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A stacked pyrazolo[3,4-*d*]pyrimidine-based flexible molecule: the effect of a bulky benzyl group on intermolecular stacking in comparison with methyl and ethyl groups[1]

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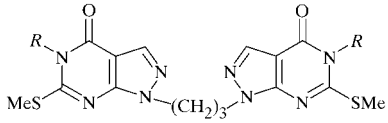
In the crystal structure of 1,1′-(1,3-propanediyl)bis(5-benzyl-6-methylsulfanyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one), $C_{29}H_{28}N_8O_2S_2$, the pairs of pyrazolo[3,4-*d*]pyrimidine rings stack as a result of intramolecular π–π interactions between the heterocyclic rings. The folded molecules are further stacked in pairs, due to intermolecular aromatic π–π interactions and C—H···O hydrogen bonds.

Comment

Interactions between aromatic units play a significant role in chemistry (Muller-Dethlefs & Hobza, 2000; Hunter *et al.*, 2001; Tsuzuki *et al.*, 2002), crystal engineering (Desiraju, 1995) and biology. In recent years, we have reported the convenient syntheses (Avasthi *et al.*, 1995, 1998; Avasthi, Rawat *et al.*, 2001) and the X-ray structures (Biswas *et al.*, 1995; Maulik *et al.*, 1998, 2000; Avasthi, Rawat *et al.*, 2001; Avasthi, Aswal & Maulik, 2001) of several novel 'propylene-linker' compounds based on the pyrazolo[3,4-*d*]pyrimidine core, which is isomeric with biologically important purine, as flexible new models for studying aromatic π–π interactions (APPI). Two of these compounds, *viz.* 1,1′-(1,3-propanediyl)bis(5-methyl-6-methylthio-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one), (I), and 1,1′-(1,3-propanediyl)bis(5-ethyl-6-methylthio-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one), (II), show inter- and intramolecular stacking due to APPI (Maulik *et al.*, 1998; Avasthi, Aswal & Maulik, 2001) when studied using X-ray crystallography. Since the X-ray structures of (I) and (II) are quite similar in having a U-motif for the demonstration of inter- and intramolecular stacking, it was considered worthwhile to replace the *N*-methyl/ethyl group of (I) and (II) with a bulky *N*-benzyl group, to determine the robustness of the U-motif and its consequence for the intermolecular stacking from a crystal engineering point of view. In this communication, we report the X-ray structure of 1,1′-(1,3-propanediyl)bis(5-benzyl-6-methylsulfanyl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-one), (III), the synthesis of which was described previously by Avasthi *et al.* (1998).



(I) R = Me
(II) R = Et
(III) R = CH_2Ph

The molecular structure and conformation of (III) are shown in Fig. 1. The structure is folded at the centre of the bridge [C10—C11—C12 114.0 (2)°] due to an intramolecular APPI between the pyrazolo[3,4-*d*]pyrimidine rings. For comparison, the folding angles in (I) and (II) are 115.2 (2) and 114.9 (2)°, respectively. In compound (III), as in (I) and (II), the folded pyrazolo[3,4-*d*]pyrimidine rings are positioned in

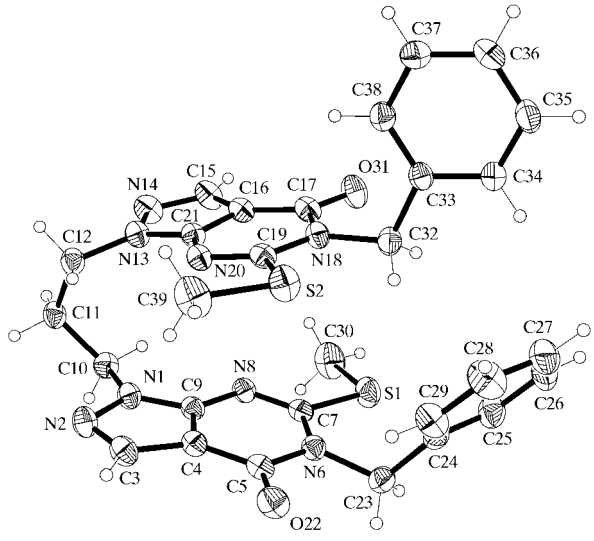


Figure 1
A displacement ellipsoid plot (30% probability), showing the molecular structure of (III) and the atom-labelling scheme.

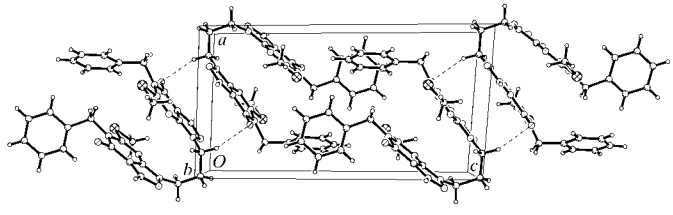


Figure 2
A crystal-packing diagram for (III), showing the intra- and intermolecular π–π stacking between the pyrazolo[3,4-*d*]pyrimidine rings and the intermolecular C—H···O hydrogen bonding (dashed lines).

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such a way that the pyrimidinyl rings overlap only partially. The overlapping six-membered rings are separated by an average distance of 3.428 (3) Å [*cf.* 3.37 (1) Å in (I) and 3.415 (3) Å in (II)], thus confirming the presence of intramolecular APPI.

The pyrazolo[3,4-*d*]pyrimidine rings in (III) are nearly planar [maximum deviation = −0.048 (2) Å] and the angle between the least-squares planes is 14.5 (1)° [*cf.* 12.4 (5)° in (I) and 12.5 (1)° in (II)]. The crystal packing (Fig. 2) shows further independent intermolecular stacking between the pyrazolo[3,4-*d*]pyrimidine systems due to π–π interactions. Pairs of pyrazolo[3,4-*d*]pyrimidine rings [related by symmetry code $(1-x, 1-y, -z)$] overlap, with an interplanar separation of 3.370 (2) Å in a 'parallel-displaced' orientation [the dihedral angle of a stacking pair is 1.0 (1)°].

Interestingly, these stacked pyrazolo[3,4-*d*]pyrimidine rings are also connected by intermolecular C—H···O hydrogen bonding (Table 1; Desiraju & Steiner, 1999). Thus, the combination of intra- and intermolecular APPI and intermolecular hydrogen bonding results in the formation of a stacked dimeric unit of (III). The continuous intermolecular stacking present in (I) and (II) is absent in (III). The crystal structure of (III) is stabilized mainly by C—H···O bonding, π–π interactions and van der Waals forces.

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

D—H···A	D—H	H···A	D···A	D—H···A
C10—H10A···O22^{i}	0.97	2.47	3.367 (3)	154

Symmetry code: (i) $1-x, 1-y, -z$.

Experimental

Compound (III) was synthesized according to the method of Avasthi *et al.* (1998). Diffraction-quality crystals were obtained by slow evaporation of an ethyl acetate solution at room temperature.

Crystal data

$C_{29}H_{28}N_8O_2S_2$
M_r = 584.71
Triclinic, $P\overline{1}$
a = 9.150 (1) Å
b = 9.491 (1) Å
c = 16.839 (2) Å
α = 83.01 (1)°
β = 85.26 (1)°
γ = 76.39 (1)°
V = 1408.5 (3) Å^3
Z = 2
D_x = 1.379 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 38 reflections
θ = 4.8–12.5°
μ = 0.23 mm^{-1}
T = 293 (2) K
Rectangular, colourless
0.35 × 0.28 × 0.25 mm

Data collection

Bruker $P4$ diffractometer
$\theta/2\theta$ scans
6623 measured reflections
5527 independent reflections
3716 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 26°
$h = -1 \rightarrow 11$
$k = -11 \rightarrow 11$
$l = -20 \rightarrow 20$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.121
S = 1.01
5527 reflections
372 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0470P)^2 + 0.5548P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Bruker, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: VJ1169). Services for accessing these data are described at the back of the journal.

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