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A dimeric layered structure of a 4-oxo-4,5-dihydropyrazolo[3,4-*d*]pyrimidine compound[1]

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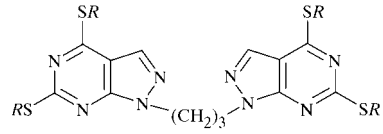
The title compound, 6-methylsulfanyl-1-(3-phenylpropyl)-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one, $C_{15}H_{16}N_4OS$, crystallizes in space group *Pbca*, with two molecules of similar structure in the asymmetric unit. The molecular structure shows the absence of intramolecular stacking in the crystalline state, as indicated by earlier ^{1}H NMR analysis in solution. In addition, the crystal packing reveals the formation of a layered structure, due mainly to intermolecular N—H···O═C hydrogen bonding and arene–arene interactions.

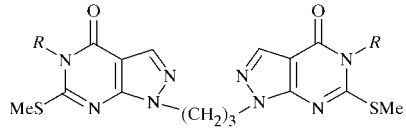
Comment

Interactions between aromatic units play a significant role in chemistry (Hunter, 1994), crystal engineering (Desiraju, 1995) and biology. Recently, we have reported the convenient syntheses of 1,3-bis(4,6-dimethylthio-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)propane, (I) (Avasthi *et al.*, 1995), and 1,1′-(1,3-propanediyl)bis(5-methyl-6-methylthio-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one, (II) (Avasthi *et al.*, 1998), and X-ray studies (Biswas *et al.*, 1995; Maulik *et al.*, 1998) of two novel 'propylene-linker' compounds based on pyrazolo[3,4-*d*]-pyrimidines. More recently, the ethyl analogues 1,3-bis(4,6-diethylthio-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)propane, (III), and 1,1′-(1,3-propanediyl)bis(5-ethyl-6-methylthio-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one, (IV), of compounds (I) and (II) have been synthesized, and X-ray analysis of these compounds also showed inter- and intramolecular stacking (Avasthi, Rawat *et al.*, 2001; Avasthi, Aswal & Maulik, 2001).

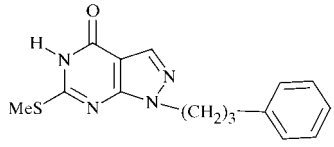
Efforts to crystallize the intermediate compound, (V), obtained during the transformation of (I) to (II) or (I) to (IV), were not successful. This common intermediate, (V), is a cyclic amide (lactam) and is capable of intermolecular dimerization similar to that of 2(1*H*)-pyridone (Gallant *et al.*, 1991) and 4(3*H*)-pyrimidone (Vaillancourt *et al.*, 1998). Due to the fact that all four compounds, (I)–(IV), showed inter- and intramolecular stacking, it became important to obtain more structural information about the common intermediate, (V). In this communication, we present an indirect strategy for the structural analysis of intermediate (V).



(I) *R*=Mc
(III) *R*=Et



(II) *R*=Mc
(IV) *R*=Et
(V) *R*=H



(VI)

Since hydrogen bonding is a much stronger non-covalent interaction than stacking interactions (Muller-Dethlefs & Hobza, 2000; Desiraju & Steiner, 1999), synthesis of the new title compound, (VI), was envisioned. This compound is capable of hydrogen bonding similar to that in intermediate (V), from a crystal engineering point of view (Desiraju, 1995). Structurally, the new compound, (VI), is obtained by the replacement of one pyrazolo[3,4-*d*]pyrimidinyl moiety in intermediate (V) by another typical aromatic moiety, namely phenyl, which is well known for its stacking interactions (Desiraju & Steiner, 1999).

Fig. 1 shows the molecular structure and conformation of (VI) with the atomic numbering scheme. There are two molecules in the asymmetric unit. Selected torsion angles are

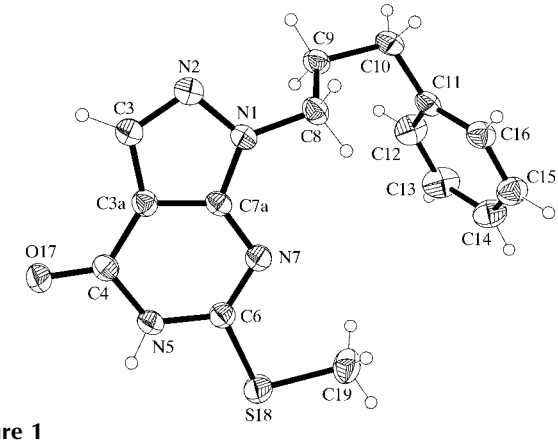


Figure 1
A view of (VI) showing the molecular structure and crystallographic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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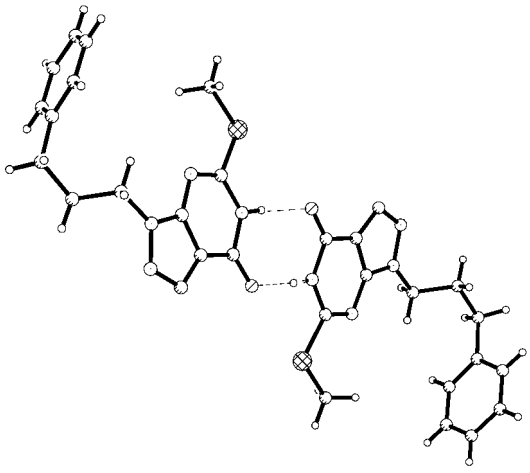

Figure 2
A view of (VI) showing the dimerization due to C—H···O bonding.

listed in Table 1. The planar phenyl rings make angles of 70.7 (1) and 80.7 (1)° with the heterocyclic ring systems in the two molecules. The central angles at the trimethylene bridge, C8—C9—C10 111.1 (2)° and C8′—C9′—C10′ 112.3 (2)°, are quite similar in the two molecules. For comparison, these angles for the intramolecularly stacked (folded) compounds (I)–(IV) are 114.1 (2), 115.2 (2), 113.5 (2) and 114.9 (2)°, respectively.

In the molecule of (VI), intramolecular stacking is absent. However, the molecule is not fully extended. The phenyl ring is somewhat tilted towards the heterocyclic ring, due to C—H···π and C—H···N interactions (Fig. 1). One H atom on C8 shares hydrogen bonding with atoms C11 and C16 of the phenyl ring, due to C—H···π interactions (H8*A*···C11 2.67 and H8*A*···C16 2.89 Å).

The molecule of (VI) can be visualized as consisting of one polar end (with the lactam moiety as the head group) capable of strong intermolecular hydrogen bonding, and a non-polar end (with the phenyl moiety as the tail group) capable of stacking interactions. Strong intermolecular hydrogen bonding of the type N—H···O=C [N5—H5···O17, with N···O distances of 2.794 (3) and 2.796 (3) Å, and angles of 168.9 and 174.8°] among the lactam moieties of the two molecules results in the formation of a dimeric structure (Fig. 2). At the non-polar end, phenyl C atoms interact with neighbouring phenyl C atoms (minimum C···C distance 3.94 Å) and a methylene H atom (C10···C14 3.88 Å, H10*A*···C14 2.98 Å and C10—H10*A*···C14 155.4°) through a C—H···π interaction. Thus, strong intermolecular hydrogen bonding among the polar lactam moieties and weak intermolecular C—H···π interactions in the non-polar moieties result in the formation of a layered structure with head-to-head and tail-to-tail packing arrangements (Fig. 3). To the best of our knowledge, this is the first such example based on the pyrazolo-[3,4-*d*]pyrimidine heterocycle where a layered structure is formed by involvement of a bilayer-type structure.

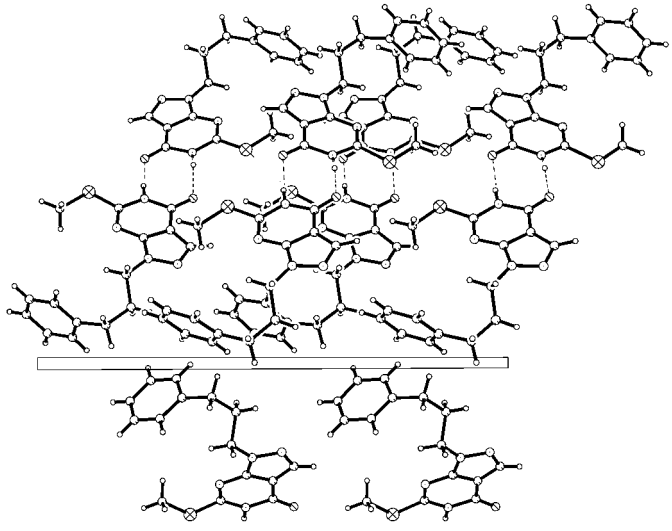

Figure 3
A packing diagram for (VI) showing the layered structure consisting of alternate columns formed by strong intermolecular dimeric hydrogen bonding (dashed lines) and weak stacking interactions (bar).

In conclusion, the crystal structure of (VI) clearly shows that the simultaneous presence of inter- and/or intramolecular stacking interactions, along with hydrogen bonding in intermediate (V), are the most likely reasons for not allowing the formation of a single crystal of (V) for crystallography. As compound (VI) does not have competing intramolecular stacking interactions, stronger hydrogen-bonding interactions take full control during crystallization, resulting in the formation of a beautiful dimeric layered structure. It is also important to mention here that the observation of such a dimeric structure for (VI) is significant, due to its isomeric relationship with purines and pyrimidines, which play a critical biological role in the self-association of nucleic acids.

Experimental

Compound (VI) was synthesized (Avasthi & Rawat, 2001) by the reaction of 4,6-bis(methylthio)-1*H*-pyrazolo[3,4-*d*]pyrimidine (Taylor *et al.*, 1966) with commercial 1-bromo-3-phenylpropane using the general methodology described earlier by Avasthi *et al.* (1993). Diffraction quality crystals of (VI) were obtained by slow evaporation of an ethyl acetate–hexane solution at room temperature.

Crystal data

$C_{15}H_{16}N_4OS$
M_r = 300.38
Orthorhombic, *Pbca*
a = 9.4742 (8) Å
b = 19.287 (1) Å
c = 33.032 (2) Å
V = 6035.8 (7) Å^3
Z = 16
D_x = 1.322 Mg m^{-3}
Cu *K*α radiation
Cell parameters from 25 reflections
θ = 9.1–11.9°
μ = 1.94 mm^{-1}
T = 293 (2) K
Block, colourless
0.35 × 0.25 × 0.15 mm

Table 1
Selected torsion angles (°).

C7a—N1—C8—C9	110.9 (3)	C7a′—N1′—C8′—C9′	−130.1 (3)
N2—N1—C8—C9	−68.2 (3)	N2′—N1′—C8′—C9′	50.3 (4)
N1—C8—C9—C10	−173.7 (2)	N1′—C8′—C9′—C10′	173.2 (2)
C8—C9—C10—C11	65.4 (3)	C8′—C9′—C10′—C11′	−67.7 (4)
C9—C10—C11—C16	−106.1 (3)	C9′—C10′—C11′—C12′	−76.0 (3)
C9—C10—C11—C12	71.8 (3)	C9′—C10′—C11′—C16′	100.3 (3)

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.703, T_{max} = 0.747
5179 measured reflections
5179 independent reflections
4176 reflections with $I > 2\sigma(I)$
θ_{max} = 67.9°
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 20$
$l = 0 \rightarrow 39$
2 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.190
S = 1.52
5179 reflections
380 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.39 e Å^{-3}
Extinction correction: *SHELXTL-NT* (Bruker, 1997)
Extinction coefficient: 0.00029 (8)

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXTL-NT* (Bruker, 1997); molecular graphics: *SHELXTL-NT*; software used to prepare material for publication: *SHELXTL-NT*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE1182). Services for accessing these data are described at the back of the journal.

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