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

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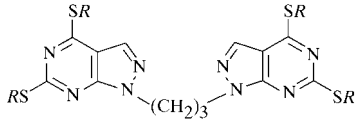
In the crystal structure of 1,3-bis(4,6-diisopropylsulfanyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)propane, $C_{25}H_{36}N_8S_4$, the pairs of pyrazolo[3,4-*d*]pyrimidine rings in the molecule stack as a result of intramolecular π–π interactions between the heterocyclic rings. The crystal packing also exhibits an intermolecular C—H$\cdots\pi$ interaction between one methyl group of an isopropyl group and a pyrazolo[3,4-*d*]pyrimidine ring.

Comment

Interactions between aromatic moieties are known to play an important role in chemistry (Desiraju & Steiner, 1999; Hunter *et al.*, 2001; Tsuzuki *et al.*, 2002), stabilization of DNA/RNA structures (Hobza & Sponer, 1999), crystal engineering (Desiraju, 1995) and drug development (Meyer *et al.*, 2003). Use of a polymethylene and especially a trimethylene linker for demonstrating intramolecular stacking was pioneered by Browne *et al.* (1968) and early work was reviewed by Leonard (1979). In 1995, we reported the first synthesis (Avasthi *et al.*, 1995) and crystal structure determination (Biswas *et al.*, 1995) of a trimethylene-linker molecule, (I), based on the pyrazolo[3,4-*d*]pyrimidine core, which is isomeric with the biologically important purine system. The crystal structure exhibits both an unusual intramolecular stacking (U-motif) and intermolecular stacking. The robustness of the U-motif in (I) has been further demonstrated by the crystal structure determination of the ethyl analog, (II) (Avasthi, Rawat *et al.*, 2001), and other related propylene-linker compounds (Maulik *et al.*, 1998; Avasthi, Aswal & Maulik, 2001; Avasthi, Tewari *et al.*, 2002). Interestingly, no intramolecular stacking is observed when the trimethylene linker is replaced by an ethylene (Avasthi, Rawat *et al.*, 2001) or tetramethylene linker (Maulik *et al.*, 2000; Avasthi, Farooq *et al.*, 2002). We report here the structure of 1,3-bis(4,6-diisopropylsulfanyl-1*H*-pyrazolo[3,4-*d*]-pyrimidin-1-yl)propane, (III).



(I) $R = CH_3$
(II) $R = C_2H_5$
(III) R = i-C_3H_7

The conformation of (III) is shown in Fig. 1. The asymmetric unit contains only half of the molecule, which is related to the other half by the crystallographic symmetry operation $(1-x, y, \frac{1}{2}-z)$. The molecule is folded at the centre of the bridge [C8—C9—C8*A* = 113.9 (2)°] as a result of intramolecular stacking between the pyrazolo[3,4-*d*]pyrimidine rings. For comparison, the corresponding angles in (I) and (II) are 114.1 (2) and 113.5 (2)°, respectively. In (III), as in (I) and (II), the two pyrazolo[3,4-*d*]pyrimidine rings are positioned in such a way that only part of the pyrimidine rings overlap (Fig. 1). The overlapping six-membered rings are separated by an average distance (the mean value of the distances of all the atoms in one ring from the least-squares plane through the atoms in the other ring) of 3.555 (2) Å [3.4 (4) and 3.37 (4) Å in (I) and (II), respectively], thus confirming the presence of an intramolecular π–π interaction. The pyrazolo[3,4-*d*]-pyrimidine rings in (III), like those in (I) and (II), are nearly planar [maximum deviation = −0.036 (1) Å] and the angle between the least-squares planes is 21.96 (4)° [13.2 (1)° in both (I) and (II)]. It appears that because the isopropyl group is bulkier than the methyl/ethyl groups, the average intramolecular distance [3.555 (2) Å] and angle [21.96 (4)°] between the least-squares planes have increased appreciably. However, the most striking effect of the presence of the isopropyl group instead of the methyl/ethyl groups found in (I) and (II) is seen

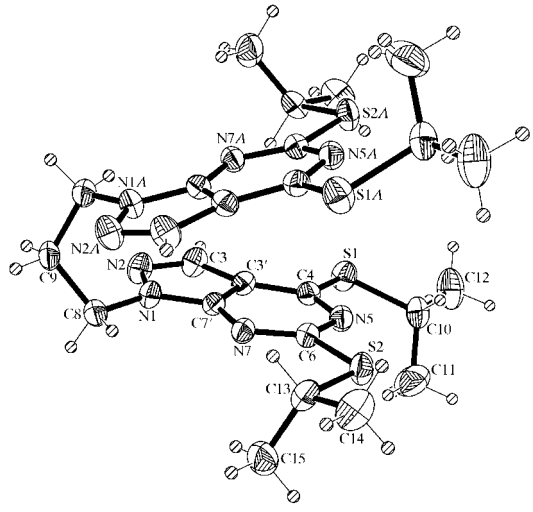


Figure 1
Displacement ellipsoid plot (30% probability) showing the molecular structure of (III) and the atomic labelling scheme. [Symmetry code: (*A*) $1-x, y, -z+\frac{1}{2}$.]

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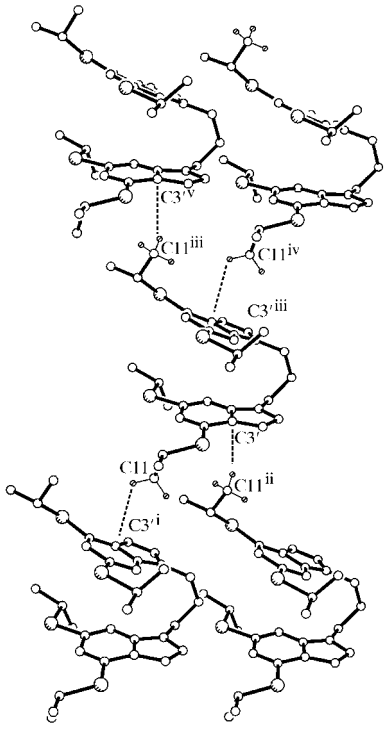

Figure 2
Crystal-packing diagram of (III), showing the intermolecular C—H···π-stacking interactions (dashed lines) between the pyrazolo[3,4-*d*]pyrimidine rings. [Symmetry codes: (i) $\frac{3}{2}-x,\frac{1}{2}-y,\frac{1}{2}-z$; (ii) $\frac{3}{2}-x,\frac{1}{2}+y,\frac{1}{2}-z$; (iii) $1-x,y,\frac{1}{2}-z$; (iv) $x-\frac{1}{2},\frac{1}{2}+y,z$; (v) $x-\frac{1}{2},y-\frac{1}{2},z$.]

in the packing diagram of (III) (Fig. 2). Molecule (III) does not exhibit intermolecular stacking due to the π–π interaction but instead exhibits an intermolecular C—H···π interaction (Fig. 2) between one methyl group of an isopropyl group and the adjacent C3′ atom of the pyrazolo[3,4-*d*]pyrimidine ring (H···C3′ = 3.14 Å). In conclusion, replacement of the methyl or ethyl group in (I) or (II) by a bulky isopropyl group does not seriously affect the robustness of the U-motif formed by intramolecular stacking due to the aromatic π–π interaction. However, the parallel mode of intermolecular stacking seen in (I) and (II) is not present in (III) but is replaced by a C—H···π interaction.

Experimental

Compound (III) was prepared by stirring a mixture of 4,6-diisopropylsulfanyl-1*H*-pyrazolo[3,4-*d*]pyrimidine and 1,3-dibromopropane in dimethylformamide in the presence of anhydrous potassium carbonate (Avasthi *et al.*, 1995). Diffraction-quality crystals were prepared by slow evaporation from a 1:1 solution of methanol and butanol at room temperature.

Crystal data

$C_{25}H_{36}N_8S_4$
M_r = 576.90
Monoclinic, *C*2/*c*
a = 21.044 (2) Å
b = 8.814 (1) Å
c = 18.953 (2) Å
β = 118.07 (1)°
V = 3101.9 (6) Å^3
Z = 4
D_x = 1.235 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 44 reflections
θ = 3.9–12.5°
μ = 0.34 mm^{-1}
T = 293 (2) K
Rectangle, colourless
0.30 × 0.28 × 0.20 mm

Data collection

Bruker *P*4 diffractometer
θ–2θ scans
3403 measured reflections
2738 independent reflections
2352 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 25.0°
$h = -24 \rightarrow 1$
$k = -1 \rightarrow 10$
$l = -20 \rightarrow 22$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.094
S = 1.03
2738 reflections
173 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0402P)^2 + 1.8299P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0045 (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: DE1217). Services for accessing these data are described at the back of the journal.

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