

## 8-Chloro-7-(2,6-dichlorobenzyl)-1,3-dimethyl-7H-purine-2,6(1H,3H)-dione

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Received 29 July 2004

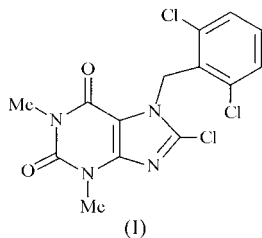
Accepted 17 September 2004

Online 18 December 2004

The title compound,  $C_{14}H_{11}Cl_3N_4O_2$ , consists of two planar fragments which are nearly perpendicular to one another. The crystal packing is controlled by intra- and intermolecular C—H $\cdots$ O hydrogen bonds, and Cl $\cdots$ phenyl-ring-centroid and weak stacking interactions.

## Comment

The presence of an *ortho*-halogen-substituted phenyl ring in purine systems is characteristic of many marketed (*e.g.* Adipiodone, Guanfacine or Loviride) or emerging drugs in pharmacology. Knowledge of the three-dimensional structures of these compounds forms the basis for understanding the mechanism of their pharmaceutical action, and it is also necessary for the modeling of docking in the study of the biological activity of these compounds. Against this background, we present here the crystal structure of 8-chloro-7-(2,6-dichlorobenzyl)-1,3-dimethyl-7H-purine-2,6-dione, (I).



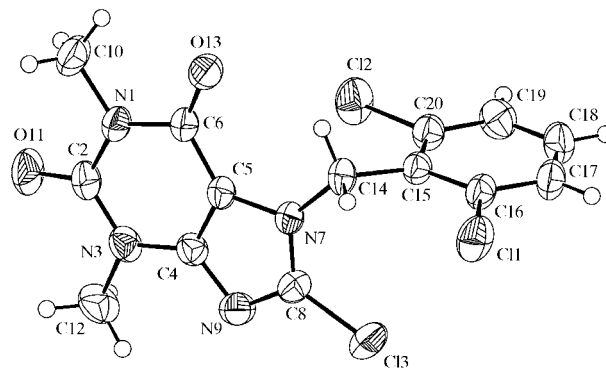
The molecular structure of (I) (Fig. 1) is characterized by two planar fragments, one formed by the heterocyclic system (N1/C2/N3/C4—C6/N7/C8/N9/C14) and the other based on the benzyl substituent (C14—C20); the dihedral angle between these two planes is 86.75 (4)°. A search of the Cambridge Structural Database (CSD, Version 5.25; Allen, 2002) revealed 126 derivatives of 7H-purine-2,6-dione. The bond lengths and angles of (I) have values which are characteristic of these compounds.

The molecular packing of (I) (Fig. 2) is characterized by two C—H $\cdots$ O hydrogen bonds, one intramolecular and the other

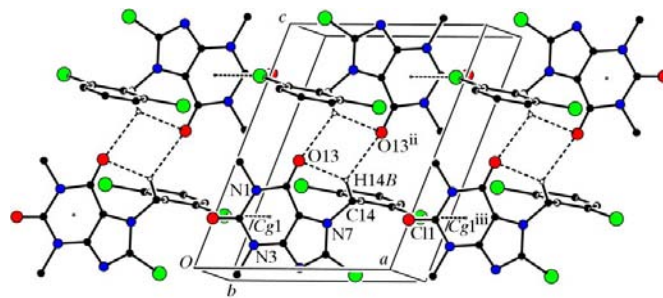
intermolecular; details are given in Table 1. The intramolecular C—H $\cdots$ O bond corresponds to a moderate hydrogen bond (Gilli, 2002) and results in an additional five-membered ring in the molecule, coplanar with the purine system; the C8—N7—C14—C15 torsion angle is 58.3 (2)°. The formation of the hydrogen bond is promoted by electron-acceptor substituents at C14. Most probably, the same type of hydrogen bond also occurs in the molecule of 7-(2,6-dichlorobenzyl)-8-(3-oxocyclopentyl)-1,3-dipropyl-7H-purine-2,6-dione (Bolte, 1996).

An estimate of the hydrogen-bond energy has been undertaken by the quantum-chemical AM1 method (MOPAC7; Stewart, 1993), which is suitable for systems with hydrogen bonds (Dewar *et al.*, 1985). The AM1 heat of formation for (I) is 96.78 kJ mol<sup>-1</sup> and the hydrogen bond order is 0.0048. For a virtual molecule of (I), with a C8—N7—C14—C15 torsion angle of 90°, where a hydrogen bond is impossible, the heat of formation is 105.94 kJ mol<sup>-1</sup>. Thus, the energy of the intramolecular hydrogen bond in (I) can be estimated to be 9.16 kJ mol<sup>-1</sup>. This is a relatively high value, especially for a C—H $\cdots$ O bond. The theoretically calculated geometry of the hydrogen bond for an isolated molecule of (I) (C $\cdots$ O = 3.115 Å, H $\cdots$ O = 2.24 Å and C—H $\cdots$ O = 133°) differs slightly from that obtained by our X-ray analysis (Table 1).

As shown in Fig. 2, inversion-related molecules [at (x, y, z) and (1 - x, 1 - y, 1 - z), hereafter (ii)] are linked by a pair of



**Figure 1**  
The molecular structure of (I) showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.



**Figure 2**  
Perspective view of the molecular packing in (I), showing the C—H $\cdots$ O and Cl $\cdots$ centroid interactions as dashed lines. [Symmetry codes: (ii) 1 - x, 1 - y, 1 - z; (iii) 1 + x, y, z.]

bifurcated C—H···O hydrogen bonds involving O13 and C14—H14B. These dimers are then linked by chlorine···ring-centroid interactions to generate ribbons which extend in the [100] direction; Cl1 is 3.258 Å from the centroid of the phenyl ring (Cg1) at (1 + x, y, z), hereafter (iii), and the C16—Cl1···Cg1<sup>iii</sup> angle (Fig. 2) is 162°. Analogous interactions are observed in the crystal structure of 3-(2,6-dichlorobenzyl)-N,N-dimethyladenine (Mishnev *et al.*, 1991), where the distance between the Cl atom and the plane of the six-membered ring is 3.25 Å. The only other significant intermolecular interaction in the crystal structure of (I) is between pairs of inversion-related phenyl rings [at (x, y, z) and (1 - x, 1 - y, 1 - z)]; the centroids of these rings are separated by 4.261 Å, but the shortest atom–atom contact is C19···C19<sup>ii</sup> of 3.392 (3) Å.

### Experimental

The title compound was prepared for the synthesis of a series of 7,8-disubstituted theophyllines, as reported by Dolman *et al.* (1965). The compound was recrystallized from ether. The colourless crystals thus obtained were filtered off and dried in air.

#### Crystal data

C <sub>14</sub> H <sub>11</sub> Cl <sub>3</sub> N <sub>4</sub> O <sub>2</sub>	Mo K $\alpha$ radiation
$M_r = 373.63$	Cell parameters from 11 449 reflections
Triclinic, $P\bar{1}$	$\theta = 1.0\text{--}30.0^\circ$
$a = 8.4073 (2) \text{ \AA}$	$\mu = 0.61 \text{ mm}^{-1}$
$b = 8.6544 (3) \text{ \AA}$	$T = 293 \text{ K}$
$c = 11.8014 (4) \text{ \AA}$	Prism, colourless
$\alpha = 71.8140 (14)^\circ$	$0.39 \times 0.28 \times 0.26 \text{ mm}$
$\beta = 70.7538 (13)^\circ$	
$\gamma = 82.343 (2)^\circ$	
$V = 769.74 (4) \text{ \AA}^3$	
$Z = 2$	
$D_x = 1.612 \text{ Mg m}^{-3}$	

#### Data collection

Nonius KappaCCD diffractometer	4339 independent reflections
$\varphi$ and $\omega$ scans	3637 reflections with $I > 2\sigma(I)$
Absorption correction: by Gaussian integration based on 12 indexed crystal faces (NUMABS; Coppens, 1970)	$R_{\text{int}} = 0.070$
$T_{\text{min}} = 0.838$ , $T_{\text{max}} = 0.905$	$\theta_{\text{max}} = 30.0^\circ$
10 330 measured reflections	$h = -11 \rightarrow 11$
	$k = -12 \rightarrow 12$
	$l = -15 \rightarrow 16$

#### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0524P)^2 + 0.2719P]$
$R(F) = 0.049$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.130$	$(\Delta/\sigma)_{\text{max}} = 0.002$
$S = 1.02$	$\Delta\rho_{\text{max}} = 0.39 \text{ e \AA}^{-3}$
4339 reflections	$\Delta\rho_{\text{min}} = -0.36 \text{ e \AA}^{-3}$
211 parameters	Extinction correction: SHELXL97
H-atom parameters constrained	Extinction coefficient: 0.009 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
C14—H14B···O13	0.97	2.44	3.170 (2)	132
C14—H14B···O13 <sup>i</sup>	0.97	2.55	3.196 (2)	124

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

All H atoms were revealed in difference maps and were allowed for in the refinement as riding atoms, with C—H = 0.93–0.97 Å and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{CH or CH}_2)$  or  $1.5U_{\text{eq}}(\text{methyl C})$ .

Data collection: *KappaCCD Server Software* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97* and *maXus* (Mackay *et al.*, 1999).

The authors acknowledge financial support from the Latvian Council of Science (grant Nos. 167 and 193).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1201). Services for accessing these data are described at the back of the journal.

### References

- Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.
- Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
- Bolte, M. (1996). *Acta Cryst.* **C52**, 1985–1987.
- Coppens, P. (1970). In *Crystallographic Computing*, edited by F. R. Ahmed, S. R. Hall & C. P. Huber, pp. 255–270. Copenhagen: Munksgaard.
- Dewar, M. J. S., Zoebisch, E. G. & Healy, E. F. (1985). *J. Am. Chem. Soc.* **107**, 3902–3909.
- Dolman, H., van der Goot, J. & Moed, H. D. (1965). *Recl Trav. Chim.* **84**, 193–196.
- Gilli, G. (2002). In *Fundamentals of Crystallography*, edited by C. Giacovazzo, pp. 585–666. Oxford University Press.
- Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Mackay, S., Gilmore, C. J., Edwards, C., Stewart, N. & Shankland, K. (1999). *maXus*. Bruker–Nonius, The Netherlands, MacScience, Japan, and The University of Glasgow, Scotland.
- Mishnev, A. F., Belyakov, S. V., Ramzaeva, N. P., Goldberg, Yu. Sh. & Lidaka, M. J. (1991). *Acta Cryst.* **C47**, 343–345.
- Nonius (1999). *KappaCCD Server Software*. Nonius BV, Delft, The Netherlands.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography, Part A*, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
- Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
- Stewart, J. J. P. (1993). *MOPAC7*. QCPE Program No. 455. Quantum Chemistry Program Exchange, Indiana University, Bloomington, Indiana, USA.