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3-Methyl-7-(2-thienyl)pyrido[2,3-*d*]-pyrimidine-2,4(1*H*,3*H*)-dione: π-stacked bilayers built from N—H···O, C—H···O and C—H···π hydrogen bonds

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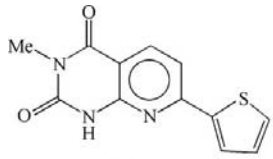
In the title compound, $C_{12}H_9N_3O_2S$, the thienyl substituent is disordered over two sets of sites with occupancies of 0.749 (3) and 0.251 (3). A combination of N—H···O, C—H···O and C—H···π hydrogen bonds links the molecules into bilayers and these bilayers are themselves linked into a continuous structure by π–π stacking interactions.

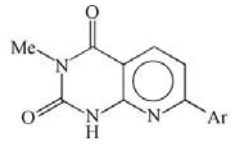
Comment

Pyrido[2,3-*d*]pyrimidines are interesting heterocycles because of their potential as bioactive derivatives, and as part of a general study of such systems we have recently reported the molecular and supramolecular structures of four 7-aryl substituted pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-diones, prepared by cyclocondensation of the corresponding 6-amino-pyrimidine-5-carbaldehyde and acetophenones under a BF_3–Et_2O catalysed fusion protocol (Trilleras *et al.*, 2009). Using a similar procedure, we have now prepared the title compound, (I), which is the 7-(2-thienyl) analogue of the compounds previously reported. The present synthesis utilized the cyclocondensation between 6-amino-5-formyl-2-methoxy-3-methylpyrimidin-4(3*H*)-one and 2-acetylthiophene, where the condensation was accompanied by the hydrolytic cleavage of the methoxy group at the 2-position. We report here the structure and supramolecular aggregation of (I) (Fig. 1).

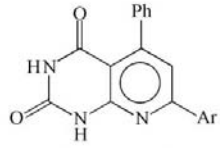
As commonly observed in systems containing 2-thienyl substituents, this group was found to be disordered over two sets of sites, corresponding to a 180° rotation about the C—C bond linking the thienyl and pyridine ring; the refined site occupancies are 0.749 (3) and 0.251 (3). The dihedral angles between the planes of the pyridine ring and the major and minor components of the 2-thienyl ring are 9.4 (3) and 6.1 (7)°, respectively, indicating that, for both orientations of the thienyl ring, the entire molecule is nearly planar, apart from the H atoms of the methyl group. The bond distances and angles throughout the molecule present no unusual values.



(I)



(II) Ar = 4-FC_6H_4
(III) Ar = 4-$MeOC_6H_4$



(IV) Ar = 4-ClC_6H_4

Three different types of hydrogen bond are present in the structure of (I) (Table 1). An N—H···O hydrogen bond links molecules related by translation into *C*(6) (Bernstein *et al.*, 1995) chains running parallel to the [001] direction, while two C—H···O hydrogen bonds, involving atoms C75 and C84 in the major and minor components of the 2-thienyl substituent, respectively, link molecules related by translation into *C*(10) chains running parallel to the [100] direction. The combination of these two chain motifs then generates an almost planar sheet of $R_4^4(28)$ rings lying parallel to (010) (Fig. 2).

Pairs of such sheets related by a *c*-glide plane are linked by a C—H···π(pyridine) hydrogen bond (Table 1) to form a bilayer (Fig. 3). Two such bilayers pass through each unit cell. The reference bilayer comprising sheets related by the *c*-glide plane at $y = \frac{3}{4}$ lies in the domain $\frac{1}{2} < y < 1.0$, and a second bilayer, related to the first by inversion and comprising sheets related to one another by the *c*-glide plane at $y = \frac{1}{4}$, lies in the

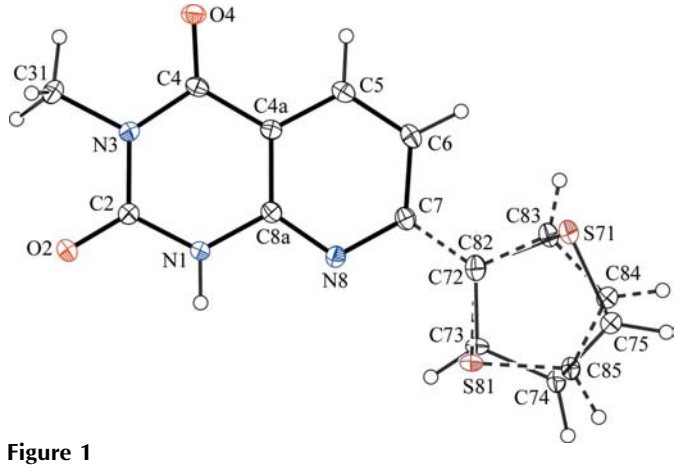


Figure 1
The molecular structure of compound (I), showing the disorder of the 2-thienyl group and the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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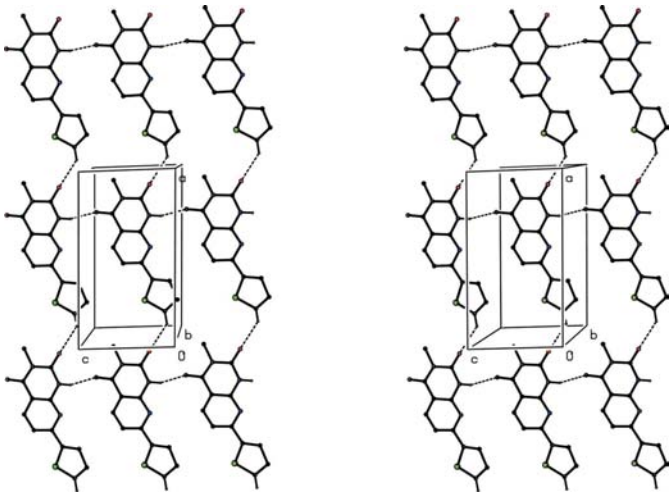

Figure 2
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded sheet of $R_4^4(28)$ rings lying parallel to (010). For the sake of clarity, only the major orientation of the 2-thienyl group has been shown and H atoms not involved in the motifs shown have been omitted.

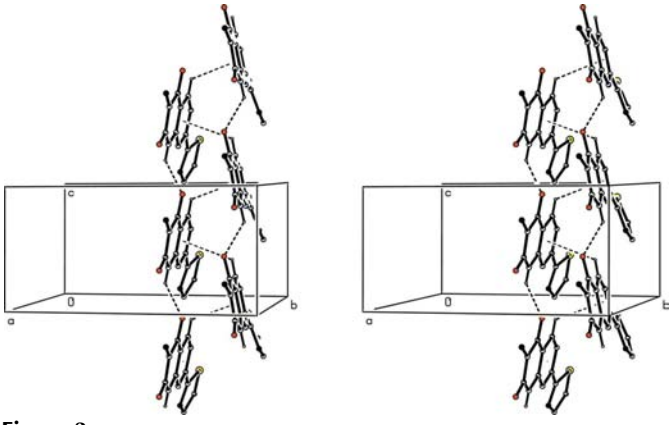

Figure 3
A stereoview of part of the crystal structure of compound (I), showing the C—H···π(pyridine) hydrogen bonds linking pairs of (010) sheets into bilayers. For the sake of clarity, only the major orientation of the 2-thienyl group has been shown and H atoms not involved in the motifs shown have been omitted.

domain $0.0 < y < \frac{1}{2}$. Each bilayer is linked to the two adjacent bilayers by means of a π–π stacking interaction. The pyridine rings in the molecules at (x, y, z) and $(1 - x, 1 - y, 1 - z)$ are strictly parallel, with an interplanar spacing of 3.420 (2) Å. The ring-centroid separation is 3.600 (2) Å, corresponding to a ring-centroid offset of 1.124 (2) Å (Fig. 4). Hence, all of the bilayers are linked into a single continuous structure.

In the analogues (II) and (III) (Trilleras *et al.*, 2009), which differ from compound (I) only in the identity of the substituent at position 7, the supramolecular aggregation is simpler than that in (I). In the 7-(4-fluorophenyl) compound, (II), the molecules are linked into $C(6)$ chains by an N—H···O hydrogen bond, and these chains are linked into sheets by a π–π stacking interaction, while in the 7-(4-methoxyphenyl) analogue, (III), similarly formed $C(6)$ chains are linked into sheets by two C—H···π(arene) hydrogen bonds.

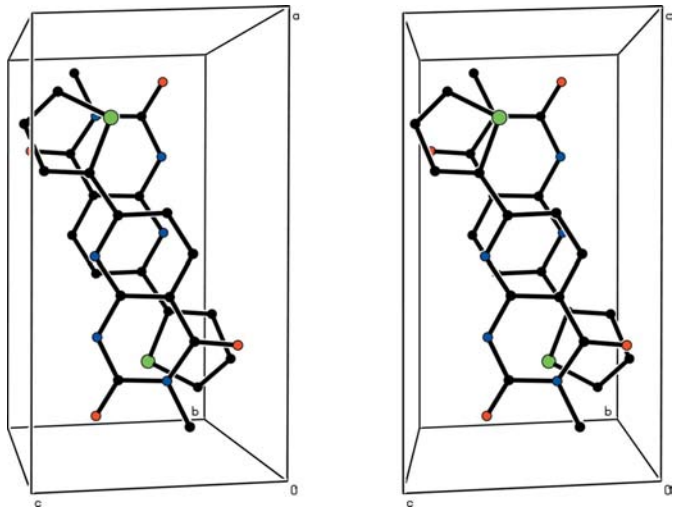

Figure 4
A stereoview of part of the crystal structure of compound (I), showing the π–π stacking interaction which links each hydrogen-bonded bilayer to its two immediate neighbours. For the sake of clarity, only the major orientation of the 2-thienyl group has been shown and all H atoms have been omitted.

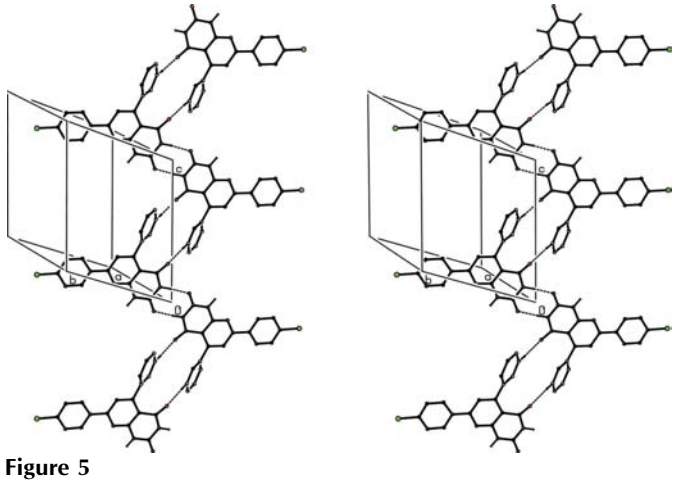

Figure 5
A stereoview of part of the crystal structure of compound (IV), showing the formation of a chain of centrosymmetric $R_2^2(8)$ and $R_2^2(16)$ rings. The original atomic coordinates (Wang *et al.*, 2006) have been employed. For the sake of clarity, the dimethylformamide component has been omitted, and H atoms not involved in the motifs shown have been omitted.

Somewhat similar in constitution to compounds (I)–(III) is the 7-(4-chlorophenyl)-5-phenyl analogue, (IV) [Cambridge Structural Database (Allen, 2002) refcode XEBCUD (Wang *et al.*, 2006)], which contains no *N*-methyl substituents and which crystallizes as a stoichiometric 1:1 solvate with dimethylformamide. Although the original report lists a number of hydrogen bonds, several of these are probably better described as short intermolecular contacts. However, no description was given of the structural consequences of these interactions. In fact, one of the N—H bonds is solely engaged in linking together the two independent molecular components by means of an N—H···O hydrogen bond, so that (IV) has just one N—H bond available for intermolecular hydrogen-bond formation, just as in compound (I). Analysis of the crystal structure of (IV) shows that a combination of

one N—H···O hydrogen bond and one C—H···O hydrogen bond [*cf.* the interactions in compound (I)] links the heterocyclic components in a chain of centrosymmetric rings running parallel to the [001] direction. Rings of $R_2^2(8)$ type centred at $(0, 0, n)$, where n represents an integer, alternate with rings of $R_2^2(16)$ type centred at $(0, 0, n+\frac{1}{2})$, where n again represents an integer (Fig. 5). The dimethylformamide molecules are pendent from this chain, but play no further role in the supramolecular aggregation. A single π–π stacking interaction, involving the pyridyl and chlorinated aryl rings, links adjacent chains of rings into sheets lying parallel to $(1\bar{1}0)$ Although the original authors (Wang *et al.*, 2006) provided a packing diagram for compound (IV), their selected view is of a plane normal to the [001] chain of rings, so that the formation of this chain is not readily apparent.

Hence, the combination of one N—H···O hydrogen bond and one C—H···O hydrogen bond gives rise to different structures in compounds (I) and (IV). A sheet generated solely by translation is formed in (I), and a chain of rings generated solely by inversion is formed in compound (IV). Similarly, the effects of the π–π stacking interactions are wholly different between compounds (I) and (IV).

Experimental

Equimolar quantities of 6-amino-5-formyl-2-methoxy-3-methyl-3*H*-4-pyrimidone and 2-acetylthiophene were mixed in the absence of solvent. Three drops of BF_3–Et_2O were added and the mixture was then heated in an oil bath at 443 K for 30 s. The resulting dark-brown solution was diluted with ethanol and cooled to ambient temperature to afford a precipitate that was collected by filtration, washed with fresh ethanol and then recrystallized from dimethylformamide to give the pure title compound as yellow crystals suitable for single-crystal X-ray diffraction (yield 60%, m.p. >573 K). HR–MS found: 259.0414; $C_{12}H_9N_3O_2S$ requires: 259.0415.

Crystal data

$C_{12}H_9N_3O_2S$
M_r = 259.29
Monoclinic, $P2_1/c$
a = 12.1969 (15) Å
b = 13.4010 (13) Å
c = 6.6071 (8) Å
β = 92.134 (11)°
V = 1079.2 (2) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.30 mm^{-1}
T = 120 K
0.20 × 0.20 × 0.20 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.885, T_{max} = 0.936
26230 measured reflections
2486 independent reflections
1746 reflections with $I > 2\sigma(I)$
R_{int} = 0.051

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.129
S = 1.06
2486 reflections
177 parameters
5 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

It was apparent from an early stage in the refinement that the 2-thienyl substituent was disordered. This ring was modelled using two sets of sites, corresponding to a 180° rotation about the inter-ring C—C bond, but it was found necessary to apply DFIX restraints (*SHELXL97*; Sheldrick, 2008) to the S—C and C—C distances in the minor component of this ring. In addition, the anisotropic displacement parameters for each pair of non-H atoms occupying essentially the same physical site (see Fig. 1) were set to be equal. Subject to these conditions, the site occupancies refined to 0.749 (3) and 0.251 (3), respectively, for the major and minor orientations. All H atoms were located in difference maps, apart from those in the minor component of the 2-thienyl ring, which were generated in calculated positions. All H atoms were then treated as riding atoms in geometrically idealized positions, with C—H = 0.98 (CH_3) or 0.95 Å (all other C—H), and N—H = 0.88 Å, with U_{iso}(H) = kU_{eq}(carrier), where k = 1.5 for the methyl group, which was permitted to rotate but not to tilt, and 1.2 for all other H atoms.

Table 1
Hydrogen-bond geometry (Å, °).

*Cg*1 is the centroid of the N8/C7/C6/C5/C4a/C8a ring.

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O4^{i}	0.88	2.13	2.839 (2)	137
C75—H75···O2^{ii}	0.95	2.39	3.155 (5)	138
C84—H84···O2^{ii}	0.95	2.21	3.116 (18)	160
C5—H5···*Cg*1^{iii}	0.96	2.89	3.478 (2)	121

Symmetry codes: (i) $x, y, z-1$; (ii) $x-1, y, z$; (iii) $x, -y+\frac{3}{2}, z+\frac{1}{2}$.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); structure solution: *SHELXS97* (Sheldrick, 2008); structure refinement: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3317). Services for accessing these data are described at the back of the journal.

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