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Structure of 8-(Dicyclopropylmethyl)-1,3-dipropylxanthine

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Abstract

The title compound, 8-(dicyclopropylmethyl)-1,3-dipropyl-3,7-dihydro-1*H*-purine-2,6-dione, is a potent antagonist of the adenosine A_1 receptor. The dicyclopropylmethyl group adopts a conformation with the H atom of the methyl group located almost on the plane of the xanthine ring. Two *n*-propyl groups have fully extended conformations.

Comment

Xanthine derivatives block adenosine receptors and exhibit varied pharmacological activity. Because these compounds act as antagonists it is obvious that their three-dimensional structures are very important in the binding process to the receptors. To discover the structure–activity relationships of xanthine derivatives we have undertaken the X-ray analysis of a series of these derivatives. The title compound is one example and shows a high potency against the adenosine A_1 receptor (Shimada, Suzuki, Nonaka & Ishii, 1992).

The exocyclic bond angles around C6 are remarkably asymmetric. A similar asymmetry is observed in 3-isobutyl-1-methylxanthine (Srikrishnan & Parthasarathy, 1988). The N7—C8 bond is relatively long. All other bond lengths and angles in the xanthine skeleton are within normal ranges. An H atom is attached to N7. The two *n*-propyl chains are on opposite sides of and perpendicular to the xanthine ring. An H atom attached to C9 is almost eclipsed by N9. C10*a* and C10*b* are *gauche* and *gauche* to N7 and they are located on the N7 side. The dihedral angles between the xanthine ring and the two cyclopropane rings (composed of C10*a*, C11*a* and C12*a*, and C10*b*, C11*b* and C12*b*) are 116 and 57°, respectively. The dihedral angle between the two cyclopropane rings is 59°.

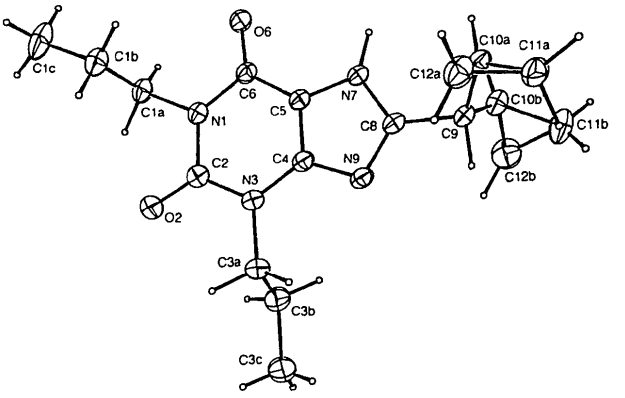

Fig. 1. *ORTEP*II drawing (Johnson, 1976) of the title molecule with heavy atoms represented as 30% probability ellipsoids and H atoms as spheres of arbitrary radii.

Experimental

Crystal data

$C_{18}H_{26}N_4O_2$
M_r = 330.43
Triclinic
$P\bar{1}$
a = 9.718 (1) Å
b = 9.830 (1) Å
c = 10.731 (1) Å
α = 99.26 (1)°
β = 105.30 (1)°
γ = 72.90 (1)°
V = 941.2 (3) Å^3
Z = 2
D_x = 1.17 Mg m^{-3}
D_m = 1.19 Mg m^{-3}

Cu $K\alpha$ radiation
λ = 1.54184 Å
Cell parameters from 25 reflections
θ = 35–47°
μ = 0.591 mm^{-1}
T = 295 K
Prism
0.3 × 0.3 × 0.2 mm
Colourless
Crystal source: from ethanol solution

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3994 measured reflections
3795 independent reflections
3041 observed reflections [$|F_o| > 3.0\sigma(|F_o|)$]

R_{int} = 0.046
θ_{max} = 75°
h = 0 → 12
k = −12 → 12
l = −13 → 12
3 standard reflections
frequency: 83.3 min
intensity variation: 0.021%

Refinement

Refinement on F
Final R = 0.073

$\Delta\rho_{max}$ = 0.35 (5) e Å^{-3}
$\Delta\rho_{min}$ = −0.28 (5) e Å^{-3}

$wR = 0.072$
$S = 0.686$
3041 reflections
218 parameters
H-atom parameters not refined
Unit weights applied
$(\Delta/\sigma)_{max} = 0.01$
Extinction correction: Zachariasen (1963)
Extinction coefficient: 2.14×10^{-6}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

$B_{eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O2	0.1840 (3)	0.0786 (3)	1.0647 (3)	6.31 (7)
O6	0.4983 (3)	0.3600 (3)	1.1180 (2)	5.83 (6)
N1	0.3375 (3)	0.2230 (3)	1.0912 (3)	4.34 (6)
N3	0.1338 (3)	0.2313 (3)	0.9106 (3)	4.45 (6)
N7	0.3124 (3)	0.4700 (3)	0.8568 (3)	4.34 (6)
N9	0.1139 (3)	0.3922 (3)	0.7531 (3)	4.28 (6)
C1*a*	0.4199 (4)	0.1636 (4)	1.2170 (3)	4.79 (9)
C1*b*	0.5409 (4)	0.0291 (4)	1.1990 (4)	6.0 (1)
C1*c*	0.6202 (6)	−0.0270 (6)	1.3322 (5)	8.9 (2)
C2	0.2145 (4)	0.1724 (4)	1.0243 (3)	4.68 (8)
C3*a*	−0.0032 (4)	0.1905 (4)	0.8425 (4)	5.47 (9)
C3*b*	−0.1364 (4)	0.2928 (5)	0.8878 (5)	7.5 (1)
C3*c*	−0.2773 (5)	0.2463 (6)	0.8140 (7)	11.1 (2)
C4	0.1781 (3)	0.3306 (3)	0.8664 (3)	3.95 (7)
C5	0.2996 (3)	0.3741 (3)	0.9321 (3)	4.01 (7)
C6	0.3874 (4)	0.3246 (4)	1.0514 (3)	4.29 (8)
C8	0.1977 (3)	0.4759 (4)	0.7509 (3)	4.08 (7)
C9	0.1750 (3)	0.5640 (4)	0.6413 (3)	4.36 (8)
C10*a*	0.3083 (4)	0.5197 (4)	0.5819 (3)	5.22 (9)
C10*b*	0.1369 (4)	0.7208 (4)	0.6833 (4)	5.9 (1)
C11*a*	0.3433 (5)	0.3735 (5)	0.5104 (4)	6.4 (1)
C11*b*	−0.0141 (6)	0.7934 (6)	0.6989 (5)	8.5 (2)
C12*a*	0.2862 (4)	0.5039 (5)	0.4372 (4)	6.7 (1)
C12*b*	0.0363 (6)	0.8237 (5)	0.5888 (5)	8.6 (2)

Table 2. *Geometric parameters* (Å, °)

O2—C2	1.218 (5)	N7—C5	1.388 (5)
O6—C6	1.236 (4)	N7—C8	1.360 (4)
N1—C1*a*	1.487 (4)	N9—C4	1.360 (4)
N1—C2	1.405 (4)	N9—C8	1.324 (5)
N1—C6	1.395 (5)	C4—C5	1.354 (4)
N3—C2	1.376 (4)	C5—C6	1.408 (4)
N3—C3*a*	1.474 (5)	C8—C9	1.504 (5)
N3—C4	1.366 (5)		
C1*a*—N1—C2	116.4 (3)	N9—C4—C5	112.1 (3)
C1*a*—N1—C6	117.5 (3)	N7—C5—C4	105.5 (3)
C2—N1—C6	126.1 (3)	N7—C5—C6	131.1 (3)
C2—N3—C3*a*	118.9 (3)	C4—C5—C6	123.4 (4)
C2—N3—C4	119.7 (3)	O6—C6—N1	120.3 (3)
C3*a*—N3—C4	121.4 (3)	O6—C6—C5	127.4 (4)
C5—N7—C8	105.5 (3)	N1—C6—C5	112.3 (3)
C4—N9—C8	103.9 (3)	N7—C8—N9	113.0 (3)
O2—C2—N1	120.9 (3)	N7—C8—C9	122.6 (3)
O2—C2—N3	122.3 (3)	N9—C8—C9	124.4 (3)
N1—C2—N3	116.8 (3)	C8—C9—C10*a*	111.0 (3)
N3—C4—N9	126.0 (3)	C8—C9—C10*b*	111.7 (3)
N3—C4—C5	121.8 (3)	C10*a*—C9—C10*b*	111.5 (4)

Program used throughout the analysis: CAD-4 *SDP-Plus* (Frenz, 1985). Program used to solve structure: *MULTAN*11/82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). Molecular graphics: *ORTEP*II (Johnson, 1976). Refinement was by full-matrix least-squares methods. The reflection 001 was excluded from the refinement because it seemed to suffer from strong secondary extinction.

Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71027 (22 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1014]

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