Therefore, in this report, we focused on the seven-membered ring derivatives and the molecular structure of hydrochloride of 2-phenyl aminotetrahydro-1,3-thiazepine (HPAT) and 2-phenylimino hexahydro-1,3-thiazepine (PIT) was determined by the single crystal X-ray diffraction method. Furthermore, Hirshfeld surface analysis was performed to determine the nature of the intermolecular contacts that stabilize the crystal structures of HPAT and PIT.

2. Experimental

2.1. Synthesis of hydrogenated 1,3-thiazepines

2.1.1. 1-(4-Hydroxybutyl)-3-phenylthiourea

1-(4-Hydroxybutyl)-3-phenylthiourea was synthesized by the interaction of phenyl isothiocyanate (PITC) with 4-amino-1-buthanol according to known methods (Scheme 1) [5,7]. To a solution of 4-aminobutanol-1 (8.91 g, 0.1 mol) in THF (25 mL) added drop-wise of phenyl isothiocyanate (0.1 mol, 13.5 g) in THF (15 mL) with vigorous stirring at a temperature of 15 to 20 °C. The reaction mixture was left to stand for 24 hours at room temperature. Then, the obtained white solids were purified by recrystallization from aqueous ethanol mixture. Yield: 90%. The spectral characteristics were identical to the data from the literature [7].

2.1.2. Hydrochloride of 2-phenylaminotetrahydro-1,3-thiazepine (HPAT)

Cyclization of 1-(4-hydroxybutyl)-3-phenylthiourea in an acidic medium (HCl) was carried out according to the method described in references (Scheme 1) [5,7,11]. 0.05 mol of thiourea were added to 300 mL of concentrated HCl and boiled for 5 h. To the evaporated half-reaction mixture was added 100 mL of water and, upon cooling, neutralized Sodium bicarbonate (0.1 N). The oily product obtained was separated from the reaction mixture. It dissolved in chloroform and was placed in a dark place for evaporation of chloroform. The product was crystallized in chloroform within one week. The yield of HPAT is 53%.

2.1.3. 2-Phenyliminohexahydro-1,3-thiazepine (PIT)

2-Phenyliminohexahydro-1,3-thiazepine was obtained from HPAT. HPAT (3 g, 0.11 mol) was dissolved in water and neutralized with 0.01 N sodium bicarbonate (Scheme 1). The obtained white precipitates were filtered off and dissolved in chloroform. Yield: 96% (2.27 g). The suitable colorless crystals were obtained in chloroform within one week for single-crystal X-ray analysis.

2.2. Single crystal X-ray diffraction analysis

Single crystal X-ray diffraction (XRD) data were collected by using CuKα radiation (λ = 1.54184 Å) on a CCD Xcalibur Ruby diffractometer (Oxford Diffraction) at room temperature. Data reduction including multi-scan absorption correction was done using CrysAlisPRO [20]. The structure was solved by a direct method using the SHELXT program [21], integrated into the OLEX2 package [22], and refined by full-matrix least squares using the SHELXL program [23]. All non-H atoms were refined anisotropically. Hydrogen atoms were inserted at calculated positions and constrained with isotropic thermal parameters, except for hydrogen atoms of nitrogen and water molecules, which were located from a Fourier-difference map and refined isotropically. Molecular and crystal structures are plotted using XP [24] and MERCURY program packages [25].

2.3. Theoretical studies

Hirshfeld surfaces and fingerprint plots were calculated for the title compounds based on the crystallographic information file (CIF) using the CrystalExplorer program [26]. 2D fingerprint plots displayed using the standard 0.7-2.6 Å view with the d_e and d_i distance scales displayed on the graph axes. The function d_{norm} is a ratio that encloses the distances of any surface point to the nearest interior (d_i) and exterior (d_e) atoms and the van der Waals (vdW) radii of the atoms. Hirshfeld surfaces were obtained using a standard (high) surface resolution with the three-dimensional d_{norm} surfaces mapped over a fixed color scale of -0.492 (red) to 1.265 (blue). Points with a contribution to the Hirshfeld surface are colored by blue for a small contribution and by green to red for points with the greatest contributions.

3. Results and discussion

3.1. Single crystal X-ray diffraction analysis

The general reaction scheme for the preparation of hydrogenated 1,3-thiazepines is shown in Scheme 1. The main crystallographic data of both obtained products **HPAT** and **PIT** are summarized in Table 1. The molecular structure of **HPAT** and **PIT** with atom labeling is presented in Figure 1.

HPAT crystallizes in the orthorhombic $P2_12_12_1$ space group (Table 1). The asymmetric unit contains one protonated molecule, a chlorine anion, and one water molecule (Figure 1).

Table 1. Crystal data and parameters for structure refinement of **HPAT** and **PIT**.

Parameter/Compound	HPAT	PIT
Empirical formula	$C_{11}H_{17}N_2OClS$	$C_{11}H_{14}N_2S$
Formula weight (g/mol)	260.77	206.30
Temperature (K)	296(2)	293(2)
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1/n$
a, (Å)	4.97183(14)	9.6303(9)
b, (Å)	15.1169(4)	9.8938(6)
c, (Å)	17.7376(5)	11.5627(9)
β (°)	90	103.419(8)
Volume (Å^3)	1333.14(6)	1071.62(14)
Z	4	4
ρ_{calc} (g/cm^3)	1.299	1.279
μ (mm^{-1})	3.859	2.357
F(000)	552.0	440.0
Crystal size (mm^3)	0.25 × 0.22 × 0.16	0.3 × 0.25 × 0.16
Radiation	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection (°)	7.684 to 152.042	10.798 to 152.328
Index ranges	$-6 \le h \le 4, -16 \le k \le 19, -21 \le l \le 22$	$-11 \le h \le 11, -7 \le k \le 12, -14 \le l \le 10$
Reflections collected	9243	3938
Independent reflections	2749 [R_{int} = 0.0314, R_{sigma} = 0.0255]	2172 [R_{int} = 0.0288, R_{sigma} = 0.0330]
Data/restraints/parameters	2749/0/162	2172/0/132
Goodness-of-fit on F^2	1.023	1.044
Final R indexes [I≥2σ (I)]	R_1 = 0.0351, wR_2 = 0.0881	R_1 = 0.0431, wR_2 = 0.1146
Final R indexes [all data]	R_1 = 0.0387, wR_2 = 0.0911	R_1 = 0.0521, wR_2 = 0.1219
Largest diff. peak/hole (e.Å^{-3})	0.19/-0.17	0.29/-0.25
Flack parameter	0.391(7)	-
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Table 2. Bond lengths and angles for **HPAT** and **PIT**.

Compound	Atom	Atom	Length (Å)	Atom	Atom	Length (Å)
HPAT	S1	C2	1.749(3)	C6	C7	1.504(5)
	S1	C7	1.823(4)	C1'	C2'	1.381(4)
	N3	C2	1.301(4)	C1'	C6'	1.373(5)
	N3	C4	1.468(4)	C2'	C3'	1.385(4)
	N8	C2	1.326(4)	C3'	C4'	1.366(5)
	N8	C1'	1.437(4)	C4'	C5'	1.373(5)
	C4	C5	1.508(4)	C5'	C6'	1.383(5)
	C5	C6	1.520(5)			
PIT	S1	C2	1.7845(18)	C6	C7	1.512(3)
	S1	C7	1.817(2)	C1'	C2'	1.393(2)
	N3	C2	1.357(2)	C1'	C6'	1.391(3)
	N3	C4	1.461(2)	C2'	C3'	1.380(3)
	N8	C2	1.283(2)	C3'	C4'	1.376(3)
	N8	C1'	1.412(2)	C4'	C5'	1.380(3)
	C4	C5	1.505(3)	C5'	C6'	1.378(3)
	C5	C6	1.508(3)			
Compound	**Atom**	**Atom**	**Atom**	**Angle (°)**	**Atom**	**Atom**	**Atom**	**Angle (°)**
HPAT	C2	S1	C7	103.31(16)	C6	C7	S1	116.1(3)
	C2	N3	C4	125.9(3)	C2'	C1'	N8	120.5(3)
	C2	N8	C1'	125.2(2)	C6'	C1'	N8	118.7(3)
	N3	C2	S1	122.5(2)	C6'	C1'	C2'	120.7(3)
	N3	C2	N8	122.7(3)	C1'	C2'	C3'	119.0(3)
	N8	C2	S1	114.8(2)	C4'	C3'	C2'	120.6(3)
	N3	C4	C5	115.1(3)	C3'	C4'	C5'	120.0(3)
	C4	C5	C6	114.7(3)	C4'	C5'	C6'	120.3(3)
	C7	C6	C5	114.0(3)	C1'	C6'	C5'	119.4(3)
PIT	C2	S1	C7	103.79(10)	C6	C7	S1	116.07(15)
	C2	N3	C4	123.75(17)	C2'	C1'	N8	118.73(17)
	C2	N8	C1'	121.80(15)	C6'	C1'	N8	123.08(16)
	N3	C2	S1	116.24(13)	C6'	C1'	C2'	118.04(17)
	N8	C2	S1	123.03(14)	C3'	C2'	C1'	120.69(18)
	N8	C2	N3	120.68(16)	C4'	C3'	C2'	120.74(19)
	N3	C4	C5	115.07(18)	C3'	C4'	C5'	118.96(19)
	C4	C5	C6	114.40(17)	C6'	C5'	C4'	120.8(2)
	C5	C6	C7	114.35(18)	C5'	C6'	C1'	120.68(18)

The bond lengths of C2-N3 and C2-N8 were found as 1.301(4) and 1.326(4) Å, respectively (Table 2). The torsion angle of N3-C2-N9-C1′ is 14.58°. The seven-membered heterocycle has a chair conformation.

PIT crystallizes in the monoclinic $P2_1/n$ space group. Crystal data, data collection and structure refinement details are summarized in Table 1. The asymmetric unit contains one crystallographically independent molecule. The displacement ellipsoid plots and the numbering scheme for **PIT** molecule is provided in Figure 1. The bond lengths for the endocyclic and exocyclic C-N bonds found as 1.357(2) and 1.283(2) Å, respectively, indicate that in the crystal state the molecule was organized as an imine form (Table 2). The seven-membered heterocycle has a twist-chair conformation. In **PIT** molecule, S1, C2, N3, N8, and C1′ lay in the same plane with a RMS deviation of the fitted atoms of 0.023 Å and the dihedral angle between this plane and the benzene ring is 56.20(4)°. In the crystal, the intermolecular N-H···N hydrogen bonds link molecules to dimers (Figure 2). The geometry of the H-bonds is given in Table 3.

Table 3. Parameters of hydrogen bonds in the crystal for **HPAT** (Å, °) *.

D-H···A	d(D-H)	d(H···A)	d(D···A)	∠D-H···A
N3-H3···Cl1	0.92(4)	2.26(4)	3.131(3)	159(3)
N8-H···O1W	0.86	1.93	2.780(4)	168.00
O1W-H1W···Cl1^{i}	0.98(6)	2.15(6)	3.122(4)	177(5)
O1W-H2W···Cl1^{ii}	0.91(5)	2.26(5)	3.163(4)	171(4)
C2'-H2'A···Cl1^{iii}	0.93	2.80	3.712(3)	167

* Symmetry codes: (i) 1-*x*, -1/2+*y*, 3/2-*z*; (ii) -*x*, -1/2+*y*, 3/2-*z*; (iii) 1+*x*, *y*, *z*.

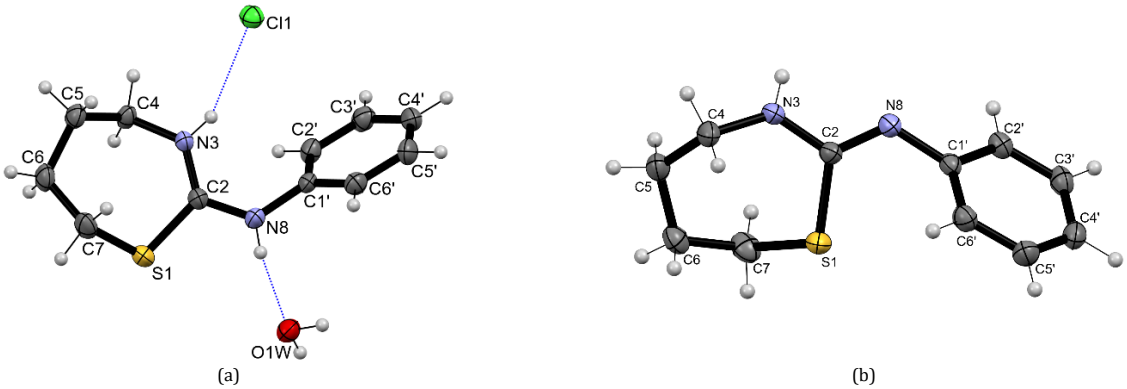

Figure 1. The molecular structure of **HPAT** (a) and **PIT** (b) with atom labelling.

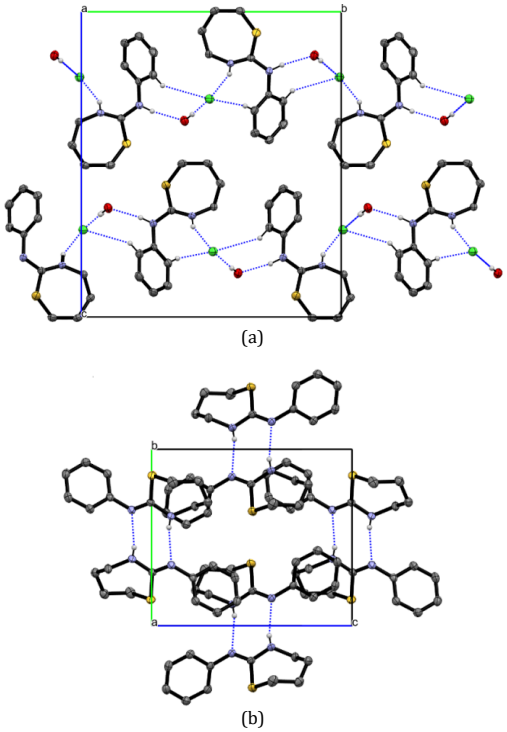

Figure 2. Intermolecular hydrogen bonding of molecules in the crystal of **HPAT** (a) and **PIT** (b).

The packing analysis of **HPAT** shows that chlorine anions and water molecules form a zigzag-shaped H-bonded chain along the *a*-axis. Protonated thiazepine molecules links to this chain through N-H···O and N-H···Cl hydrogen bonds from different sides, resulting in H-bonded layers parallel to the *ab* plane (Figure 2). The geometry of the H-bonds is given in Table 3.

3.2. Hirshfeld surface analysis

The Hirshfeld surface mapped in 3D d_{norm} [27-29] for studied compounds is given in Figure 3, where red spots represent short contacts. The longest contacts are represented by blue. The white color represents the contacts around the van der Waals radii [27,28]. The closest intermolecular interactions in the crystal of **HPAT** and **PIT** are N-H···Cl/O and N-H···N H-bonds, respectively.

According to 3D Hirshfeld surface and 2D fingerprints [30] for **HPAT** were found the main contribution of close contacts H···H (59.6%), C···H/H···C (14.3%), S···H/H···S (9.5%), Cl···H/H···Cl (7.9%), O···H/H···O (5.0%) to intermolecular stabilization in the crystal. But the contributions of other contacts including N···H/H···N (1.2%) to the Hirshfeld surface are negligible (Figure 4). In the case of **PIT**, the contribution of H···H (64.7%) and C···H/H···C (19.6%) contacts are higher relatively to the contacts of **HPAT**. In addition, N···H (8.0%) and S···H (7.4%) contacts make a significant contribution to close contacts of **PIT** (Figure 5).

(a) (b)

Figure 3. Hirshfeld surfaces of **HPAT** (a) and **PIT** (b) mapped with d_{norm}.

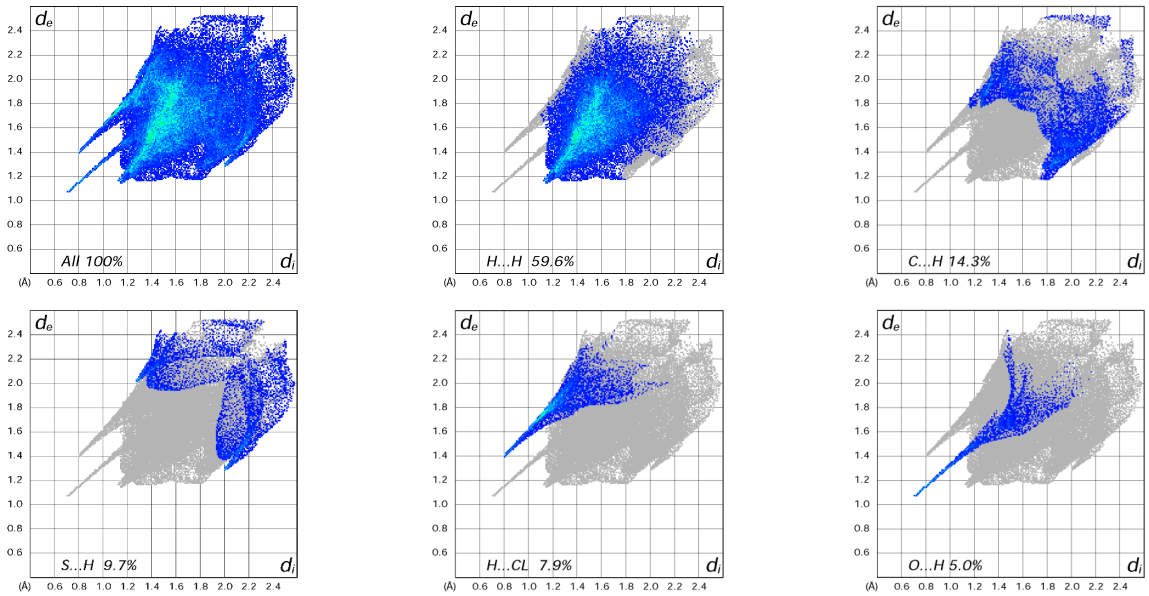

Figure 4. The 2D fingerprint plots of the **HPAT**.

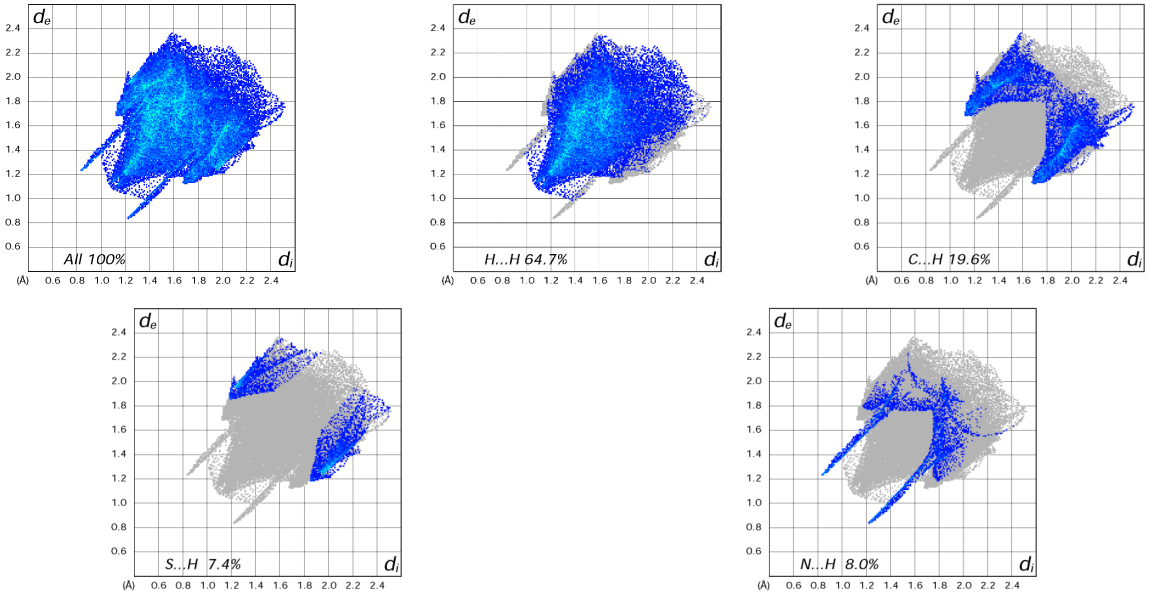

Figure 5. The 2D fingerprint plots of the **PIT**.

4. Conclusions

For the first time, 2-phenylaminotetrahydro-1,3-thiazepine hydrochloride has been obtained by cyclization of 1-(4-hydroxy butyl)-3-phenylthiourea in an acidic medium and it's structure was elucidated trough single crystal X-ray analysis. The crystal unit cell of **HPAT** contains four molecules of protonated (on N3 atom) amine tautomer, four chlorine anion, and four water molecules. Chlorine anion and water molecules play the role of a bridge connecting protonated amine molecules through the H-bond with hydrogen atoms of N3 and N8 nitrogen atoms. Neutralization efforts of the hydrochloride of the amine tautomer by sodium bicarbonate to obtain a neutral amine tautomer led to the formation of an imine tautomer. The structure of the imine form was also elucidated by X-ray analysis and it was found that in the crystal, pairs of 2-phenyl iminohexahydro-1,3-thiazepine are linked via N-H···N hydrogen bonds, forming centrosymmetric dimers. The type and main contribution of intermolecular interactions are visualized through Hirshfeld surface analysis and 2D fingerprint plots.

Supporting information

The CCDC-2203212 and 2203213 contain 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 CB2 1EZ, UK; fax: +44(0)1223-336033.

Disclosure statement

Conflict of interest: The authors declare that they have no conflict of interest.
Ethical approval: All ethical guidelines have been adhered.
Sample availability: Sample of the compounds are available from the author.

CRediT authorship contribution statement

Conceptualization: Alisher Eshimbetov, Khamid Khodjaniyazov; Methodology: Mukhriddin Umirov, Alisher Eshimbetov; Software: Jamshid Ashurov; Kambarali Turgunov; Validation: Alisher Eshimbetov; Formal Analysis: Alisher Eshimbetov; Investigation: Mukhriddin Umirov, Alisher Eshimbetov; Resources: Mukhriddin Umirov; Data Curation: Mukhriddin Umirov; Alisher Eshimbetov; Writing - Original Draft: Mukhriddin Umirov, Alisher Eshimbetov, Kambarali Turgunov; Writing - Review and Editing: Alisher Eshimbetov, Jamshid Ashurov, Khamid Khodjaniyazov; Visualization: Jamshid Ashurov, Kambarali Turgunov; Funding acquisition: Mukhriddin Umirov; Supervision: Alisher Eshimbetov; Project Administration: Jamshid Ashurov.

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References

[1]. Remko, M.; Walsh, O. A.; Richards, W. G. Ab initio and DFT study of molecular structure and tautomerism of 2-amino-2-imidazoline, 2-amino-2-oxazoline and 2-amino-2-thiazoline. *Chem. Phys. Lett.* **2001**, *336*, 156–162.
[2]. Shishkin, O. V.; Konovalova, I. S.; Zubatyuk, R. I.; Palamarchuk, G. V.; Shishkina, S. V.; Biitseva, A. V.; Rudenko, I. V.; Tkachuk, V. A.; Kornilov, M. Y.; Hordiyenko, O. V.; Leszczynski, J. Remarkably strong polarization of amidine fragment in the crystals of 1-imino-1H-isoindol-3-amine. *Struct. Chem.* **2013**, *24*, 1089–1097.
[3]. Aly, A. A.; Brase, S.; Gomaa, M. A.-M. Amidines: their synthesis, reactivity, and applications in heterocyclic synthesis. *ARKIVOC* **2018**, *2018*, 85–138.
[4]. Sondhi, S. M.; Rani, R.; Gupta, P. P.; Agrawal, S. K.; Saxena, A. K. Synthesis, anticancer, and anti-inflammatory activity evaluation of methanesulfonamide and amidine derivatives of 3,4-diaryl-2-imino-4-thiazolines. *Mol. Divers.* **2009**, *13*, 357–366.
[5]. Toldy, L. G. Biologically active heterocyclic analogs of thiourea (review). *Chem. Heterocycl. Compd. (N. Y.)* **1978**, *14*, 705–714.
[6]. Eshimbetov, A.; Adizov, S.; Kaur, I.; Reymov, A. Is it possible to differentiate between 2-phenylaminodihydro-1,3-thiazine from 2-phenyliminotetrahydro-1,3-thiazine by spectral methods? New glance to the old problem. *Eur. J. Chem.* **2021**, *12*, 77–80.
[7]. Ambartsumova, R. F.; Levkovich, M. G.; Mil'grom, E. G.; Abdullaev, N. D. 1,3-Thiazepines. 1. Synthesis and spectral properties of 2-imino hexahydro-1,3-thiazepines. *Chem. Heterocycl. Compd. (N. Y.)* **1997**, *33*, 112–117.
[8]. Ambartsumova, R. F.; Tashkhodzhaev, B.; Makhmulov, M. K. 1,3-Thiazepines: 4. Reactions of 2-iminothiazepines with methyl acrylate. Crystal and molecular structure of 2-phenylimino-3-(β-methoxy carbonylethyl)- and 2-benzyliminohexahydro-1,3-thiadiazepines. *Chem. Heterocycl. Compd. (N. Y.)* **1997**, *33*, 475–480.
[9]. Levkovich, M. G.; Abdullaev, N. D.; Ambartsumova, R. F. 1,3-Thiazepines. 5. Study of 2-Phenyl(benzyl)iminohexahydro-1,3-thiazepines and Their Derivatives by 13C Spectroscopy. *Chem. Heterocycl. Compd. (N. Y.)* **2002**, *38*, 612–615.
[10]. Kristallovich, E. L.; Eshimbetov, A. G.; Ambartsumova, R. F. 1,3-Thiazepines. 6. UV Spectroscopic and Theoretical Study of the Electronic Structures of 2-Aminotetrahydro- and 2-Iminotetrahydro-1,3-thiazepines. *Chem. Heterocycl. Compd. (N. Y.)* **2003**, *39*, 368–373.
[11]. Olszenko-Piontkowa, Z.; Urbanski, T. 1-Thia-3-azacycloheptane derivatives. *Org. Prep. Proced. Int.* **1971**, *3*, 27–32.
[12]. Levkovich, M. G.; Abdullaev, N. D.; Ambartsumova, R. F. 1,3-Thiazepines. 3.* Conformational dynamics of 2-aminotetrahydro and 2-iminohexahydro derivatives of 1,3-thiazepine. *J. Struct. Chem.* **1997**, *38*, 497–499.
[13]. Groom, C. R.; Bruno, I. J.; Lightfoot, M. P.; Ward, S. C. The Cambridge Structural Database. *Acta Crystallogr. B Struct. Sci. Cryst. Eng. Mater.* **2016**, *72*, 171–179.
[14]. Kieć-Kononowicz, K.; Karolak-Wojciechowska, J.; Michalak, B.; Pekala, E.; Schumacher, B.; Müller, C. E. Imidazo[2,1-b]thiazepines: synthesis, structure and evaluation of benzodiazepine receptor binding. *Eur. J. Med. Chem.* **2004**, *39*, 205–218.
[15]. Kieć-Kononowicz, K.; Zatorski, A.; Karolak-wojciechowska, J. Reaction of 5,5-diphenyl-2-thiohydantoin with 1,4-dibromobutane. The crystal and molecular structure of 2,3,4,5-tetrahydro-7,7-diphenylimidazo-[2,1-b]-thiazepine-8(7H)-one. *Phosphorus Sulfur Silicon Relat. Elem.* **1989**, *42*, 191–200.
[16]. Moussaif, A.; Essassi, E. M.; Pierrot, M. 2,3,4,5-Tetrahydro-1,3-thiazepino[3,2-a][1,3]benzimidazole. *Acta Crystallogr. Sect. E Struct. Rep. Online* **2001**, *57*, o364–o365.
[17]. Geng, X.; Liu, S.; Wang, W.; Qu, J.; Wang, B. Tert-amino effect-promoted rearrangement of aryl isothiocyanate: A versatile approach to benzimidazothiazepines and benzimidazothioethers. *J. Org. Chem.* **2020**, *85*, 12635–12643.
[18]. Struga, M.; Kossakowski, J.; Miroslaw, B.; Koziol, A. E.; Zimniak, A. Synthesis of new 1,3-thiazepine derivatives. *J. Heterocycl. Chem.* **2009**, *46*, 298–302.
[19]. Struga, M.; Kossakowski, J.; Koziol, A. E.; Kedzierska, E.; Fidecka, S.; La Colla, P.; Ibba, C.; Collu, G.; Sanna, G.; Secci, B.; Loddo, R. Synthesis, pharmacological and antiviral activity of 1,3-thiazepine derivatives. *Eur. J. Med. Chem.* **2009**, *44*, 4960–4969.
[20]. Agilent (2014). CrysAlis PRO. Agilent Technologies Ltd, Yarnton, Oxfordshire, England.
[21]. Sheldrick, G. M. SHELXT - integrated space-group and crystal-structure determination. *Acta Crystallogr. A Found. Adv.* **2015**, *71*, 3–8.
[22]. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* **2009**, *42*, 339–341.
[23]. Sheldrick, G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr. C Struct. Chem.* **2015**, *71*, 3–8.
[24]. Bruker, AXS Inc., "SHELXTL. Version 6.10, XP" Bruker AXS Inc., Madison, 2000.
[25]. Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T. A.; McCabe, P.; Pidcock, E.; Platings, M.; Shields, G. P.; Stevens, J. S.; Towler, M.; Wood, P. A. Mercury 4.0: from visualization to analysis, design and prediction. *J. Appl. Crystallogr.* **2020**, *53*, 226–235.
[26]. Spackman, P. R.; Turner, M. J.; McKinnon, J. J.; Wolff, S. K.; Grimwood, D. J.; Jayatilaka, D.; Spackman, M. A. CrystalExplorer: a program for

Hirshfeld surface analysis, visualization and quantitative analysis of molecular crystals. *J. Appl. Crystallogr.* **2021**, *54*, 1006–1011.
[27]. Spackman, M. A.; McKinnon, J. J.; Jayatilaka, D. Electrostatic potentials mapped on Hirshfeld surfaces provide direct insight into intermolecular interactions in crystals. *CrystEngComm* **2008**, *10*, 377–388.
[28]. Spackman, M. A.; Jayatilaka, D. Hirshfeld surface analysis. *CrystEngComm* **2009**, *11*, 19–32.
[29]. Minaeva, V. A.; Karaush-Karmazin, N. N.; Panchenko, A. A.; Heleveria, D. N.; Minaev, B. F. Hirshfeld surfaces analysis and DFT study of the structure and IR spectrum of N-ethyl-2-amino-1-(4-chlorophenyl) propan-1-one (4-CEC) hydrochloride. *Comput. Theor. Chem.* **2021**, *1205*, 113455.
[30]. Spackman, M. A.; McKinnon, J. J. Fingerprinting intermolecular interactions in molecular crystals. *CrystEngComm* **2002**, *4*, 378–392.