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ORIGINAL ARTICLE

Synthesis and crystal structure analysis of 2-(4-fluorobenzyl)-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole and its chlorophenyl derivative

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KEYWORDS

Imidazo[2,1-*b*][1,3,4]thiadiazole derivative;
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Weak interactions;
C–H···N;
C–H···F;
π–π Interactions

Abstract Preparations of 2-(4-fluorobenzyl)-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole (**3a**) and its chlorophenyl derivative (**3b**) are described. Preliminary analysis was done spectroscopically by means of ^{1}H NMR, ^{13}C NMR spectra, mass spectra and elemental analyses. Further the structures were confirmed by X-ray crystal structure analyses. The compound (**3a**) has crystallized in a triclinic P-1 space group with three independent molecules in the asymmetric unit, while the compound (**3b**) belongs to $P2_1/c$ space group with one molecule in the asymmetric unit. The molecule (**3b**) differs from molecule (**3a**) by the presence of chlorine substituent. Additionally, the imidazo-thiadiazole entity is as usual planar. Intramolecular C–H···N hydrogen bonding between the imidazole and the phenyl ring of the molecule can be observed in (**3a**) & (**3b**). The molecules of (**3a**) are linked into two dimensional supramolecular hexagonal hydrogen bonded network sustained by C–H···F interaction, while those of (**3b**) are linked by bifurcated C–H···N interactions. Further, the molecular packing of both the compounds is stabilized by π–π stacking interactions between the benzene and imidazo-thiadiazole ring systems.

1. Introduction

A large number of imidazo[2,1-*b*][1,3,4]thiadiazole derivatives have been reported to possess diverse medicinal properties which can be classified as anthelmintic, antimicrobial, anti-inflammatory, antipyretic, analgesic and they also have other characteristics of therapeutic significance (Khazi et al., 2004; Palagiano et al., 1995). 1,3,4-Thiadiazoles are known for their promising biological and pharmacological activities, possibly due to the presence of pharmacophoric isothioamide (S–C═N–) unit (Banu et al., 2010) in the thiadiazole nucleus. Secondly, the thiadiazole ring is bioisosteric with the thiazole moiety of the novel broad spectrum anthelmintic tetramisole

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(Kumar et al., 2010). Some thiadiazole derivatives are reported to possess anti-cancer properties (Sanff et al., 2004; Rzeski et al., 2007). They appeared to be the most feasible route to fused imidazo[2,1-*b*][1,3,4] thiadiazole rings of interest in potential applications (Amery et al., 1984).

Apart from this, fluorinated compounds in general and fluorinated heterocyclic compounds in particular, are the focus of much interest in modern medicinal chemistry. In other classes of antitumour compounds, e.g. the anthracycline antibiotics (Miller and Stoodley, 2010), the substitution of a hydrogen atom for a fluorine atom in the tetracyclic ring system was found to possess better antitumour properties (Animati et al., 1996).

Moreover the presence of a fluoro substituent in the molecule enhances its biological activity. Accumulation of fluorine (Strunecka et al., 2004) on carbon leads to increased oxidative and thermal stability. Further it leads to increased lipid solubility which enhances the rate of absorption and transport of the drug *in vivo*. These findings prompted the synthesis of the title compounds. A single crystal X-ray diffraction analysis was carried out to establish the crystal structure and to understand the self-aggregation in terms of possible intermolecular interactions.

In the course of our structural studies of the family of imidazo-thiadiazole derivatives, we report here the structures of two such compounds, namely 2-(4-fluorobenzyl)-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole and its 6-(4-chlorophenyl) derivative. The syntheses of these compounds were followed by measurement of their analytical data and subsequent spectroscopic analyses using ^{1}H NMR, ^{13}C NMR spectra, mass spectra and elemental analyses techniques to confirm the presence of the supposed ring systems, presence of fluoro and chloro substituents as well as the signals for the existence of various protons. A single crystal X-ray diffraction analysis was carried out for the two compounds in order to establish the crystal as well as molecular structures and to understand the self-aggregation in terms of possible intermolecular interactions. The analyses revealed structural features such as the orthogonal orientation of the fluorobenzyl group to the rest of the molecule, presence of various intermolecular interactions involving the hexagonal hydrogen bond network and π–π interactions.

2. Experimental

2.1. Materials

All reagents were obtained from commercial sources. Solvents were dried and purified with known conventional methods.

2.2. Analytical methods

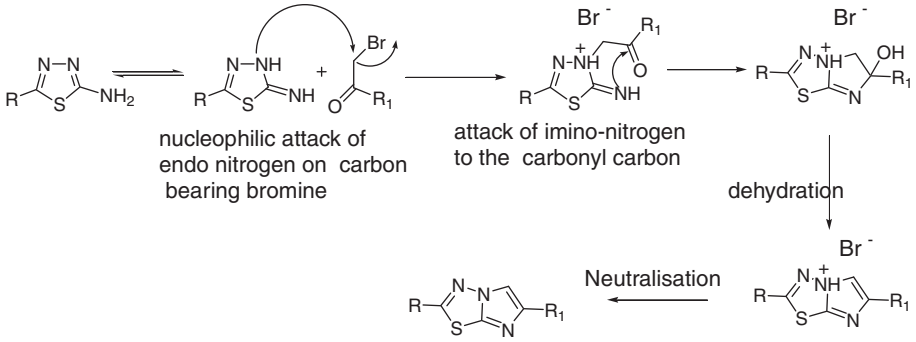
The melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded as KBr discs using a Nicolet FT-IR 410 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian RXZ-300 MHz spectrometer using TMS as internal reference compound. C, H and N were estimated on a Heraus CHN rapid analyzer at Karnatak University, Dharwad, India. The title compounds were prepared following the procedure given below and as shown in Scheme 1.

2.3. Procedure for the preparation of 2-(4-fluorobenzyl)-6-phenylimidazo[2,1-b][1,3,4]thiadiazole (**3a**) and its chlorophenyl derivative (**3b**)

A mixture of 5-(4-fluorobenzyl)-1,3,4-thiadiazol-2-amine (**1**) (Khazi et al., 2004) (2.69 g, 0.01 mol) and phenacyl bromide (**2a**) (0.01 mol) was refluxed in dry ethanol for 12 h. The excess of solvent was distilled off and the solid hydrobromide salt that separated was collected by filtration, suspended in water and neutralized by aqueous sodium carbonate solution to get the free base (**3a**). It was filtered, washed with water, dried and recrystallized from ethyl acetate to afford white needles with good yield of 75% (2.98 g).

The same procedure was followed to obtain (**3b**) wherein (**1**) was treated with *p*-chloro phenacyl bromide (**2b**). The crystals of (**3b**) were obtained by recrystallization using ethanol solvent. Yield 70% (3.08 g).

2.3.1. Mechanism



2.3.2. 2-(4-Fluorobenzyl)-6-phenylimidazo[2,1-b][1,3,4]-thiadiazole (**3a**)

Brown crystalline Solid (ethanol + dioxan), yield 75%, m.p. 168–170 °C; IR (KBr) ν cm^{-1}: 3124 (=CH), 2923, 2853 (–CH), 1602, 1507 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.29 (s, 2H, CH_2), 7.06–7.44 (m, 7H, Ar–H), 7.83 (d, J = 7.2 Hz, 2H, Ar–H), 7.98 (s, 1H, C_5–H, imidazole). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13C NMR (75 MHz, $CDCl_3$) δ: 37.8 (–CH_2–), 109.6–164.4 (C of imidazo-thiadiazole and 2 Ars), MS (m/z): 309. Anal. calcd. for $C_{17}H_{12}FN_3S$: C, 66.01; H, 3.88; N, 13.59. Found: C, 66.10; H, 3.82; N, 13.62%.

2.3.3. 6-(4-Chlorophenyl)-2-(4-fluorobenzyl)imidazo[2,1-b][1,3,4]thiadiazole (**3b**)

Shining white needles (ethanol + dioxan), yield 70%, m.p. 173–175 °C; IR (KBr) ν cm^{-1}: 3016, 2859, 2817, 1603, 1504;

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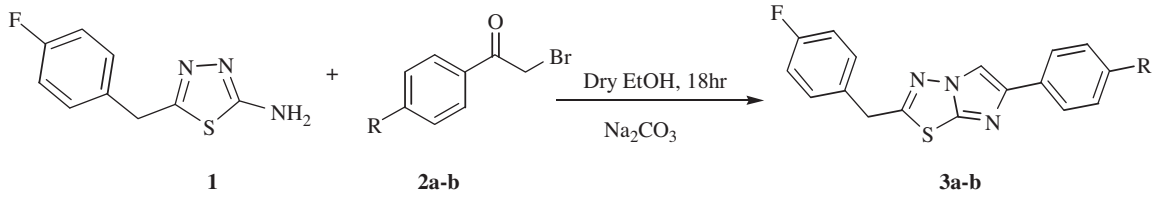

1 **2a-b** **3a-b**

a, R = H; **b,** R = Cl

Scheme 1 Syntheses of compounds **3a** and **3b**.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.29 (s, 2H, CH_2), 7.05–7.42 (m, 6H, Ar–H), 7.64 (d, J = 7.3 Hz, 2H, Ar–H), 7.96 (s, 1H, C_5–H, imidazole). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13C NMR (75 MHz, $CDCl_3$) δ: 37.8 (–CH_2–), 109.6–164.4 (C of imidazo-thiadiazole and 2 Ars), MS (m/z): 343. Anal. calcd. for $C_{17}H_{11}FClN_3S$: C, 59.47; H, 3.20; N, 20.58. Found: C, 59.28; H, 3.24; N, 20.51%.

3. X-ray diffraction analysis

The X-ray diffraction data, for both compound (**3a**) and compound (**3b**) were collected on a Bruker Smart CCD Area Detector System at I.I.Sc., Bangalore, using MoKα (0.71073 Å) radiation for the crystal. The data were reduced using SAINTPLUS (Bruker, 1998). The structure was solved by direct methods using SHELXS97 (Sheldrick, 2008) and difference Fourier synthesis using SHELXL97 (Sheldrick, 2008). The positions and anisotropic displacement parameters of all non-hydrogen atoms were included in the full-matrix least-square refinement using SHELXL97 (Sheldrick, 2008) and the procedures were carried out for a few cycles until convergence was reached. The H atoms were placed at calculated positions in the riding model approximation (C–H 0.93 Å); their temperature factors were set to 1.2 times those of the equivalent isotropic temperature factors of the parent atoms. All other non-H atoms were refined anisotropically. Molecular diagrams were generated using ORTEP (Farrugia, 1997). The mean plane calculation was done using the program PARST (Nardelli, 2010).

*3.1. Compound (**3a**)*

Intensity data were collected up to a maximum of 27.00° for the compound in the ω–ϕ scan mode. A total of 13113 reflections were collected, resulting in 9234 independent reflections of which the number of reflections satisfying $I > 2\ \sigma(I)$ criteria were 7000. These were treated as observed. The R factor for observed data finally converged to R = 0.0857 with wR_2 = 0.2363 in the compound. The maximum and minimum values of residual electron density were 2.870 and −0.687 e Å^{-3}.

*3.2. Compound (**3b**)*

Intensity data were collected up to a maximum of 27.00° for the compound in the ω–ϕ scan mode. A total of 8553 reflections were collected, resulting in 3238 independent reflections of which the number of reflections satisfying $I > 2\ \sigma(I)$ criteria were 2307. These were treated as observed. The R factor for observed data finally converged to R = 0.0540 with wR_2 = 0.1394 in the compound. The maximum and minimum values of residual electron density were 0.484 and −0.419 e Å^{-3}.

4. Results and discussion

4.1. Chemistry

The reaction of 2-amino-5-(4-fluoro-benzyl)-1,3,4-thiadiazole (**1**) (Giri et al., 1964) and phenacyl bromide (**2**) in boiling ethanol afforded the 2-(4-fluoro-benzyl)-6-phenyl-imidazo[2,1-*b*][1,3,4]thiadiazole (**3**) as hydrobromide salt, which was neutralized by sodium carbonate solution to get the free base. It is well established that this reaction proceeds via the intermediate iminothiadiazole which under reflux temperature spontaneously undergoes dehydrocyclisation to form the desired fused heterocycle (Gadad et al., 2000). Various α-haloaryl ketones were prepared by the bromination of the corresponding ketones.

Structures of imidazothiadiazole derivatives (**3a–b**) were established by the absence of υ_{N-H} band in the IR spectra and appearance of imidazole proton (C_5–H) around δ 8 in the ^{1}H NMR spectra. The ^{13}C NMR and mass spectra of these compounds further confirmed the assigned structures. A number of compounds containing 2-benzyl-6-phenyl-imidazo[2,1-*b*][1,3,4] thiadiazole as the basic structural unit with various substituents have been synthesized earlier and spectroscopically analyzed and reported (Badiger et al., 2009; Gupta et al., 1993). Good quality single crystals for compounds (**3a**) and (**3b**) were prepared by slow evaporation method using ethyl acetate and ethanol solvents. Crystals grown are stable for a long-time in normal conditions of temperature and humidity. The chemical formula was determined when resolving the crystal structure by X-ray diffraction. In the present work, we report the synthesis and spectroscopic analysis of the two title compounds with more emphasis laid on weak interactions.

4.2. Crystallography

The details of crystal data and refinements are given in Tables 1 and 2 for the compounds (**3a**) and (**3b**) respectively. The selected bond distances and angles for compound (**3a**) and (**3b**) are given in Tables 3 and 4, respectively. Tables 5 and 6 give their respective hydrogen bond interactions. The ORTEP diagrams of the molecules **3a** and **3b** are shown in Figs. 1 and 2, respectively. Figs. 3–5 show the hydrogen bond interactions in crystal structure of (**3a**) and (**3b**), respectively.

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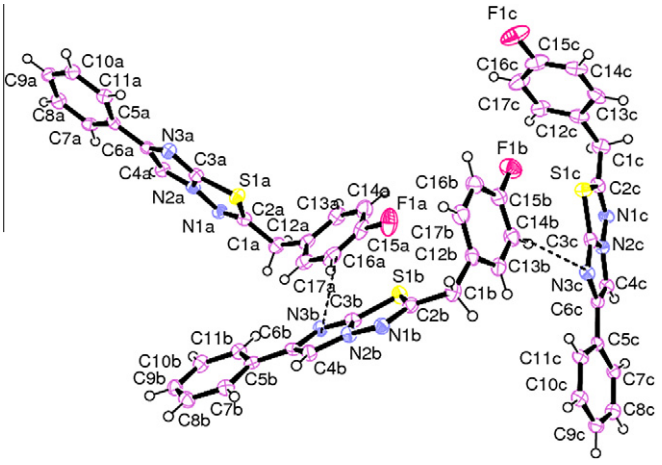

Figure 1 ORTEP diagram of the three independent molecules present in the asymmetric unit of compound (**3a**), showing 50% probability displacement ellipsoids and the atom-numbering scheme. Dotted line indicates C—H···N interaction.

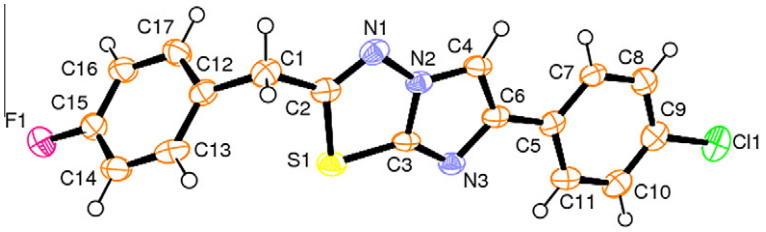

Figure 2 ORTEP diagram of compound (**3b**), showing 50% probability displacement ellipsoids and the atom-numbering scheme.

Table 1 Crystal data and structure refinement for (**3a**).

Empirical formula	$C_{17}H_{12}FN_3S$
Formula weight	309.36
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, $P\bar{1}$
Unit cell dimensions	
a = 5.582 Å α = 117.06°	
b = 20.888 Å β = 94.81°	
c = 21.405 Å γ = 94.89°	
Volume	2193.0 Å^3
Z	6
Calculated density	1.405 mg/m^3
Absorption coefficient	0.231 mm^{-1}
F(0 0 0)	960
Crystal size	0.18 × 0.16 × 0.16 mm
Theta range for data collection	1.91–27.00 °
Limiting indices	$-7 \le h \le 7$, $-19 \le k \le 26$, $-27 \le l \le 23$
Reflections collected/unique	13,113/9234 [R(int) = 0.0413]
Completeness to theta	27.00, 96.6%
Absorption correction	Multi scan
Max. and min. transmission	0.9639 and 0.9596
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	9234/0/595
Goodness-of-fit on F^2	1.144
Final R indices [$I > 2\ \sigma(I)$]	$R1$ = 0.0857, $wR2$ = 0.2363
R indices (all data)	$R1$ = 0.1101, $wR2$ = 0.2800
Largest diff. peak and hole	2.870 and −0.687 e Å^{-3}

Table 2 Crystal data and structure refinement for (**3b**).

Empirical formula	$C_{17}H_{11}ClFN_3S$
Formula weight	343.80
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	
a = 10.255(4) Å	
b = 5.618(3) Å	
c = 26.044(1) Å	
β = 91.438(8)°	
Volume	1499.9(11) Å^3
z	4
Calculated density	1.523 mg/m^3
Absorption coefficient	0.406 mm^{-1}
F(000)	704
Crystal size	0.18 × 0.16 × 0.16 mm
Theta range for data collection	2.15–27.00°
Limiting indices	$-12 \le h \le 13$, $-7 \le k \le 7$, $-33 \le l \le 19$
Reflections collected/unique	8553/3238 [R(int) = 0.0549]
Completeness to theta	27.00, 99.3%
Max. and min. transmission	0.9379 and 0.9305
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3238/0/212
Goodness-of-fit on F^2	1.080
Final R indices [$I > 2\ \sigma(I)$]	$R1$ = 0.0540, $wR2$ = 0.1394
R indices (all data)	$R1$ = 0.0805, $wR2$ = 0.1705
Largest diff. peak and hole	0.484 and −0.419 e Å^{-3}

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Table 3 Selected bond lengths [Å] and angles [°] for compound (**3a**).

C1–C12	1.509(6)/1.516(6)/1.503(6)	N3–C3–S1	138.0(3)/138.2(3)/138.6(3)
C1–C2	1.502(6)/1.515(6)/1.513(6)	N2–C3–S1	109.1(3)/108.9(3)/108.6(3)
C2–N1	1.300(5)/1.297(5)/1.286(5)	N2–C4–C6	104.7(4)/104.9(4)/104.5(4)
C2–S1	1.750(4)/1.743(4)/1.751(4)	C11–C5–C7	118.7(4)/118.8(4)/117.9(4)
C3–N3	1.314(5)/1.317(5)/1.312(5)	C11–C5–C6	120.8(4)/121.1(4)/120.9(4)
C3–N2	1.362(5)/1.365(5)/1.360(5)	C7–C5–C6	120.5(4)/120.1(4)/121.2(4)
C3–S1	1.729(4)/1.734(4)/1.732(4)	C4–C6–N3	111.7(4)/112.0(4)/111.6(4)
C4–N2	1.362(5)/1.379(5)/1.367(5)	C4–C6–C5	127.9(4)/127.4(4)/128.2(4)
C4–C6	1.365(5)/1.370(5)/1.372(6)	N3–C6–C5	120.4(4)/120.6(4)/120.2(4)
C5–C11	1.394(5)/1.394(5)/1.390(6)	C8–C7–C5	120.7(4)/119.8(4)/122.0(4)
C5–C7	1.395(5)/1.393(6)/1.399(5)	C7–C8–C9	120.6(4)/121.2(5)/119.5(4)
C5–C6	1.481(6)/1.477(5)/1.466(5)	C8–C9–C10	118.8(4)/119.6(4)/119.2(4)
C6–N3	1.393(5)/1.391(5)/1.393(5)	C11–C10–C9	120.7(4)/119.8(4)/120.4(4)
C7–C8	1.383(6)/1.395(6)/1.383(6)	C10–C11–C5	120.6(4)/120.7(4)/121.0(4)
C8–C9	1.392(6)/1.368(6)/1.392(6)	C17–C12–C1	118.6(5)/119.6(5)/118.2(5)
C9–C10	1.394(6)/1.385(6)/1.392(6)	C17–C12–C1	120.9(5)/120.5(4)/121.4(4)
C10–C11	1.387(6)/1.397(6)/1.394(6)	C13–C12–C1	120.3(4)/119.7(5)/120.4(5)
C12–C13	1.395(7)/1.389(6)/1.393(6)	C14–C13–C12	121.3(5)/121.1(5)/121.9(5)
C12–C17	1.370(6)/1.380(6)/1.394(7)	C13–C14–C15	117.9(5)/116.8(5)/117.7(5)
C13–C14	1.377(7)/1.397(7)/1.373(7)	F1–C15–C16	119.1(5)/117.8(5)/118.2(5)
C14–C15	1.380(7)/1.374(6)/1.379(7)	F1–C15–C14	118.2(5)/118.4(5)/118.9(5)
C15–C16	1.375(7)/1.374(6)/1.374(7)	C16–C15–C14	122.7(5)/123.8(5)/122.9(5)
C16–C17	1.387(7)/1.386(7)/1.382(7)	C15–C16–C17	117.7(5)/118.4(5)/118.5(5)
C15–F1	1.364(5)/1.369(5)/1.356(6)	C12–C17–C16	121.6(5)/120.2(5)/120.8(5)
N1–N2	1.375(5)/1.363(4)/1.374(5)	C2–N1–N2	108.3(4)/108.4(4)/108.0(4)
		C4–N2–C3	107.6(4)/106.7(4)/107.7(4)
C12–C1–C2	111.4(4)/110.5(4)/111.9(4)	C4–N2–N1	134.5(4)/135.5(4)/133.9(4)
N1–C2–C1	122.9(4)/122.3(4)/123.1(4)	C3–N2–N1	117.8(4)/117.4(4)/117.7(4)
N1–C2–S1	116.6(3)/120.4(4)/117.2(3)	C3–N3–C6	103.0(3)/103.5(4)/103.5(4)
C1–C2–S1	120.5(3)/117.3(3)/119.8(3)	C3–S1–C2	88.1(2)/87.7(2)/87.8(2)
N3–C3–N2	112.9(4)/112.8(4)/112.8(4)		

* The values given after 1st/corresponds to molecule B whereas 2nd/to molecule C.

The compound (**3a**) has three independent molecules in the asymmetric unit. The central imidazo-thiadiazole unit is linked to the fluorobenzyl group at one end and the phenyl ring at the other. The dihedral angles between fluorobenzyl and imidazo-thiadaizole rings is orthogonally inclined at an angle 88.25(6)°/81.43(2)°/82.79(8)° (the three values corresponds to the three independent molecules) and angles between imidazo-thiadiazole and phenyl ring 8.65(3)°/10.21(6)°/10.21(6)° represent the co-planarity of the molecule.

The average value of the bond distances is 1.388(6) Å while the exocyclic bond angles [120.6(8)°] in the phenyl rings of the molecule have normal values which agree quite well with the values reported in the literature for some analogous structures (Toda et al., 1998; Li et al., 1992). The survey of the structure at a molecular level reveals the usual geometrical parameters for the S–C bond of 1.731(5) Å. The N–C and N–N bonds of the three independent molecules A, B and C are 1.360(6) Å/1.354 Å/1.358 Å and 1.380 Å/1.352(2) Å/1.375 Å, respectively which are shorter than typical bond lengths due to the π-electron delocalization. The C═N bond length of 1.310(7) Å confirms it as a double bond. The orientation of fluorobenzyl group is characterized by torsion angles C(17A)-C(12A)-C(1A)-C(2A) of 85.1(6)°, C(17B)-C(12B)-C(1B)-C(2B) of 83.7(5)° and C(13C)-C(12C)-C(1C)-C(2C) of 86.0(6)° in molecules A, B and C, respectively.

The most interesting feature of this compound is the analyzes of the crystal packing indicating intra and intermolecular interactions. All the three molecules in the asymmetric unit are primarily stabilized by two strong intramolecular C–H···N hydrogen bonds in the crystal structure leading to the formation of a pseudo-five-membered hydrogen bonded pattern with graph set S(5) which locks the molecular conformation while eliminating conformational flexibility.

The crystal structure of compound (**3a**) is further stabilized by intermolecular C–H···N and C–H···F hydrogen bonds. There are two C–H···N interactions, the former generates bifurcated bonds from two donor atoms, C4 and C14 to the same acceptor, N3 linking the dimers into a tape like pattern while the latter leads to the formation of centrosymmetric head to head dimers corresponding to graph set notation $R_2^2(14)$ (Bernstein et al., 1995) along '*a*' axis (Fig. 3). These C–H···N hydrogen bonds have been extensively used in crystal engineering (Desiraju, 1991, 1995, 1996, 1997a,b; Steiner, 1996).

The intermolecular C–H···F interaction of the molecule leads to the two dimensional supramolecular porous network of hexagonal hydrogen bond pattern in the crystal structure where the six molecules connects themselves into a perfect cyclohexagonal ring pattern along '*a*' axis (Fig. 4). The function of the C–F group in crystal packing helps in the understanding of the binding of a fluorinated substrate to a macromolecular receptor (Evans and Seddon, 1997; Glusker, 1995). The C–H···F interaction (3.284 Å) has the least donor–acceptor distance compared to C–H···N (3.536 Å), which makes the C–H···F bond a successful competitor for the C–H donor. This is unusual since

Table 4 Selected bond lengths [Å] and angles [°] for compound (**3b**).

C(1)–C(2)	1.497(4)	N(2)–C(3)–S(1)	109.0(2)
C(1)–C(12)	1.499(4)	N(2)–C(4)–C(6)	104.6(3)
C(2)–N(1)	1.289(4)	C(11)–C(5)–C(7)	117.8(3)
C(2)–S(1)	1.750(3)	C(11)–C(5)–C(6)	120.7(3)
C(3)–N(3)	1.330(4)	C(7)–C(5)–C(6)	121.5(3)
C(3)–N(2)	1.357(4)	C(4)–C(6)–N(3)	111.4(3)
C(3)–S(1)	1.729(3)	C(4)–C(6)–C(5)	127.6(3)
C(4)–N(2)	1.371(4)	N(3)–C(6)–C(5)	121.0(3)
C(4)–C(6)	1.375(4)	C(8)–C(7)–C(5)	121.7(3)
C(5)–C(11)	1.392(4)	C(7)–C(8)–C(9)	118.9(3)
C(5)–C(7)	1.404(4)	C(10)–C(9)–C(8)	121.3(3)
C(5)–C(6)	1.462(4)	C(10)–C(9)–Cl(1)	119.5(3)
C(6)–N(3)	1.395(4)	C(8)–C(9)–Cl(1)	119.2(3)
C(7)–C(8)	1.378(4)	C(9)–C(10)–C(11)	119.3(3)
C(8)–C(9)	1.386(5)	C(5)–C(11)–C(10)	121.0(3)
C(9)–C(10)	1.376(5)	C(13)–C(12)–C(17)	117.9(3)
C(9)–Cl(1)	1.746(3)	C(13)–C(12)–C(1)	121.7(3)
C(10)–C(11)	1.395(5)	C(17)–C(12)–C(1)	120.4(3)
C(12)–C(13)	1.388(4)	C(14)–C(13)–C(12)	122.0(3)
C(12)–C(17)	1.388(4)	C(15)–C(14)–C(13)	117.9(3)
C(13)–C(14)	1.382(5)	F(1)–C(15)–C(14)	119.3(3)
C(14)–C(15)	1.370(4)	F(1)–C(15)–C(16)	118.7(3)
C(15)–F(1)	1.355(4)	C(14)–C(15)–C(16)	122.0(3)
C(15)–C(16)	1.374(4)	C(17)–C(16)–C(15)	119.2(3)
C(16)–C(17)	1.374(4)	C(16)–C(17)–C(12)	120.9(3)
N(1)–N(2)	1.372(3)	C(2)–N(1)–N(2)	108.1(2)
		C(3)–N(2)–C(4)	108.1(2)
C(2)–C(1)–C(12)	114.9(3)	C(3)–N(2)–N(1)	118.1(2)
N(1)–C(2)–C(1)	122.2(3)	C(4)–N(2)–N(1)	133.8(2)
N(1)–C(2)–S(1)	116.9(2)	C(3)–N(3)–C(6)	103.5(2)
C(1)–C(2)–S(1)	120.9(2)	C(3)–S(1)–C(2)	87.81(14)
N(3)–C(3)–N(2)	112.3(3)		
N(3)–C(3)–S(1)	138.7(2)		

Table 5 Non-bonded interactions and possible hydrogen bonds (Å, °) for compound (**3a**) (D-donor; A-acceptor; H-hydrogen).

D–H···A	D–H	H···A	D···A	D–H···A
C16a–H16a···N3b	0.930(5)	2.537(4)	3.434(7)	162
C14b-H14b···N3c	0.930(5)	2.641(4)	3.536(6)	162
C4a-H4a···.N3a^{i}	0.930(6)	2.917(4)	3.527(6)	124
C14C–H14c···N3a^{ii}	0.930(6)	2.663(4)	3.536(8)	156
C17C–H17c···F1b^{i}	0.930(6)	2.570(4)	3.344(8)	141
C13a–H13a···F1c^{iii}	0.930(5)	2.523(3)	3.351(6)	148
C17b–H17b···F1a^{iv}	0.930(6)	2.445(4)	3.284(7)	150
C7b–H7b···N1b^{v}	0.930(4)	2.740(3)	3.607(5)	155

Symmetry code: (0) x, y, z; (i) $x-1, +y, +z$; (ii) $-x, -y, -z+1$; (iii) $-x-1, -y, -z+1$; (iv) $x+1, +y, +z$; (v) $-x+2, -y+1, -z+1$.

Table 6 Non-bonded interactions and possible hydrogen bonds (Å, °) for compound (**3b**) (D-donor; A-acceptor; H-hydrogen).

D–H···A	D–H	H···A	D···A	D–H···A
C11–H11···N3	0.930(3)	2.567(3)	2.894(4)	101
C1–H1b···N3^{i}	0.970(3)	2.571(2)	3.431(4)	148
C4–H4···N3^{ii}	0.977(3)	2.658(4)	3.501(4)	147

Symmetry code: (0) x, y, z (i) $-x+1/2, +y-1/2, -z+1/2$; (ii) $x, +y-1, +z$.

it happens in the presence of oxygen and nitrogen which are strong acceptor atoms, thus making the C–H···F interaction an important structure-directing entity. The molecular packing is further stabilized by π–π stacking interactions between the benzene and imidazothiadiazole ring systems with C2–C7 atoms of the two molecules being separated by a distance of 3.757(4) Å (symmetry code: ½$-x, y, -z$) strengthening the supramolecular assembly in the crystal structure. In the molecular packing of compound (**3a**), the C–H···F interactions play important role in the formation of the supramolecular network influencing the conformation and property of imidazo-thiadiazole derivatives.

The compound (**3b**) has a chloro group substituted at the para position of the phenyl ring. The dihedral angle between fluorobenzyl and imidazo-thiadaizole is 79.54(3)° indicating

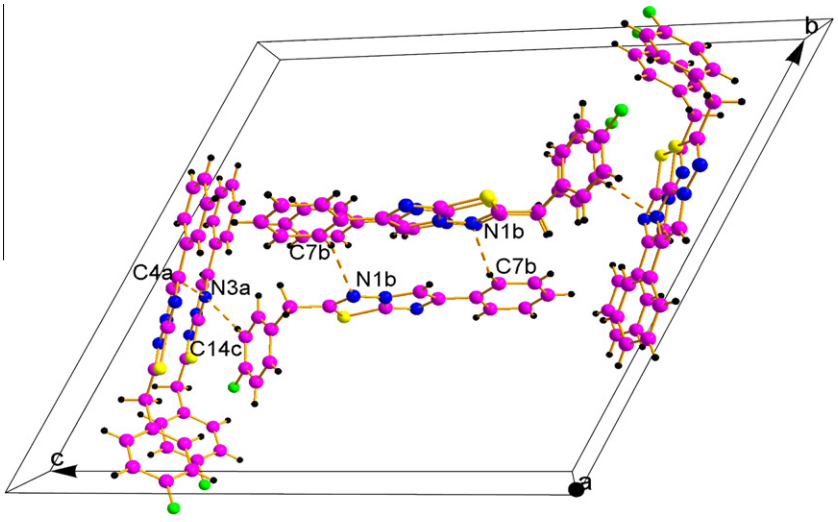

Figure 3 Packing of the molecules in crystal of (**3a**) viewed along '*a*' axis. Dotted lines indicate C–H···N intermolecular interactions resulting in dimers and bifurcated bond.

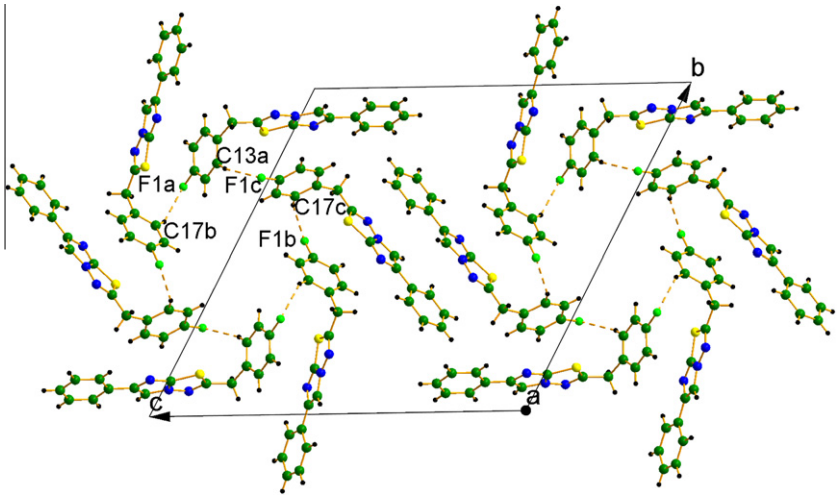

Figure 4 Packing of the molecules of (**3a**) with dotted lines indicating C–H···F intermolecular interactions generating hexagonal hydrogen bond along '*a*' axis.

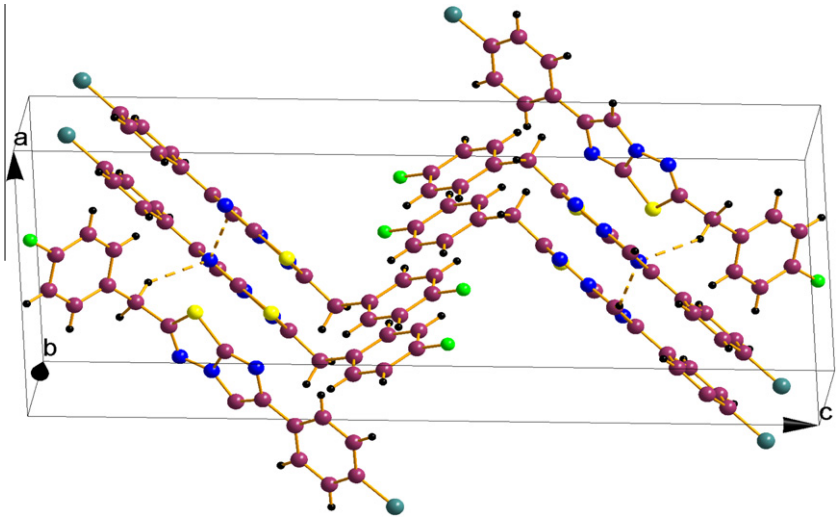

Figure 5 View of the molecular packing in (**3b**), showing bifurcated C–H···N interactions along *'b'* axis.

that the two are oriented orthogonally. Chlorophenyl and imidazothiadiazole are coplanar; the dihedral angle is 7.73(4)° between them. The C3═N3 bond length of 1.330(4) Å confirms it as a double bond. The C2–N1 bond length of 1.289(4) Å and the N1–N2 bond length of 1.372(3) Å are relatively short, suggesting some degree of delocalization in the imidazothiadiazole system. The *cis* orientation of the fluorobenzyl group and thiadiazole moiety is characterized by the torsion angle C(12)–C(1)–C(2)–S(1) [−41.5(3)°] in the molecule. The imidazole part of this imidazothiadiazole system is more resonance stabilized due to the difference in bond lengths S1–C3 [1.729(3) Å] and S1–C2 [1.750(3) Å]. Additionally, the imidazothiadiazole entity is as usual planar and rigid. Most of the imidazothiadiazole derivatives posses near or total planarity locking the molecules conformationally into pseudo ring moieties, and self-aggregates through weak C–H···N interactions (Begum et al., 2006, 2007).

Despite the presence of elements like chlorine; sulphur fluorine etc, there are no interesting intermolecular interactions in the crystal structure of compound (**3b**). However, the molecular packing of this compound is rendered cohesive by molecules linked via two C–H···N hydrogen bond interactions (Begum et al., 2007).

The intra and intermolecular packing features seen in **3b** are very similar to the one observed in molecule **3a** by the presence of bifurcated and π–π stacking interactions (Fig. 5). The π–π stacking interaction between the imidazothiadiazole and benzene rings (Begum et al., 2007) being separated by a distance of 3.785(2) Å (symmetry code:$-\frac{1}{2}+x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$) further strengthens the supramolecular structure. So the supramolecular aggregation in this structure is limited to the formation of these bifurcation and π–π stacking interactions.

5. Conclusion

The synthesis as well as the characterization of imidazo[2,1-*b*][1,3,4]thiadiazole and its chlorophenyl derivative are described with promising biological and pharmacological

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activities. Additionally, the single crystal X-ray diffraction analysis revealed certain interesting features such as the non-planarity of the molecule due to the orthogonal orientation of fluorobenzyl with the imidazo-thiadiazole ring, presence of a strong intramolecular hydrogen bond and the conformational rigidity of the pseudo five-membered ring. The stabilization of the structure due to intermolecular C–H···F and C–H···N interactions were analyzed wherein the supramolecular aggregation in the molecule highlights a very interesting molecular packing feature on C–H···F interaction where the six molecules connect themselves into a perfect hexagonal geometry depicting a cyclohexagonal ring pattern in order to establish the construction of crystalline superstructures.

Supplementary material

Crystallographic data for the structures (**3a**) and (**3b**) reported in this paper have been deposited with the Cambridge data centre. The deposition numbers are CCDC 787336 and CCDC 763066.

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