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Synthesis, Characterization and Crystal Structures of [4-substituted(aryl)-piperazin-1-yl](thieno[2,3-*c*]pyridin-5-yl)methanone derivatives

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ABSTRACT

*Four [4-substituted(aryl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanones, namely, 4-(methoxyphenyl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanone (**1**), 4-(fluorophenyl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanone (**2**), 4-(methylphenyl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanone (**3**) and 4-(3,4-dimethylphenyl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanone (**4**) were synthesized and characterized by FTIR, ^{1}H NMR and LC-MS spectroscopic techniques. The single crystals of all the compounds were grown, and their molecular & crystal structures were determined by single crystal X-Ray diffraction. The molecular structure of all the compounds features an intramolecular hydrogen bond of the type C-H…N which closes into a S(6) motif. The crystal structures of these compounds display several secondary interactions of the type C-H…O, C-H…F, C-H…π and π…π, and the combination of these interactions results in adopting different supramolecular architectures. Three different structure directing C-H…O interactions in **1** builds a three dimensional architecture, while in **2**, two C-H…F and one C-H…O interactions generate a three dimensional structure. Several C-H…π interactions give additional stability to the crystal structures of **1** and **2**and have no structure directing features. Unlike **1** and **2**, the supramolecular structures of **3** and **4**are two dimensional networks formed by a combination of C-H…O and C-H…π interactions. The C-H…π interactions in **3** and **4** are structure directing in nature and extends the one dimensional architecture formed by C-H…O interactions into two dimensional.*

Keywords: Thienopyridine; X-Ray diffraction; C-H…π interactions; C-H…F interactions; π…π interactions

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INTRODUCTION

Thienopyridine derivatives occupy a special place in medicinal chemistry and have attracted considerable attention because of their broad pharmacological activities, including anti-cancer [1-3], antiviral [4-6], anti-inflammatory [7-9], anti-diabetic [12,13], anti-hypertensive [14-16] and osteogenic activities [17,18] in addition to the treatment of CNS disorders [19,20].Also, thienopyridines are identified as a selective, irreversible ADP receptor/P2Y12 inhibitors used for their anti-platelet activity [21]. Further, Ticlopidine and Clopidogrel are two highly effective thienopyridine based drugs used for the treatment of cardiac disease [22,23]. Both of them are good inhibitors of platelet activation by a more effective mechanism compared to that of aspirin, thereby, limiting complications like stroke and myocardial infarction. Thus, owing to the promising biological activities of thienopyridines, it would be worth to synthesize the derivatives of thienopyridinei.e.,4-(aryl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanones. Therefore, herein we report the synthesis of four4-substitutedaryl-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanones (**1-4)**, their characterization by FTIR, ^{1}H NMR & LC-MS spectroscopic techniques and also by single crystal X-ray diffraction studies.

MATERIALS AND METHODS

1.1. Analytical Methods

Melting points were determined in open capillaries and are reported as such. The molecular structures of the synthesized compounds were established using IR, ^{1}H NMR and LC-MS studies. Solid state FT-IR Spectra were recorded as KBr discs on Jasco FT-IR Spectrometer. ^{1}H NMR spectra were recorded in DMSO at 400.37 MHz on Bruker model Avance II. All the chemical shifts were reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. Mass spectra of the compounds were recorded on Shimadzu LC-2010EV with ESI probe.

1.2. X-Ray Data Collection and Structure Refinement Details

The single crystal X-ray diffraction data of all the compounds were collected on a Bruker SMART CCD diffractometer with Cu Kα (λ=1.54178 Å) X-rays at 23°C. Crystal structures were solved using SHELXTL [24].All non-hydrogen atoms were located from the difference Fourier map using geometrical constraints and were refined anisotropically. The least-squares refinement cycles on F^2were performed until the model converged. The H atoms were positioned with idealized geometry using a riding model with C(Ar)-H = 0.93 Å, C(methyl)-H = 0.96 Å and C(methylene)-H = 0.97 Å. All H atoms were refined with isotropic displacement parameters (set to 1.2-1.5 times of the Ueq of the parent carbon atom). To improve considerably the values of R1, wR2, and GOOF the bad reflections (0 2 0, 0 2 1, 2 3 7) in **1**, (0 2 0) in **2**, (0 2 0) in **3** and (0 0 1, -2 2 2, 3 2 6, 1 4 0, -1 -4 1, 0 1 2, 5 0 3, 3 2 11, 3 2 13, 4 3 13, 4 -4 2, -3 -2 8, 3 2 14, -2 2 6, 3 2 2, 4 -4 3, 1 0 2, -4 -3 4, 2 -2 11, -4 4 13)in **4** were omitted from the final refinement. The ORTEP diagrams and the crystal packing diagrams were drawn using the MERCURY software [25].

1.3. Synthesis

Step 1: Synthesis of Methyl (acetylamino)(dimethoxyphosphoryl)acetate

To a solution of methyl {[(benzyloxy)carbonyl]amino}(dimethoxyphosphoryl)acetate (22g,66.46mmol)in ethyl acetate (250mL), acetic anhydride (10g,99.69mmol)was added. Palladium on carbon (2g, 10% wet) was added to the above mixture carefully and was stirred in an autoclave under hydrogen atmosphere (3Kg) for 5 h. After the completion of reaction the mixture was filtered through a celite bed and washed with ethyl acetate (100mL x 3). The filtrate was concentrated and the excess acetic acid was azeotropically removed using toluene as a co solvent to get the title compound as white crystalline solid (**Scheme 1**). Yield: 73.34%, 11g.

Step 2:Synthesis of Methyl thieno[2,3-c]pyridine-5-carboxylate

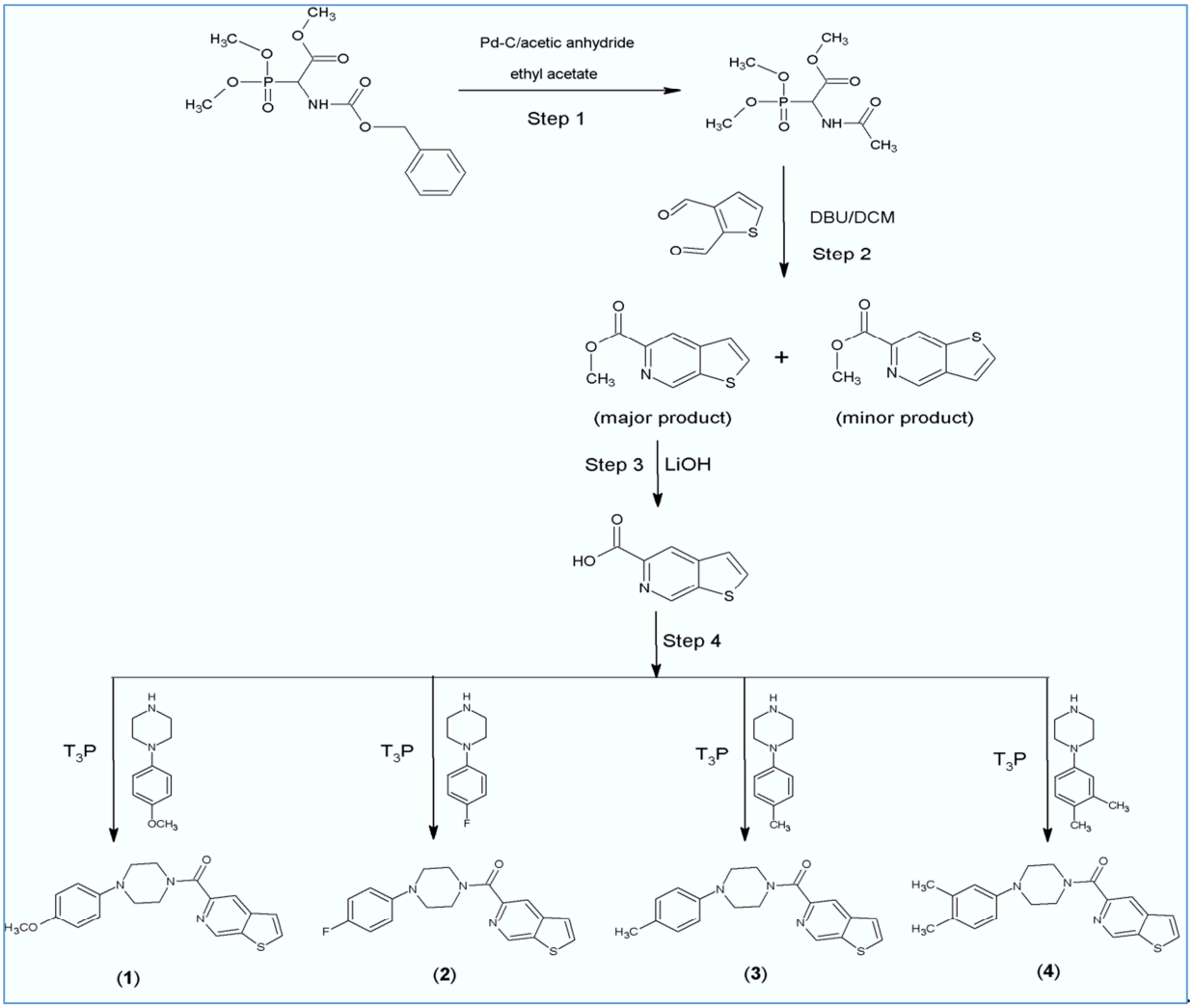
To an ice cooled solution of methyl(acetylamino)(dimethoxyphosphoryl)acetate (10g,41.84mmol) in dichloromethane (150mL) was added DBU (9.5g,62.76mmol) followed by the drop wise addition of thiophene-2,3-dicarbaldehyde (7g,62.76mmol) dissolved in dichloromethane (30mL)over a period of 20 min. The reaction mass was allowed to come to room temperature and stirred for 16h. It was then diluted with water (50mL) and the crude product was extracted intodichloromethane (50mL x 3). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated to obtain the crude compound containing the regio isomers (**Scheme 1**). The desired isomer was eluted out in the pure form by using SiO_2 flash column chromatography with 30% ethyl acetate /petroleum ether. The solution was concentrated and dried to get the desired compound as a pale yellow solid. Yield: 50%, 4g.

Step 3: Synthesis of thieno[2,3-c]pyridine-5-carboxylic acid

A solution of methyl thieno[2,3-*c*]pyridine-5-carboxylate (4.0g,20.72mmol) in a mixture of methanol-water (25mL : 10mL) was cooled in an ice bath and LiOH (0.750g,31.08mmol) was added. The reaction mixture was stirred at room temperature for 5 h. Methanol was evaporated off after completion of the reaction and the reaction mass was acidified to pH 2-3 using dilute HCl. The solid obtained was filtered, washed with water (15mL x 2) and finally with diethyl ether to afford the desired compound as a light brown solid. Yield: 82%, 3.02g.

Step 4:General procedure for the synthesis of [4-(4-aryl)piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanone

A solution of thieno[2,3-c]pyridine-5-carboxylic acid (0.2g,1.11mmol) and the respective 1-(4-aryl)piperazines (1.34mmol) [4-aryl = 4-methoxyphenyl (**1**), 4-fluorophenyl (**2**), 4-methylphenyl (**3**)and 3,4-dimethylphenyl (**4**)] in dry dichloromethane (6 mL) were cooled in an ice bath. Triethylamine (0.4mL, 2.7mmol) was added to the reaction mixtures followed by the drop wise addition of poly phosphoric acid anhydride (T_3P-50% wt in EtOAc, 1.06mL,1.67mmol) and the reaction mixtures were stirred for 3h at room temperature. The reaction mixtures were diluted with water (3mL) and the crude products were extracted into dichloromethane (3mLx2), dried over Na_2SO_4, concentrated to get the crude products, and later were purified by column chromatography.



SCHEME 1. Synthesis of compounds 1-4

Single crystals of **1**-**4**suitable for X-ray diffraction studies were obtained by slow evaporation of the solutions of the compounds in ethanol at room temperature (27^{o}C).

RESULTS AND DISCUSSION

1.4. Spectral characterization

The compounds**1**-**4**were synthesized as per the reactions given in Scheme 1.All the compounds were characterized and their formation was confirmed by recording their IR, ^{1}H NMR and LCMS spectra. The FT-IR, ^{1}H NMR and LCMS spectra of all the four compounds are supplied in the Supplementary File (Fig. S1-S12). The details of the yield, melting pointand analysis of FT-IR, ^{1}H NMR and LCMS spectra of **1**-**4**are as follows:

1: Yield: 53%, 0.21g; mp: 175-177^{o}C;FTIR (KBr, cm^{-1}):3045, 2959, 2918 ($C_{Aromatic}$-H), 1620 (>C=O), 1510 (>C=N), 1460 (>C-N<), 1310 (>C-S str); ^{1}H NMR (DMSO): δ (vs. TMS):9.30 (s, 1H, Ar-H), 8.23-8.22 (d, 1H, Ar-H, *J* = 7.84 Hz), 8.13 (s, 1H, Ar-H), 7.65-7.64 (d, 1H, Ar-H,*J* = 6.5 Hz), 6.94-6.92 (d, 2H, Ar-H, *J* = 8.0 Hz), 6.84-6.82 (d, 2H, Ar-H, *J* = 7.9 Hz), 3.83 (s, 2H, CH_2), 3.69 (s, 3H, OCH_3), 3.62 (s, 3H, CH_2), 3.11 (s, 2H, Ar-N-CH_2), 2.99 (s, 2H, Ar-N-CH_2); LC-MS: m/z = 355.2.

2: Yield: 42%, 0.16 g; mp: 210-212^{o}C; FTIR (KBr, cm^{-1}):3046, 2967, 2920($C_{Aromatic}$-H), 1611 (>C=O), 1505 (>C=N), 1475 (>C-N<), 1378 (>C-S str); ^{1}H NMR (DMSO): δ (vs. TMS):9.30 (s, 1H, Ar-H),8.24-8.22 (d, 1H, Ar-H, *J* = 8.00 Hz),8.14 (s, 1H, Ar-H),7.65-7.64 (d, 1H, Ar-H,*J* = 7.4 Hz),7.09-7.02 (m, 2H, Ar-H), 7.00-6.95 (m, 2H, Ar-H), 3.83 (s, 2H, CH_2), 3.63 (s, 2H, CH_2), 3.33 (s, 2H, Ar-N-CH_2), 3.19 (s, 2H, Ar-N-CH_2); LC-MS: m/z = 342.3.

3: Yield: 40%, 0.15 g; mp: 185-187^{o}C; FTIR (KBr, cm^{-1}):3085, 2978, 2885, 2815($C_{Aromatic}$-H, C_{Methyl}-H); 1624 (>C=O), 1581 (>C=N), 1470 (>C-N<), 1376 (>C-S); ^{1}H NMR (DMSO): δ (vs. TMS):9.30 (s, 1H, Ar-H),8.23-8.22 (d, 1H, Ar-H, *J* = 8.0 Hz), 8.13 (s, 1H, Ar-H), 7.65-7.64 (d, 1H, Ar-H, *J* = 7.5 Hz), 7.05-7.03 (d, 2H, Ar-H, *J* = 8.0 Hz), 6.88-6.86 (d, 2H, Ar-H, *J*= 7.9 Hz), 3.82 (s, 2H, CH_2), 3.62 (s, 2H, CH_2), 3.33 (s, 2H, Ar-N-CH_2), 3.18 (s, 2H, Ar-N-CH_2), 2.2(s, 3H, Ar-CH_3); LC-MS: m/z = 339.2.

4: Yield: 53.8%, 0.21 g; mp: 225-227^{o}C; FTIR (KBr, cm^{-1}): 3103, 2956, 2898, 2820 ($C_{Aromatic}$-H, C_{Methyl}-H); 1613 (>C=O), 1575 (>C=N), 1483 (>C-N<), 1381 (>C-S);^{1}H NMR (DMSO): δ (vs. TMS):9.30 (s, 1H, Ar-H),8.23-8.21 (d, 1H, Ar-H, *J* = 7.8 Hz), 8.13 (s, 1H, Ar-H), 7.65-7.63 (d, 1H, Ar-H, *J* = 8.0 Hz), 6.99-6.96 (d, 1H, Ar-H, *J* = 8.4 Hz), 6.77 (s, 1H, Ar-H), 6.71-6.69 (d, 1H, Ar-H, *J* = 7.9 Hz), 3.81 (s, 2H, CH_2), 3.61 (s, 2H, CH_2), 3.39 (s, 2H, Ar-N-CH_2), 3.32 (s, 2H, Ar-N-CH_2), 2.16 (s, 3H, Ar-CH_3), 2.11 (s, 3H, Ar-CH_3); LC-MS: m/z = 353.0.

1.5. Single crystal X-ray diffraction studies

The crystal data and refinement parameters for **1**-**4** are given in Table 1, the dihedral angles between the various rings of **1**-**4** are given in Table 2, the geometries of the C-H…N intramolecular interactions in **1**-**4** are given in Table 3. The geometries of the intermolecular interactions of the type C-H…O, C-H…F and the weak interactions of the type C-H…π and π…π displayed in **1**-**4** are given in Table 4. The bond lengths and the bond angles in all the compounds are in the normal range, and hence are not discussed here.

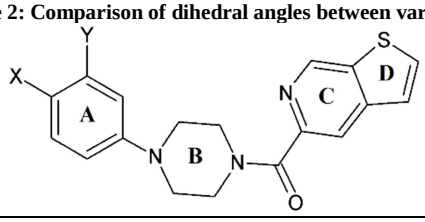
1.5.1. Molecular Conformations

The ORTEP diagrams of **1**-**4** are shown in Figure 1. The piperazine ring in all the compounds adopts chair conformation which is confirmed by Puckering analysis [26]. The puckering amplitude Q and angles θ & Φ being 0.562(3) Å, 177.2(3)^{o}, 120(7)^{o} in **1**, 0.5606(17) Å, 177.48(17)^{o}, 310(4)^{o} in **2**, 0.552(2) Å, 2.7(2)^{o}, 141(5)^{o} in **3**, and 0.564(4) Å, 3.2(4)^{o}, 58(5)^{o} in **4**. Comparison of the dihedral angles between the various rings of **1**-**4** (Table 2) shows that the dihedral angles between two particular rings in all the compounds have values in a certain definite range (Table 2), the highest being observed in compound **4** and the least in compound **3**. The carbonyl C=O bonds in all the compounds is anti to the N and S atoms of the thieno[2,3-c]pyridine rings and the molecular conformations are stabilized by intramolecular C-H…N hydrogen bonds (Table 3) with the S(6) graph set motifs [27]. The geometries of these intramolecular hydrogen bonds (Table 3)are almost same in all the compounds, the only exception being **4**, where a relatively weaker contact is observed.

TABLE 1 Crystal data and structure refinement for 1-4

Parameters	1	2	3	4
CCDC number	1060041	1060042	1060043	1060044
Empirical formula	$C_{19}H_{19}N_3O_2S$	$C_{18}H_{16}FN_3OS$	$C_{19}H_{19}N_3OS$	$C_{20}H_{21}N_3OS$
Formula weight	353.43	341.40	337.43	351.46
Temperature/K	296(2)	296(2)	296(2)	296(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/n$	P-1
a/Å	6.0631(5)	6.1000(2)	6.1289(11)	6.1711(2)
b/Å	32.969(3)	31.7836(10)	33.315(7)	7.8148(3)
c/Å	8.1522(6)	7.9838(2)	8.1055(17)	18.4645(7)
α/°	90.00	90.00	90.00	81.095(2)
β/°	93.583(6)	92.521(2)	92.173(15)	86.441(2)
γ/°	90.00	90.00	90.00	79.530(2)
Volume/Å^3	1626.4(2)	1546.40(8)	1653.8(6)	864.56(5)
Z	4	4	4	2
ρ_{calc}g/cm^3	1.443	1.466	1.355	1.350
μ/mm^{-1}	1.923	2.049	1.817	1.759
F(000)	744.0	712.0	712.0	372.0
Crystal size/mm^3	0.31 × 0.22 × 0.14	0.33 × 0.24 × 0.18	0.31 × 0.21 × 0.17	0.34 × 0.21 × 0.18
Radiation	CuKα (λ = 1.54178)	CuKα (λ = 1.54178)	CuKα (λ = 1.54178)	CuKα (λ = 1.54178)
2θ range for data collection/°	11.2 to 129.06	11.44 to 129.2	12.16 to 127.34	11.64 to 129.06
Index ranges	-5 ≤ h ≤ 7, -38 ≤ k ≤ 37, -8 ≤ l ≤ 9	-6 ≤ h ≤ 7, -36 ≤ k ≤ 36, -9 ≤ l ≤ 9	-7 ≤ h ≤ 6, -38 ≤ k ≤ 38, -9 ≤ l ≤ 9	-7 ≤ h ≤ 7, -9 ≤ k ≤ 9, -21 ≤ l ≤ 21
Reflections collected	9600	11311	12534	9831
Independent reflections	2633 [R_{int} = 0.0926, R_{sigma} = 0.0861]	2518 [R_{int} = 0.0539, R_{sigma} = 0.0439]	2617 [R_{int} = 0.0741, R_{sigma} = 0.0607]	2847 [R_{int} = 0.0633, R_{sigma} = 0.0675]
Data/restraints/parameters	2633/0/227	2518/0/217	2617/0/219	2847/0/229
Goodness-of-fit on F^2	0.994	1.070	1.061	1.105
Final R indexes [I>=2σ (I)]	R_1 = 0.0608, wR_2 = 0.1545	R_1 = 0.0370, wR_2 = 0.1237	R_1 = 0.0455, wR_2 = 0.1195	R_1 = 0.0632, wR_2 = 0.1658
Final R indexes [all data]	R_1 = 0.0808, wR_2 = 0.1659	R_1 = 0.0422, wR_2 = 0.1314	R_1 = 0.0651, wR_2 = 0.1280	R_1 = 0.0696, wR_2 = 0.1695
Largest diff. peak/hole / e Å^{-3}	0.48/-0.49	0.27/-0.42	0.21/-0.18	0.62/-0.43

Table 2: Comparison of dihedral angles between various rings



Rings	Dihedral Angles			
	1	2	3	4
A/B	13.26(15)	11.69(8)	8.59(12)	21.56(11)
A/C	82.38(15)	77.29(8)	75.20(12)	81.62(12)
A/D	81.01(15)	75.42(8)	73.51(11)	81.98(11)
B/C	71.61(16)	67.54(8)	67.83(11)	82.0(11)
B/D	70.08(16)	65.41(8)	65.82(12)	80.84(9)
C/D	2.37(15)	2.97(8)	2.59(11)	3.46(8)

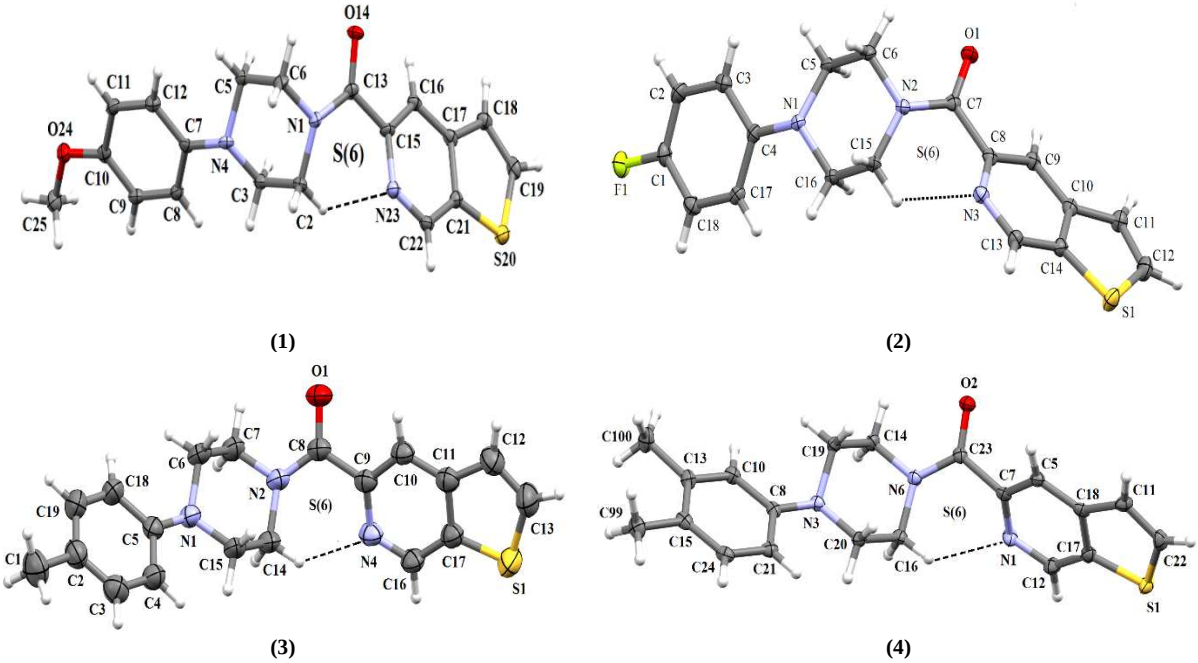


FIGURE 1 ORTEP diagrams of 1-4 drawn with 50% ellipsoidal probability. Dotted lines indicate intramolecular C-H…N hydrogen bonds

Table 3 Geometries of intramolecular C-H…N hydrogen bonds observed in 1 – 4

Compound	D-H…A	D-H/Å	H…A/Å	D…A/Å	D-H…A/°
1	C2-H2B…N23	0.97	2.25	2.912(4)	125
2	C15-H9…N3	0.97	2.25	2.917(2)	125
3	C14-H7…N4	0.97	2.24	2.907(3)	125
4	C16-H16A…N1	0.97	2.49	3.059(5)	118

1.5.2. Supramolecular architectures

In the crystal of **1**, C19-H19…O24 interactions (Table 4) between the molecules results in C(16)[27]zig-zag chains running along the crystallographic *b* axis (Figure 2). The molecules in the neighbouring chains are interlinked via C2-H2B…O14 interactions (Table 4) forming C(5) chains along *a* axis, and this results in the formation of sheets in the ab plane. The molecules in the adjacent sheets are further linked to each other through intermolecular C6-H6B…O14 (Table 4) interactions which runs into C(5) chains along *c* axis (Figure 2). The overall supramolecular architecture is three dimensional. Several C-H…π interactions (Table 4, Figure 3) (where π is the centroid of the phenyl ring C7/C8/C9/C10/C11/C12, pyridine ring C15/C16/C17/C21/C22/N23 and the thiophene ring C17/C18/C19/S20/C21) are observed in the crystal structure which gives additional stability to the crystal structure. Thus, in **1**, in the absence of strong hydrogen bonds, secondary interactions of the type C-H…O control the supramolecular architecture with C-H…π interactions giving additional stability.

The crystal structure of **2** features intermolecular C2-H16…F1 interactions (Figure 4, Table 4) connecting the molecules into $R_2^2(8)$ dimeric pairs. Structure directing C15-H9…O1interactions connects these dimers into ribbons along the diagonal of the *bc* plane. Another structure directing C12-H12…F1 interactions (Figure 4, Table 4) between the molecules in

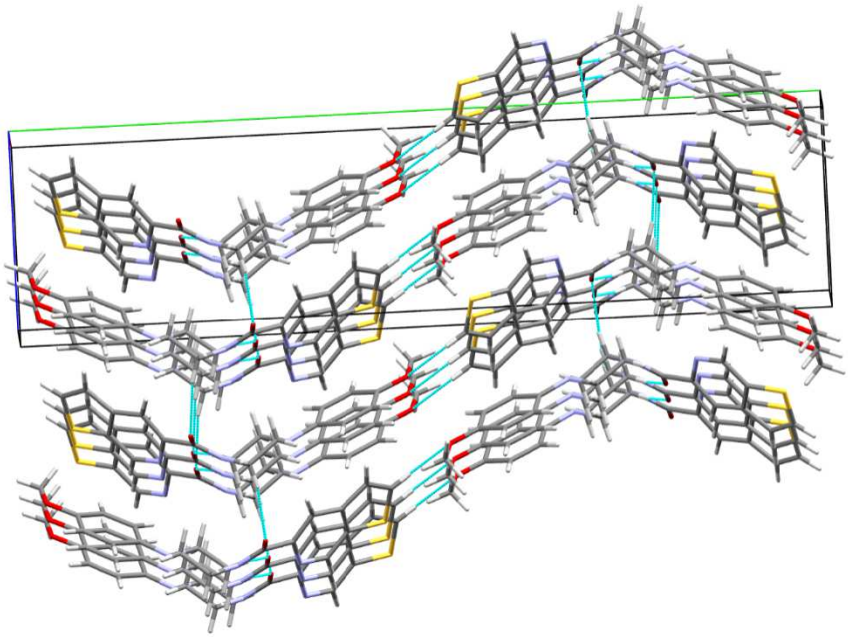


FIGURE 2 Crystal packing of 1, displaying three dimensional architecture through C-H…O interactions

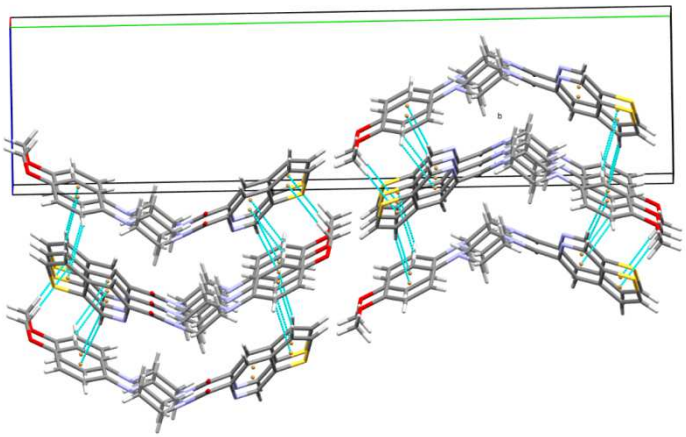


FIGURE 3C-H…π interactions in 1

The neighbouring ribbons results in the formation of sheets in the *bc* plane (Figure 4). In the final stage of the packing, the molecules in the crystal are connecting by a structure directing C6-H11…O1 interactions (Figure 4, Table 4) forming C(5) chains along *c* axis and thus completing the three dimensional architecture. Similar to **1**, the crystal structure of **2** is stabilized by several C-H…π interactions (Table 4, Figure 5) (where π is the centroid of the phenyl ring C1/C2/C3/C4/C17/C18, pyridine ring C8/C9/C10/C14/C13/N3 and the thiophene ring C10/C11/C12/S1/C14). Hence, the supramolecular architecture in **2** is controlled by structure directing secondary interactions of the type C-H…F and C-H…O, and again, C-H…π interactions having no role to play in the supramolecular aggregation.

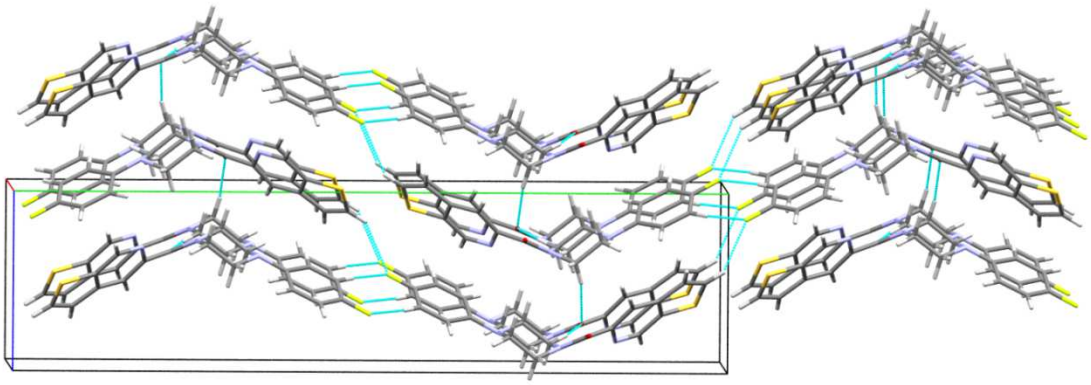


FIGURE 4Crystal packing of 2, displaying three dimensional architecture through C-H…O and C-H…F interactions

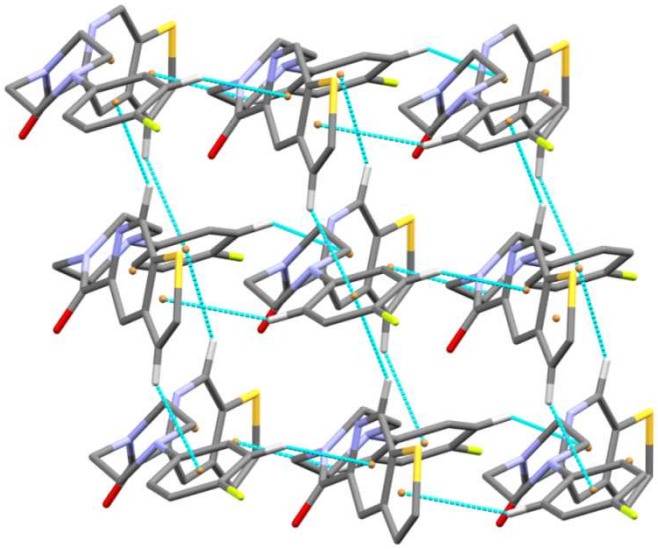


FIGURE 5C-H…*π* interactions in 2. Hydrogen atoms not involved in hydrogen bonding are omitted

In **3**, the molecules are interlinked into C(5) chains through C14-H7…O1 interactions (Figure 6, Table 4) along the crystallographic *a* axis. The molecules in the adjacent chains are connected by C3-H18…π1 and alternating C12-H8…π2 & C16-H10… π2 interactions (where π1 is the centroid of the pyridine ring C9/C10/C11/C17/C16/N4 and π2 is the centroid of the phenyl ring C2/C3/C4/C5/C18/C19) along *c* axis resulting in the formation of sheets in the *ac* plane (Figure 6). The overall structure is two dimensional. A transit in the role of C-H…π interactions in **3** is noted. Non-directing C-H…π interactions in crystals of **1** and **2**give additional stability to the crystal packing, while, in **3**,theseinteractions are structure directing in nature and extends the supramolecular architecture from one dimensional to two.

Table 4. Geometries of various intermolecular and weak interactions in 1-4

D-H…A	D-H	H…A	D…A	D-H…A	Symmetry Code
			1		
C19-H19…O24	0.93	2.49	3.282(4)	143	1/2-x,1/2+y,-1/2-z
C2-H2B…O14	0.97	2.51	3.350(4)	145	1+x,y,z
C6-H6B…O14	0.97	2.60	3.494(4)	154	1/2+x,1/2-y,1/2+z
C9-H9…cg1	0.93	2.88	3.540(3)	129	1/2+x,1/2-y,-1/2+z
C12-H12…cg2	0.93	2.90	3.686(3)	143	-1/2+x,1/2-y,1/2+z
C18-H18…cg3	0.93	2.66	3.518(3)	153	-1/2+x,1/2-y,-1/2+z
C22-H22…cg3	0.93	2.56	3.389(3)	149	1/2+x,1/2-y,1/2+z
C25-H25A…cg2	0.96	2.87	3.704(4)	146	1/2+x,1/2-y,-1/2+z
			2		
C2-H16…F1	0.93	2.46	3.384(2)	173	2-x,1-y,1-z
C15-H9…O1	0.97	2.52	3.356(2)	144	-1+x,y,z
C12-H1…F1	0.93	2.55	3.352(2)	144	-x+1/2,+y+1/2,-z+1/2
C6-H11…O1	0.97	2.60	3.489(2)	153	-1/2+x,1/2-y,-1/2+z
C11-H5…cg1	0.93	2.70	3.5025(18)	145	1/2+x,1/2-y,1/2+z
C13-H6…cg1	0.93	2.67	3.4836(19)	146	-1/2+x,1/2-y,-1/2+z
C18-H13…cg2	0.93	2.86	3.4712(19)	124	-1/2+x,1/2-y,1/2+z
C3-H15…cg3	0.93	2.95	3.7322(18)	143	1/2+x,1/2-y,-1/2+z
			3		
C14-H7…O1	0.97	2.55	3.375(2)	142	1+x,y,z
C12-H8…cg1	0.93	2.81	3.614(3)	146	-1/2+x,1/2-y,-1/2+z
C16-H10…cg1	0.93	2.76	3.579(3)	147	1/2+x,1/2-y,1/2+z
C3-H18…cg2	0.93	2.96	3.545(3)	122	1/2+x,1/2-y,-1/2+z
			4		
C21-H21…O2	0.93	2.55	3.408(5)	154	x,-1+y,z
C11-H11…O2	0.93	2.47	3.376(5)	166	2-x,2-y,-z
C16-H16B…cg1	0.97	2.51	3.419(4)	157	1+x,y,z
cg1…cg1	-	-	3.945(2)	-	3-x,2-y,-z
cg1…cg2	-	-	3.750(2)	-	3-x,2-y,-z

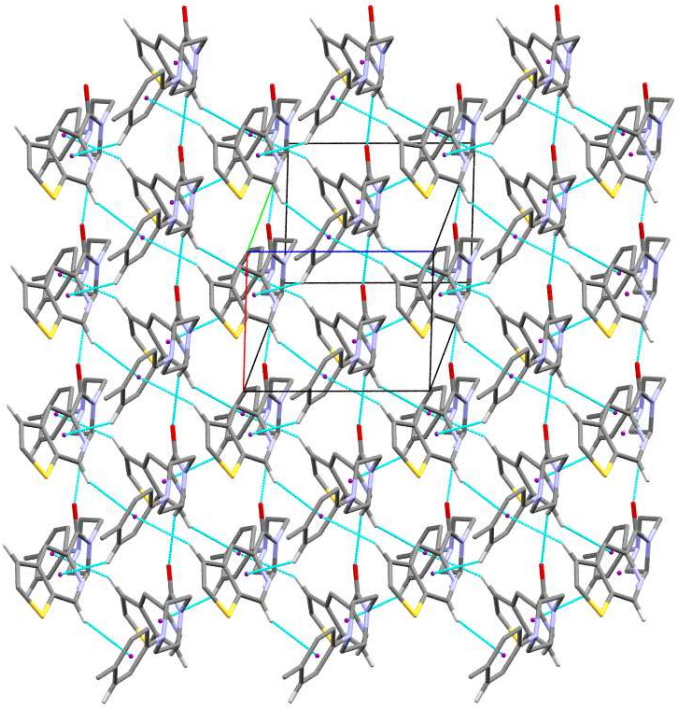


FIGURE 6Crystal packing of 3 displaying two dimensional architecture due to C-H…O and C-H…π interactions

The crystal structure of **4** features intermolecular interactions of the type C-H…O, C-H… π and π…π. The molecules of **4** are linked to one another via C21-H21…O2 interactions (Figure 7, Table 4) forming C(9) chains along *b* axis. The molecules in the adjacent chains are interconnected via C11-H11…O2 interactions to form $R_2^2(14)$ dimers (Figure 7) resulting in ribbon along *b* axis. The ribbons are stacked along *a* axis and are interconnected via C-H… π1 interactions (π1 being the centroid of the phenyl ring C13/C10/C8/C21/C24/C15) leading to a two dimensional architecture (Figure 7). Similar to **3**, C-H… π interactions in **4** play an important role in deciding the supramolecular architecture. The crystal structure is also stabilized by π2… π2 and π2… π3 interactions (Table 4)

where π2 is the centroid of the thiophene ring C18/C11/C22/S1/C17 and π3 is the centroid of the pyridine ring C7/C5/C18/C17/C12/N1.

CONCLUSION

Four 4-(aryl)-piperazin-1-yl](thieno[2,3-c]pyridin-5-yl)methanones (**1**-**4**) were synthesized and characterized by FTIR, ^{1}H NMR and LC-MS spectroscopic methods. The single crystals of all the compounds were grown, and their molecular & crystal structures were determined.

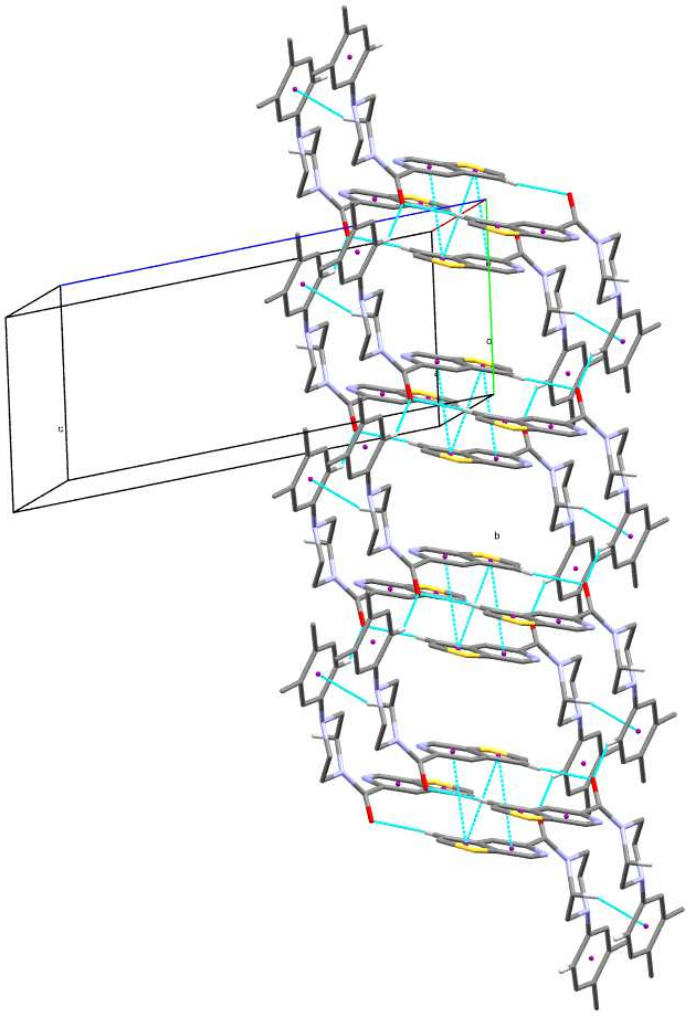


FIGURE 7Crystal packing of 4 displaying two dimensional architecture due to C-H…O and C-H…π interactions. π…π interactions are also shown

The molecular structures of all the compounds feature an intramolecular C-H…N hydrogen bond. In the crystal of **1**, three dimensional architecture is realised due to three different structure directing C-H…O interactions, while in **2**, C-H…F and C-H…O interactions generate a three dimensional structure. Several C-H…π interactions stabilize the crystal structures of both **1** and **2**andtheseinteractions have no structure directing characteristics. Unlike **1** and **2**, crystals of **3** and **4**display two dimensional networks formed by a combination of structure directing C-H…O and C-H…π interactions. Thus, the supramolecular architectures of **1**-**4** are built by various secondary interactions of the type C-H…O, C-H…F, C-H…π and π…π, and, varied combinations of these interactions directs different compounds to display different supramolecular architectures.

2. Supplementary Data

CCDC numbers 1060041, 1060042, 1060043 and 1060044 contain the supplementary crystallographic data for **1**, **2**, **3** and **4**respectively. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre 12, Union Road, Cambridge CB2 1EZ, UK; fax: (int.) +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk].

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