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N-[2-(Azepan-1-yl)-9-isopropyl-9*H*-purin-6-yl]-4-methoxybenzylamine

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.002 Å
R factor = 0.035
wR factor = 0.097
Data-to-parameter ratio = 13.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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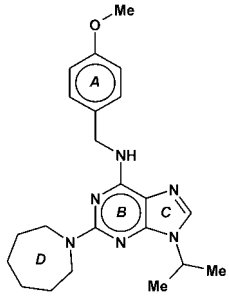
The title compound, $C_{22}H_{30}N_6O$, is a potent inhibitor of estrogen sulfotransferase which catalyses the transfer of a sulfuryl group from 3′-phosphoadenosine 5′-phosphosulfate to estrogen and estrogen-like compounds. The pyrimidine plane forms dihedral angles of 81.53 (4) and 2.99 (4)° with the benzene and imidazole rings, respectively. The crystal structure is stabilized by N—H···N hydrogen bonds connecting two adjacent molecules, thus forming centrosymmetric dimers, the N···N distance being 3.0403 (16) Å.

Comment

The search for new human anticancer drugs has resulted in the synthesis of a large series of variously 2,6,9-trisubstituted purine derivatives. Some of the organic molecules of this type, namely N6,C2,N9-adenine derivatives, belong to a group of cytokinin-derived compounds. It has been found that some of those compounds behave as potent inhibitors of cyclin-dependent kinases (CDKs) and show cytotoxic activity against some of the human cancer cell lines. In general, the CDKs are a family of serine-threonine protein kinases which control cell cycle progression in proliferating eukaryotic cells. For example, roscovitine, olomoucine and bohemine belong to this family of compounds (Veselý *et al.*, 1994; Oh *et al.*, 2001). A few years ago, we focused our attention on the preparation and characterization of such compounds and on the synthesis of transition metal complexes containing these organic molecules as ligands (Trávníček *et al.*, 2001, 2003).



(I)

The title compound, (I), also known as NG38, is a potent inhibitor of estrogen sulfotransferase (EST) which catalyses the transfer of a sulfuryl group from 3′-phosphoadenosine 5′-phosphosulfate to estrogen and estrogen-like compounds (Verdugo *et al.*, 2001). EST is one of the best characterized sulfotransferases and its X-ray structure with bound estrogen and 3′,5′-diphosphoadenosine has already been determined (Kakuta *et al.*, 1997).

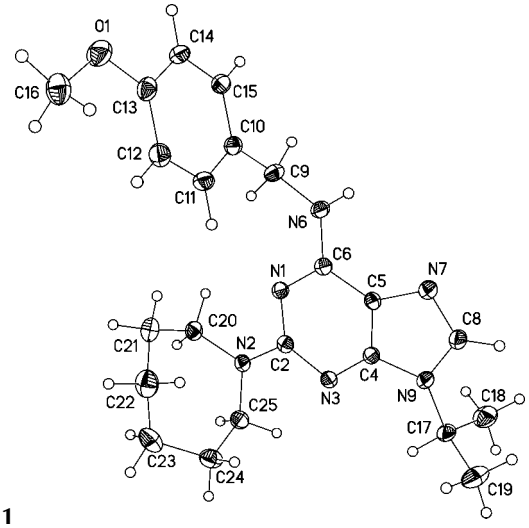


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres at arbitrary radii.

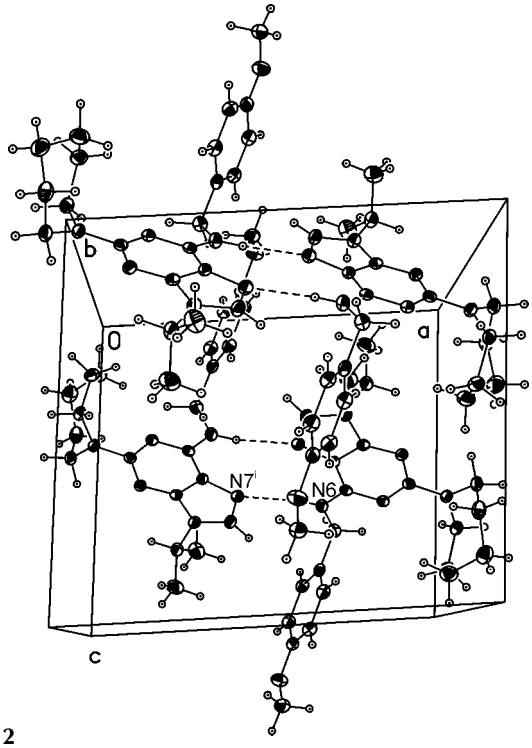


Figure 2
Part of the crystal structure of (I), showing the hydrogen bonding (as dashed lines) and molecular pairing [symmetry code: (i) $1-x, -y, 1-z$].

The crystal structure of (I) consists of discrete molecules (Fig. 1) which are linked by N6—H6$A\cdots$N7^{i} hydrogen bonds [symmetry code: (i) $1-x, -y, 1-z$] to form centrosymmetric dimers (Fig. 2 and Table 2). The molecular structure of (I) is very similar to those determined for (*R*)- and (*S*)-roscovitine (Wang *et al.*, 2001). While the interatomic parameters of the pyrimidine ring are typical for this aromatic system, a double bond is localized in the imidazole ring between atoms N7 and C8 [N7—C8 = 1.3143 (17) Å; Table 1)]. Atoms forming the benzene (*A*), pyrimidine (*B*) and imidazole (*C*) rings deviate slightly from planarity, the greatest deviations being 0.0052 (14), 0.0275 (12) and 0.0070 (12) Å, respectively. The dihedral angles between rings *A* and *B* is 81.53 (4)°, and between *B* and *C* is 2.99 (4)° (Nardelli, 1995). The torsion angles C6—N6—C9—C10, C9—N6—C6—C5 and N6—C9—C10—C15 are 115.22 (13), 172.40 (11) and 129.03 (13)°, respectively. The hexamethyleneimine ring *D* is in a chair conformation. The Cremer–Pople puckering parameters (Cremer & Pople, 1975) are Q_T = 0.7952 (17) Å, Θ_2 = 36.44 (14)°, $\varphi_2 = -124.76$ (20)° and φ_3 = 138.52 (16)°.

Experimental

The title compound, (I), was synthesized by a general procedure for preparation of 2,6,9-substituted purine derivatives as described in the literature (Imbach *et al.*, 1999). White crystals suitable for single-crystal X-ray analysis were obtained by recrystallization from ethanol. Elemental analysis (CHN Analyzer Flash EA 1112, ThermoFinnigen), calculated for $C_{22}H_{30}N_6O$: C 66.98, H 7.66, N 21.30%; found: C 66.64, H 7.58, N 21.28%.

Crystal data

$C_{22}H_{30}N_6O$
M_r = 394.52
Monoclinic, $P2_1/c$
a = 11.8709 (9) Å
b = 16.2732 (10) Å
c = 10.8433 (7) Å
β = 94.656 (6)°
V = 2087.8 (2) Å^3
Z = 4
D_x = 1.255 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4123 reflections
θ = 2.2–30.4°
μ = 0.08 mm^{-1}
T = 100 (2) K
Prism, white
0.30 × 0.30 × 0.20 mm

Data collection

Oxford Diffraction Xcalibur2 (Sapphire2 CCD) diffractometer
ω scans
Absorption correction: none
9776 measured reflections
3625 independent reflections
3104 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 25.0°
$h = -14 \rightarrow 12$
$k = -19 \rightarrow 14$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.097
S = 1.06
3625 reflections
262 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0539P)^2 + 0.4543P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C6	1.3372 (17)	C4—C5	1.3804 (18)
N1—C2	1.3571 (16)	C5—N7	1.3962 (17)
N2—C2	1.3625 (17)	C5—C6	1.4104 (18)
C2—N3	1.3482 (16)	N6—C6	1.3494 (16)
N3—C4	1.3387 (17)	N7—C8	1.3143 (17)
C4—N9	1.3751 (16)	C8—N9	1.3696 (17)
C6—N1—C2	118.99 (11)	N7—C5—C6	133.57 (12)
N3—C2—N1	127.46 (12)	N1—C6—N6	119.43 (11)
C4—N3—C2	110.77 (10)	N1—C6—C5	118.86 (11)
N3—C4—N9	125.93 (11)	N6—C6—C5	121.71 (12)
N3—C4—C5	128.19 (12)	C8—N7—C5	103.50 (11)
N9—C4—C5	105.88 (11)	N7—C8—N9	113.95 (12)
C4—C5—N7	110.71 (11)	C8—N9—C4	105.95 (10)
C4—C5—C6	115.55 (12)		
C9—N6—C6—C5	172.40 (11)	N6—C9—C10—C15	129.03 (13)
C6—N6—C9—C10	115.22 (13)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N6—H6A···N7^{i}	0.88	2.19	3.0403 (16)	164

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

H atoms attached to C and N atoms were positioned geometrically, with C—H distances of 0.95, 0.98 and 0.99 Å and an N6—H6A distance of 0.88 Å, and with U_{iso}(H) values of $1.2U_{eq}$(C,N) for CH, CH_2 and NH H atoms, and $1.5U_{eq}$(C) for methyl H atoms.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2003); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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