CRYSTAL STRUCTURE AND HIRSHFELD SURFACE ANALYSIS OF (E)-5-PHENYL-3-((4-(TRIFLUOROMETHYL)BENZYLIDENE)AMINO)THIAZOLIDIN-2-IMINIUM BROMIDE

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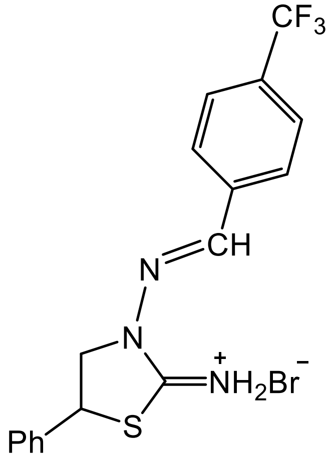
ABSTRACT

In the cation of the title salt, the central thiazolidine ring adopts an envelope conformation. In the crystal N-H ··· Br hydrogen bonds link the components into a bi-dimensional network with the cations and anions stacked parallel to plane (101). The molecular structure shows several positional disorders over -CF_3 and thiazolidine fragments and these were modeled. The weak intermolecular interactions in the crystal structure are mainly constituted by H ··· F, H ··· π and H ··· Br. Hirshfeld surface analysis were used to verify the contributions of the different intermolecular interactions.

INTRODUCTION

Schiff bases and related N-ligands attract considerable interest and play an important role in the development of the chemistry of chelate systems as potential ligands towards a large number of metal ions[1–8]. Growing interest in the synthesis of such a type of compounds are due to their potential application as catalyst in many organic transformations[9–12] and diverse useful properties, such as solvatochromism[13], molecular switching[14,15], crystal engineering[16], etc. Noncovalent interactions (hydrogen, aerogen, halogen, chalcogen, pnictogen, tetrel and icosagen bonds, as well as cation-*π*, anion-*π*, lone pair-*π*, *π*-*π* stacking, agostic, pseudo-agostic, anagostic, dispersion-driven, lipophilic, etc.) concern weak forces of attraction formed between different molecules (intermolecular) or fragments of the same molecule (intramolecular). While these weak interactions were firstly taken into consideration by van der Waals in 1873 [17], the understanding of their crucial role in synthesis, catalysis, crystal engineering, pharmaceutical design, molecular biology, molecular recognition, materials, etc. has been increasingly explored in the last few decades.

Herein we found strong charge assisted hydrogen bond and halogen bonding in (*E*)-5-phenyl-3-((4-(trifluoromethyl)benzylidene)amino)thiazolidin-2-iminium bromide (scheme 1).



Scheme 1.

EXPERIMENTAL

NMR spectra were recorded at room temperature on a Bruker Avance II + 300 (UltraShield™ Magnet) spectrometer operating at 300.130 and 75.468 MHz for proton and carbon-13, respectively. All NMR spectra are reported in parts per million (ppm, d) relative to tetramethylsilane (Me_4Si) for ^1H and ^{13}C NMR spectra, with the residual solvent proton and carbon resonances used as internal standards. Coupling constants (J) are reported in Hertz (Hz), and integrations are reported as number of protons.

The following abbreviations are used to describe peak patterns: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. ^1H and ^{13}C NMR chemical shift assignments are supported by data obtained from ^1H–^1H COSY, ^1H–^{13}C HMQC, and ^1H–^{13}C. Electrospray mass spectra (ESI-MS) were run with an ion-trap instrument (Varian 500-MS LC Ion Trap Mass Spectrometer) equipped with an electrospray ion source. For electrospray ionization, the drying gas and flow rate were optimized according to the particular sample with 35 p.s.i. nebulizer pressure. Scanning was performed from *m/z* 0 to 1100 in methanol solution. The compounds were observed in the positive mode (capillary voltage = 80–105 V).

For the molecular structure of title compound, H atoms were located in the difference Fourier map, refined with fixed individual displacement parameters, using a riding model with C—H distances of 0.93 Å (for aromatic rings), 0.92 Å; 0.96 Å (for CH_3, CH_2), with U(H) values of $1.2U_{eq}$(C, N) (for CH in aromatic rings and -NH_2^+), and $1.5U_{eq}$(C, O) (for CH_3 and -OH). Solvent molecules were restrained using Rigid body (RIGU) restrains (O1S, C1S). trifluoromethyl moiety (-CF_3) was restrained using SADI. All sigma for 1-2 distances of 0.004 Å and sigma for 1-3 distances of 0.004 Å. Finally the several disordered -CF_3, was treated with FVAR and SUMP.

X-ray diffraction patterns of title compound were collected using a Bruker SMART APEX-II CCD area detector equipped with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) at room temperature. The diffraction frames were integrated using the APEX3 package[18]. The structure of were solved by intrinsic phasing[19] using the OLEX 2 program[20].

The structure was then refined with full-matrix least-square methods based on F^2 (*SHELXL-2014*)[19]. For $C_{14}H_8BrCl_2FN_2$, non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were included in their calculated positions, assigned fixed isotropic thermal parameters and constrained to ride on their parent atoms. A summary of the details about crystal data, collection parameters and refinement are documented in Table 1, and additional crystallographic details are in the CIF files. ORTEP views were drawn using OLEX2 software[20]. CCDC 1912059 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.as.uk/data_request/cif.

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Table 1. Crystal data parameters for title compound.

Empirical Formula	$C_{18}H_{21}BrF_3N_3O_2S$
Formula mass, g mol^{-1}	480.35
Collection T, K	296.15
crystal system	monoclinic
space group	$P2_1/n$
a (Å)	5.7935(3)
b (Å)	11.6768(9)
c (Å)	31.310(2)
β (°)	95.259(4)
V (Å^3)	2109.2(2)
Z	4
ρ_{calcd} (gcm^{-3})	1.513
Crystal size (mm)	0.52 × 0.31 × 0.17
F(000)	976.0
abs coeff (mm^{-1})	2.092
2θ range (°)	2.612 – 56.186
range h,k,l	-7/7, -14/15, -41/41
No. total refl.	16972
No. unique refl.	5122 [R_{int} = 0.0504, R_{sigma} = 0.0613]
Comp. θ_{max} (%)	99.5/28.09
Data/Restraints/Parameters	5122/41/279
Final R [$I>2\sigma(I)$]	R_1 = 0.0783, wR_2 = 0.1938
R indices (all data)	R_1 = 0.1057, wR_2 = 0.2136
Goodness of fit / F^2	1.132
Largest diff. Peak/hole (eÅ^{-3})	1.52/-0.86

To the solution of 1 mmol of 3-amino-5-phenylthiazolidin-2-iminium bromide in 20 mL ethanol was added 1 mmol of 4-(trifluoromethyl)benzaldehyde and refluxed for 2 hours. Then the reaction mixture was cooled down. Reaction products was precipitated from reaction mixture as a colorless single crystals, collected by filtration and washed with cold acetone.Yield 73%. Mp 231ºC. Anal. Calcd. for $C_{17}H_{15}BrF_3N_3S$ (*Mr* =430.29): C, 47.45; H, 3.51; N, 9.77. Found: C, 47.40; H, 3.48; N, 9.71 %. ^{1}H NMR (300MHz, DMSO-*d*$_6$): 4.58 (k, 1H, CH_2, $^3J_{H-H}$=6.6); 4,89 (t, 1H, CH_2, $^3J_{H-H}$=8.4); 5.60 (t, 1H, CH-Ar, $^3J_{H-H}$=7.5); 7.39-8.29 (m, 9H, 9Ar-H); 8.51 (s, 1H, CH=); 10.51 (s, 1H, NH=). ^{13}C NMR(75MHz, DMSO-*d*$_6$): 45.45, 56.03, 125.74, 125.80, 127.86, 128.95, 129.15, 129.22, 130.72, 131.14, 136.85, 137.50, 149.54, 168.62. MS (ESI), *m/z*: 350.38 $[C_{17}H_{15}F_3N_3S]^+$ and 79.88 Br^-.

RESULTS AND DISCUSSION.

The cation structure corresponds to the *E* isomer in the solid state. All the distances and angles are normal[21,22]. The bond lengths range between measured C-C and C=N values for single and double bonds in C4-C5, C5-N1 and N1-N2 are slightly larger than the reported for similar organic compounds[23–25], depicted a potential electronic disconnection between the rings in the cation of the title compound.

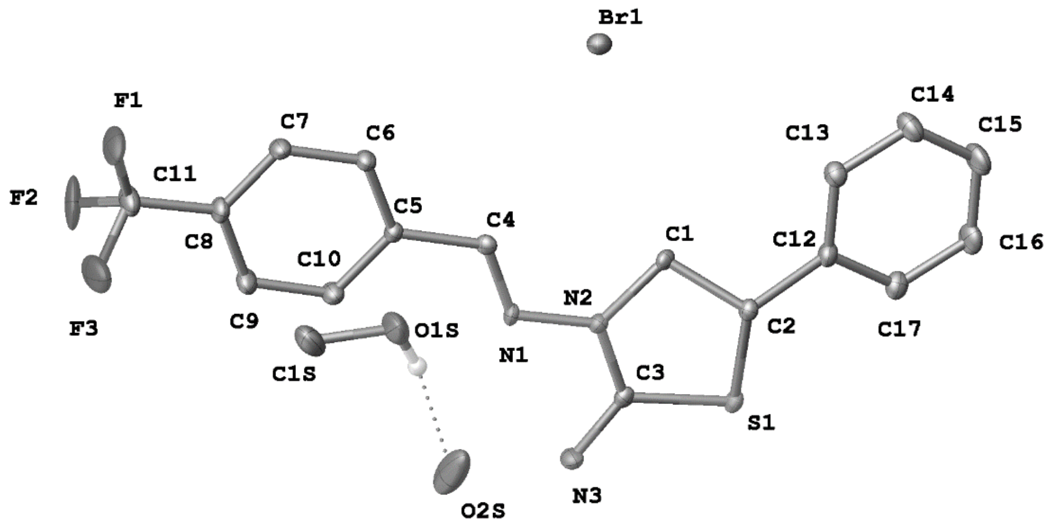

Figure 1. ORTEP plot of the title compound. Thermal ellipsoid was drawn with 30% of probability. Some hydrogen atoms were omitted for sake.

In the cation of the title salt, the central thiazolidine ring (S1/N2/C1-C3) adopts an envelope conformation with puckering parameters 0.300(6)Å, and φ(2)= 325,1(12)°. The dihedral angle between the mean plane of the central thiazolidine ring and the (4-trifluoromethyl)benzylidene ring (C5-C10) is 0.4(3) while this plane make a angle 10(2)° with the phenyl ring. The N2-N1-C4-C5 bridge that links the thiazolidine and (4-trifluoromethyl)benzylidene ring is 0.40 (3)° (see tables 3 and 4).

Table 2. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for title compound. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atoms	*x*	*y*	*z*	U(eq)
Br1	14384.5(10)	2642.6(5)	7630.0(2)	31.7(2)
S1	5698(2)	5952.5(13)	7912.1(4)	28.4(3)
F1A	13725(9)	2291(6)	5137.4(16)	72(2)
F2A	9940(40)	1910(20)	4957(6)	92(6)
F3A	11190(20)	3418(9)	4903(2)	97(4)
F1B	13110(80)	3170(50)	5005(14)	72(2)
F2B	9970(50)	2870(30)	4861(8)	97(4)
F3B	10770(40)	1435(13)	5094(5)	92(6)
O1S	4010(20)	6087(10)	6154(2)	158(6)
N1	8072(8)	4562(4)	6923.8(13)	24.0(10)
N2	7800(8)	4922(4)	7335.3(15)	24.8(10)
N3	4486(9)	5894(5)	7069.8(16)	35.7(12)
C1	9231(9)	4612(5)	7724.9(17)	24.5(11)
C3	5958(9)	5579(5)	7384.4(17)	25.6(11)
C4	9802(10)	3931(5)	6872.6(18)	26.0(11)
C5	10177(9)	3531(5)	6437.9(16)	25.2(11)
C6	12186(10)	2943(5)	6368.8(18)	31.9(13)
C7	12622(11)	2597(6)	5964.3(19)	35.2(14)
C8	11035(11)	2845(6)	5616.9(18)	38.1(15)
C9	8995(11)	3414(6)	5682.1(19)	40.3(16)
C10	8574(11)	3770(6)	6086.6(19)	37.7(15)
C11	11509(12)	2527(7)	5183(2)	55(2)
C12	9042(10)	5043(6)	8521.8(18)	35.1(14)
C13	11095(10)	4464(6)	8637.2(18)	35.9(14)
C14	11758(12)	4214(7)	9060(2)	49.8(19)
C15	10333(14)	4513(8)	9372(2)	59(2)
C16	8294(13)	5090(7)	9259(2)	49.4(19)
C17	7633(11)	5337(6)	8841.2(19)	39.4(15)
C2A	8686(13)	5497(7)	8052(2)	25.9(15)
C2B	7620(30)	4718(18)	8105(6)	25.9(15)
C1S	3780(20)	5914(9)	5728(3)	88(4)
O2S	9430(30)	7111(8)	6313(3)	169(6)

Table 3. Bond Angles for the title compound.

Atoms			Angle/°	Atoms			Angle/°
C3	S1	C2A	89.5(3)	F2A	C11	F3A	91.6(13)
C3	S1	C2B	90.7(6)	F2A	C11	C8	117.5(11)
C4	N1	N2	117.1(5)	F3A	C11	C8	112.2(7)
N1	N2	C1	127.0(4)	F1B	C11	F3B	131(2)
C3	N2	N1	116.4(4)	F1B	C11	C8	116(2)
C3	N2	C1	116.5(4)	F2B	C11	F1B	87.5(19)
N2	C1	C2A	105.1(5)	F2B	C11	F3B	87.3(17)
N2	C1	C2B	106.3(8)	F2B	C11	C8	116.8(15)
N2	C3	S1	113.3(4)	F3B	C11	C8	110.2(9)
N3	C3	S1	123.1(4)	C13	C12	C17	118.6(6)
N3	C3	N2	123.6(5)	C13	C12	C2A	116.6(5)
N1	C4	C5	119.1(5)	C13	C12	C2B	118.9(9)
C6	C5	C4	119.9(5)	C17	C12	C2A	124.0(6)
C6	C5	C10	118.8(5)	C17	C12	C2B	111.8(9)
C10	C5	C4	121.3(5)	C14	C13	C12	120.8(6)
C7	C6	C5	121.2(5)	C13	C14	C15	119.6(6)
C6	C7	C8	119.7(5)	C16	C15	C14	119.8(6)
C7	C8	C11	120.6(6)	C17	C16	C15	120.7(6)
C9	C8	C7	119.8(5)	C16	C17	C12	120.5(6)
C9	C8	C11	119.6(6)	C1	C2A	S1	106.9(5)
C10	C9	C8	120.4(5)	C1	C2A	C12	113.0(6)
C9	C10	C5	120.1(5)	C12	C2A	S1	111.4(5)
F1A	C11	F3A	99.4(7)	C1	C2B	S1	101.0(10)
F1A	C11	C8	114.7(6)	C12	C2B	S1	109.9(11)
F2A	C11	F1A	116.9(13)	C12	C2B	C1	110.8(12)

Table 4. Bond Lengths for the title compound

Atoms		Length/Å	Atoms		Length/Å
S1	C3	1.729(5)	C4	C5	1.474(7)
S1	C2A	1.826(8)	C5	C6	1.386(7)
S1	C2B	1.89(2)	C5	C10	1.401(8)
F1A	C11	1.334(8)	C6	C7	1.375(8)
F2A	C11	1.316(12)	C7	C8	1.389(8)
F3A	C11	1.362(9)	C8	C9	1.388(8)
F1B	C11	1.356(16)	C8	C11	1.458(7)
F2B	C11	1.347(14)	C9	C10	1.376(8)
F3B	C11	1.366(12)	C12	C13	1.387(8)
O1S	C1S	1.344(11)	C12	C17	1.391(8)
N1	N2	1.378(6)	C12	C2A	1.560(9)
N1	C4	1.266(7)	C12	C2B	1.53(2)
N2	C1	1.456(7)	C13	C14	1.374(8)
N2	C3	1.335(7)	C14	C15	1.381(9)
N3	C3	1.296(7)	C15	C16	1.377(10)
C1	C2A	1.508(9)	C16	C17	1.359(8)
C1	C2B	1.581(19)			

In the crystal N-H···Br hydrogen bonds link the components into a bi-dimensional network with the cations and anions stacked parallel to plane 101. The weak interactions are mainly constituted by H···F, H···π and H···Br. Moreover, In crystal structure it is found strong charge assisted hydrogen-halogen bonding and, intermolecular hydrogen-π bonding interaction along to [010] direction with 2.40 Å (Figure 2 and table 5)

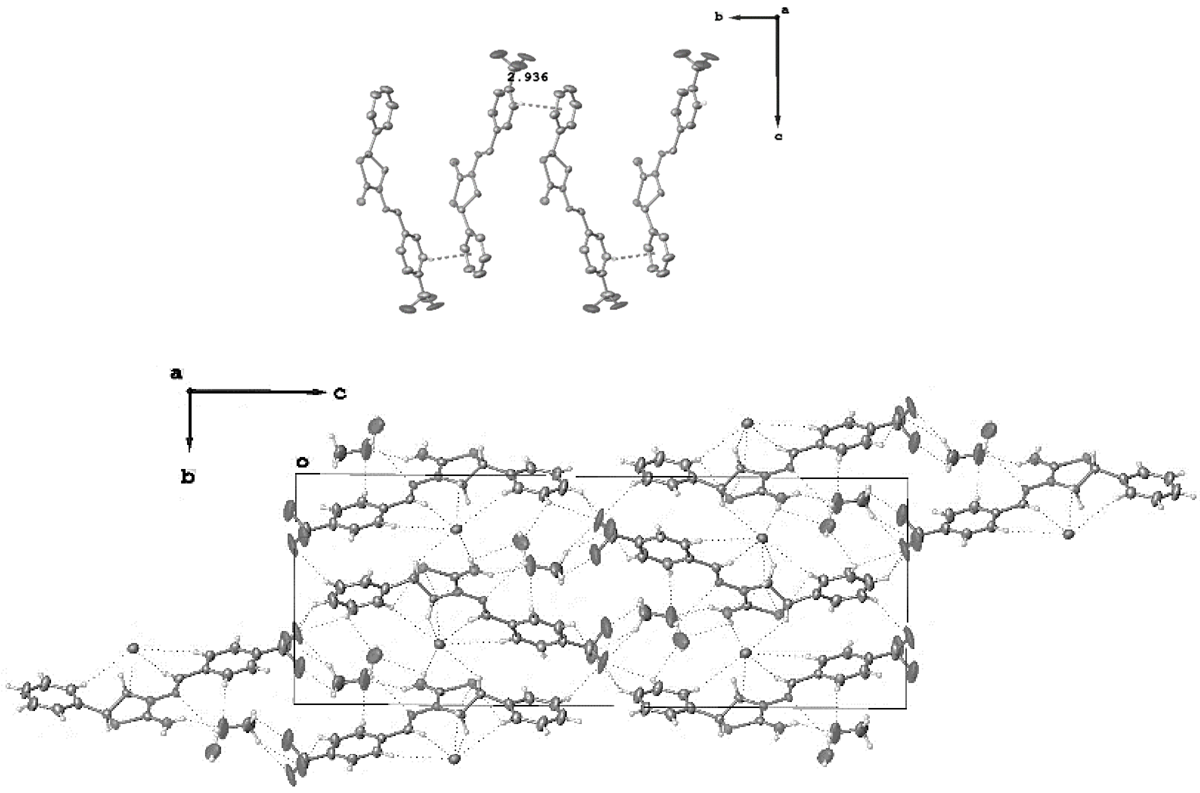

Figure 2. Non-covalent interactions in the crystal structure of the title compound.

Table 5. Hydrogen Bonds for Gul7.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
O1S	H1S	O2S[1]	0.84	2.21	2.991(16)	154.8
N3	H3A	O1S	0.88	2.10	2.863(8)	144.7

[1]-1+X,+Y,+Z

A Hirshfeld surface analysis was conducted to verify the contributions of the different intermolecular interactions. This analysis was used to investigate the presence of hydrogen bonds and intermolecular interactions in the crystal structure. The Hirshfeld surface analysis [26] was generated by CrystalExplorer 17.5 [27] and comprised d_{norm} surface plots and 2D (two-dimensional) fingerprint plots [28]. The plots of the Hirshfeld surface confirms the presence of the non-covalent interaction described below (Figure 3.), taking account the several positional disorder in the molecular structure

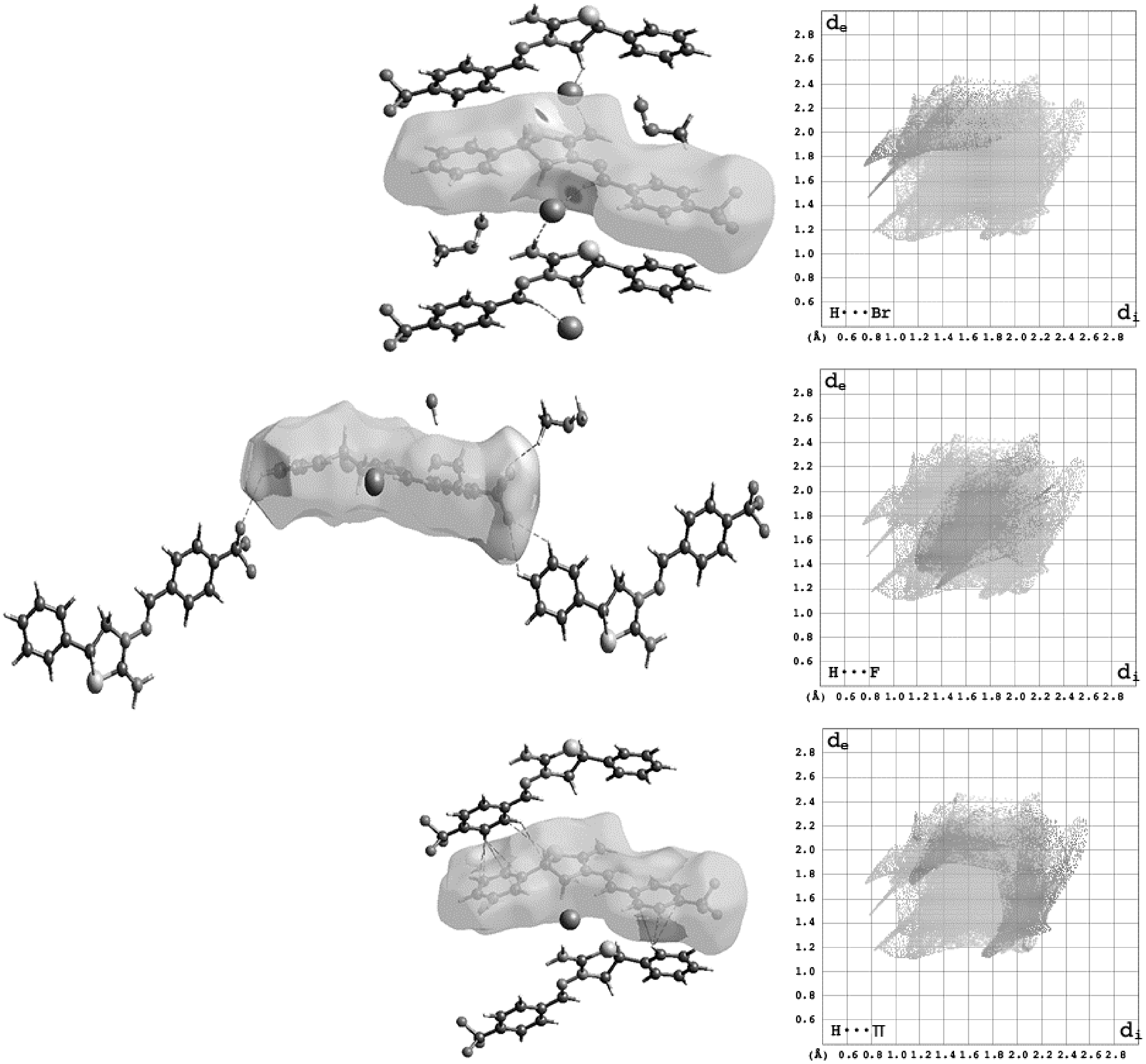

Figure 3. The two-dimensional fingerprint plots of the title compound [d_e and d_i represent the distances from a point on the Hirshfeld surface to the nearest atoms outside (external) and inside (internal) the surface, respectively].

Table 6. Contributions of interatomic contacts to the Hirshfeld surface for the title compound*.

Contact	**Contribution (%)**
Br···H	6.8%
Br···N	0.9%
Br···C	0.7%
F···F	0.5%
F···O	0.1%
F···H	24.5%
F···C	1.0%
O···H	2.9%
O···C	0.3%
H···H	32.8%
H···N	3.8%
H···C (π – H)	19.3%

*Reciprocal contacts

The weak intermolecular interactions are mainly constituted by H···F, H···π and H···Br, with a contribution of 24.5, 19.3 and 6.8%, respectively. Where the reciprocal contacts appear as a wide stain for H···F, with $d_e + d_i \simeq 2.8$ Å, for H···Br as a sharp spike with $d_e + d_i \simeq 2.3$ Å and, π ···H as asymmetrical wings with $d_e + d_i \simeq 3.0.$ Å, according to the interaction depicted in figure 2. This type of weak interactions are also observed in isostructural compounds recently reported[23–25].

CONCLUSIONS.

In this study we offer the report of synthesis, characterization and structural studies of the title compounds, showing the *E* isomer in the solid state. The weaks intermolecular interactions, were successfully verified with Hirshfeld surface analyses, being mainly constituted by H···F, H···π and H···Br, with a contribution of 24.5, 19.3 and 6.8%, respectively. The chemistry of this compound allow postulate as a good candidate for several applications such as potential biological, pharmacological and analytical applications, moreover heterocyclic amines are also widely used in the synthesis of Schiff bases, which provide different kinds of noncovalent interactions.

ACKNOWLEDGEMENTS.

Ali Khalilov thankful to Baku State University for the "50+50" individual grant support in this work. Iván Brito, Alejandro Cárdenas and Jonathan Cisterna, thank to Universidad de Antofagasta for purchase license for the Cambridge Structural Database and for the financial support. Jonathan Cisterna acknowledge to Universidad de Antofagasta for postdoctoral fellowship.

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